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Cover credit: KTSDESIGN/SCIENCE PHOTO LIBRARY / Getty Images
The cover picture shows results of an agarose gel electrophoresis experiment. Agarose gel electrophoresis separates DNA by size; the position of the band on the gel depends on its size. Under ultraviolet light, the stain on the DNA fluoresces and its intensity indicates the amount of DNA present. This is one of the many biochemical methods that have led to advances in clinical medicine.

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1. Introduction

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This book is an attempt to explain how advances in medical science will impact on law. For each topic, we will give an account of the science and medicine before putting these discoveries in a legal context. This introductory chapter will provide some groundwork on concepts which will recur in the rest of the book.

This may sound obvious, but we shall attempt to be as logical as possible, and use as much evidence as possible to back up our claims. We would also like to emphasise the impact of evolution on humans throughout our book. The theory of evolution allows us to understand processes such as decision making; it also enables us to understand how medicine is affecting our future genetically and physiologically. We therefore start with a brief introduction to the theory of evolution.

1.1 Evolution

Evolution is the theory which describes the change of living organisms over time, arising from changes in their genes, so that they become more adapted to their environments.

1.1.1 Basis

In science, when we say that a certain concept is a ‘theory’, it does not mean that it is ‘only theoretical’ in the colloquial sense. Theory means a self-consistent concept, well supported by experimental findings. So when we say that evolution is a theory, it means it is a mature scientific framework. For those parts of science which are speculative, scientists would prefer the term ‘conjecture’ or ‘hypothesis’.

Although ideas about changes in living organisms have been common from antiquity, it was Charles Darwin and Alfred Russel Wallace who put this on a scientific footing. Wallace published a preliminary form of an evolutionary theory in 1855 (Wallace 1855). Darwin had conceived of the theory before then, but had been reluctant to publish it. Darwin and Wallace had been in correspondence during this time, and Darwin wrote back to tell Wallace he had similar ideas, and was preparing something to be published in two years’ time. Wallace then sent Darwin an essay (Wallace 1858), which greatly impressed Darwin, as it contained exactly the ideas that Darwin developed himself. Darwin submitted this essay to the London Linnean Society together with two of his unpublished essays on evolution. But the complete theory of evolution had to wait till Darwin’s book \textit{On the Origin of Species} (Darwin 1859). Darwin wrote this book for the non-specialist, as he intended to write a more detailed treatise for the scientist. Unfortunately, he never found the time to write the treatise, so \textit{On the Origin of Species} became the definitive account of the theory of
evolution. It is unique amongst the scientific classics because it assumed no technical knowledge on the part of the reader, unlike Newton’s *Principia*, James Clerk Maxwell’s *A Treatise on Electricity and Magnetism* or Paul Dirac’s *Principles of Quantum Mechanics*, all of which require the reader to have a good grasp of mathematics. The logic of *On the Origin of Species* is rigorous, the argumentation extensive and the evidence compelling. Anyone willing to spend time and effort on this book will be able to understand it, and find it an intellectually rewarding experience.

In a very simplistic way, the theory of evolution starts from two axioms, both of which are strongly supported by experimental evidence. They are as follows:

1. Living organisms even within the same species display variation, arising from slightly different genes in each individual.
2. The environment of the living organisms changes over time.

We can infer that, when the environment changes, those variants of the living organisms which are more suited to the environment are more likely to survive. This process is known by the rather unfortunate name of ‘natural selection’, as if some agent is there to do the selection. The selection is ‘performed’ by the environment, and those variants which are less suited are more likely to die. Over time, these variations accumulate, and new species arise.

Although *On the Origin of Species* was published over 150 years ago, its basic ideas are still valid. Indeed, on the 150th anniversary of its publication, scientists examined this book, and found that it was essentially correct (New Scientist 2009). What Darwin could not have known were the advances in genetics and plate tectonics. *On the Origin of Species* was reticent about the molecular mechanisms underlying variation and Darwin tried to suggest mechanisms whereby similar species, most probably originating from the same ancestry, could appear in different continents. These gaps have been filled in by later scientists.

Evidence for the theory of evolution is found everywhere, from the survival of hepatitis B viruses in patients undergoing chemotherapy, to the extinction of living organisms over the aeons of time. It is the unifying concept of biology, and has found wide applications in medicine. It is rare to find a scientific book still valid 150 years after its first publication. *On the Origin of Species* thoroughly deserves its reputation as one of the greatest scientific treatises.

### 1.1.2 Implications

Some living organisms change slowly. Our genes give us attributes which allow us to survive in our environment. It is fair to say that we *Homo sapiens* first appeared as hunter-gatherers in Africa about 200,000–300,000 years ago (Bae et al. 2017), living in groups of no more than 100 people. We lived in this manner until about 12,000 years ago, when humans developed agriculture. Our genetic make-up has remained almost unchanged during these 12,000 years, so we are still best suited for a hunter-gatherer life. Our minds evolved to best survive in that environment. The effect of our actions are limited to a small area, and extend to short time-scales like a year or two.

From these origins, we humans learnt to farm, and thus build up complex cultures and civilisations. These days, our actions have far-reaching consequences, sometimes affecting the environment beyond the earth. We also carry out actions which have long-lasting effects on earth. The evolution of our minds has not quite caught up with the power to change the external environment that we have generated for ourselves. Our population exceeds 7000 million. Our actions have far-reaching repercussions, both in terms of space and in terms of time, *e.g.*, orangutans are critically endangered mainly because our need for palm oil is causing widespread deforestation in their local habitat (Ancrenaz et al. 2016; Nowak et al. 2017; Singleton et al. 2017).

One of the most obvious examples where there is incongruence between our ‘evolutionary self’ and our ‘modern self’ is in nutrition and activity level. Until the advent of
agriculture about 12,000 years ago, humans lived as hunter-gatherers. We can deduce what
their diet was by examining what modern-day hunter-gatherers eat. The hunter-gatherer
diet contains about 60% meat, about 30% vegetables and fruit, and virtually no grain nor
dairy products (Cordain et al. 2002; Eaton and Konner 1985); the exact composition
changes with respect to latitude and other factors related to the habitat (Pontzer et al.
2018). The meat consumed contains much less fat than diets in affluent countries, and we
have evolved to consume such food. In addition, our hunter-gatherer ancestors had a much
higher activity level than modern humans (Pontzer et al. 2018). Under these conditions,
since humans did not have a reliable and constant source of food, when they had access to
food, they would eat as much as they could (Eaton and Konner 1985).

In contrast, the diet in affluent countries or the ‘Western’ diet consists of more fatty
meat, grains and dairy products; it also contains much more refined sugar (Cordain et al.
2005). Humans in affluent countries have a much more sedentary lifestyle. We also have a
constant and reliable source of food from agriculture. Our instinct to gorge ourselves
whenever the opportunity arises becomes a maladaptation. It is obvious that our bodies
have not evolved for this kind of lifestyle with low activity and a reliable source of food with
a high fat or high sugar content. The high rate of obesity and related health problems in
these countries are a result of this evolutionary incongruence.

Another example of incongruence between our ‘evolutionary self’ and ‘modern self’ is in
decision making. Psychological experiments show that humans probably have two decision-
making systems (Evans 2003; Wason and Evans 1975), system 1 and system 2. System 1 is
evolutionary older and is possessed by other animals. System 2 requires working memory
and is involved with cognitive decoupling and mental simulation, and is probably uniquely
human (Stanovich and West 2000). The evolution, anatomical basis and attributes of these
decision-making systems are detailed in Sect. 3.3.3.

The repercussions of this incongruence in our ‘evolutionary self’ and our ‘modern self’
will be a constant refrain in this book.

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2. Reproduction

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2.1 Reproductive Science

Reproduction is probably one aspect of medicine where most advances will require legal input. In order to understand the emergent medical technology, it is useful to briefly review the science behind human reproduction. The interested reader is advised to consult textbooks such as Strachan and Read (2018) and Sadler (2018) for more details.

2.1.1 Chromosomes, Genes and Deoxyribonucleic Acid

Our anatomical structures and physiological functions are partly determined by our genes, and partly by the environment. We shall briefly describe how genes determine our anatomy and physiology.

The gene is the basic unit of heredity in any living organism. It is made up of deoxyribonucleic acid (DNA). In humans, most of the DNA is packaged with associated proteins into chromosomes, and exists in the cell nucleus (see Fig. 2.1). This DNA is called the chromosomal DNA or nuclear DNA. A very small proportion of DNA exists in the mitochondrion, a cellular inclusion body. Whilst the chromosomal DNA contains about 20,000 genes (Clamp et al. 2007), the mitochondrial DNA contains 37 genes (Anderson et al. 1981). DNA was first discovered in living organisms by Miescher (1871), and the four bases which made up the ‘alphabet’ of DNA were identified at different times (Kossel 1885; Kossel and Neumann 1893; Kossel and Steudel 1903; Unger 1846). Subsequent experiments by Avery et al. (1944) and Hershey and Chase (1952) showed that it contained genetic material. The structure of DNA was solved by Watson and Crick (1953b). In a subsequent paper, Watson and Crick (1953a) explained how the DNA bases match up with each other, and how that can form the basis of a linear code containing genetic information. They described how that information can be transmitted faithfully from one generation to another (see Fig. 2.2). More details can be found in Strachan and Read (2018).
Fig. 2.1 This simplified diagram shows the packaging of DNA inside human cell nuclei with the length scale on the left side. Pure DNA complexes with histone proteins to form nucleosomes; they are the bead-like structures shown in the second panel from the top. These nucleosomes are further packed to form 30-nm structures, which condense further and ultimately form the chromosome. The degree of packing and condensation depends, to some degree, on whether the DNA is being read and whether the cell is preparing to divide. Taken from Felsenfeld and Groudine (2003).

Fig. 2.2 This diagram shows the replication of DNA. The two strands of DNA part, and each becomes the template for a new strand; this is the basis for faithful replication. The original double-stranded DNA on the right (a)
Chromosomes are structures in the cell nucleus, and were first discovered to be repositories of genetic information by Boveri (1887, 1889, 1895) and Sutton (1902, 1903). In chromosomes, the DNA is associated with histones (Kossel 1884) and other proteins. A normal human cell contains 23 pairs of chromosomes (Tjio and Levan 1956), on which resides almost all the genetic material; the rest of the genetic material resides in mitochondrial DNA. Of these 23 pairs, 22 pairs are the same in men and women, and they are called the autosomes or non-sex chromosomes. There are thus two copies of the same gene on each autosome; these two copies are not always identical, and each variant form of a gene is called an allele. The other pair is XX in women and XY in men, and they are called the sex chromosomes, because they are responsible for sex determination (Guyer 1910; Painter 1921). Normal human cells are called diploid cells, because their chromosomes exist in pairs, and each half comes from one parent. Gametes, or sex cells, only contain half the number of chromosomes, and therefore they are called haploid cells.

The discovery of the structure of DNA encouraged many researchers to work on the function of DNA, and study the interaction of DNA with other molecules. It would be beyond the scope of this chapter to consider the details of these discoveries. The interested reader is referred to Judson (1979) for the history of molecular genetics, and Alberts et al. (2014) for the science. We shall briefly explain the science in the next subsections, and how they relate to new medicine.

2.1.2 Genes and Their Functions

How is genetic information used? The DNA on the chromosomes contains sequences which are to be ‘read’ by proteins, and sequences which are not ‘read’ and whose functions, if any, are still unknown. Those sequences which are to be ‘read’ usually start with three DNA bases called the ‘start codon’. This would signal to the relevant proteins to bind to that sequence and start a process called ‘transcription’. Other signals pertinent to transcription are concerned with whether the DNA bases are, for example, methylated. The cell makes changes to the DNA, but does not alter its sequence. These changes can be inherited, and the study of these processes belongs to the field of epigenetics (Allis et al. 2015).

During transcription, the DNA sequence is ‘copied’ to ribonucleic acid (RNA). The process is highly accurate because each DNA base is paired with the appropriate RNA base. The RNA is further processed and exits the nucleus. During this processing, parts of the RNA can be excised. These parts constitute the non-coding sequences, and are also called introns. Introns are important for the control of gene expression. Some introns may become non-coding RNA molecules. This processed RNA, called the messenger RNA or mRNA, then enters the cytoplasm, and is ‘read’ by a protein-RNA complex called a ribosome. The mRNA dictates the sequence of amino acids to be obtained, and causes the ribosome to synthesise a protein of that specific amino acid sequence; this process is called ‘translation’ (see Fig. 2.3). The protein may undergo post-translational modification, for example, parts of it may be excised, or sugar molecules may be added to the protein.
In the early days of molecule genetics, it was thought that each gene would code for one protein. We later discovered that this was not always true. For example, every antibody is translated from an mRNA spliced together from a number of genes (Tonegawa 1983). Indeed the genetics required to synthesise an antibody are quite complex (de Los Rios et al. 2015; Muramatsu and Honjo 2001), and involve a number of genes. An additional level of complication is that some genes code for proteins which directly affect the physiology of the person, whilst other genes code for proteins which control the genes which directly affect the physiology. Thus there are hierarchical levels of genetic control to achieve healthy functioning of the human body (Strachan and Read 2018).

Most of the genes are found on the chromosomes, and a small number in the mitochondria. The genes found on the autosomes exist in pairs, as the individual inherits one copy of the gene from the father, and another copy from the mother. In women, the sex chromosomes are XX, so they also have two copies of each gene on the X chromosome. In men, the sex chromosomes are XY, so they will have one copy of X-chromosome genes, and one copy of Y-chromosome genes.

### 2.1.3 Production of Gametes

Humans can only carry out sexual reproduction. In sexual reproduction, two sex gametes, each from a different individual of the species, fuse to form a zygote that will develop into an individual of the next generation. In humans, the man provides the spermatozoon and the woman provides the ovum or the oocyte. The spermatozoon has a ovoid head which is about 5 μm in length and about 3 μm wide, and a tail about 50 μm long, while the ovum is a spherical cell about 100 μm in diameter, and is one of the largest cells in the human body. These cells are the gametes; they fuse during fertilisation to give the zygote. The zygote develops into the human fetus in the uterus of the mother.

Not all living organisms carry out sexual reproduction. Many living organisms carry out asexual reproduction, and some living organisms can carry out both asexual and sexual reproduction. Asexual reproduction is simpler, as only one individual of the species is needed to reproduce, while sexual reproduction requires two individuals and also involves complex processes of producing the gametes, which are specialised haploid cells. So how does the more complex mode of sexual reproduction come about?

Evolutionary biologists have studied this problem for a long time. Weismann (1891b) first suggests that sex functions to provide variation for natural selection to act upon. Thereafter,
research has focused on the evolutionary costs and advantages of sexual reproduction. A recent review article (Meiman et al. 2017) explains the different hypotheses explaining why sexual reproduction predominates; the authors suggest that a ‘pluralist’ approach where different stand-alone hypotheses are considered together is probably best suited to explain the predominance of sexual reproduction.

For example, one hypothesis is called Muller’s ratchet. In a theoretical paper, Muller (1964) hypothesises that asexually reproducing lineages will suffer from the accumulation of mildly deleterious mutations and be finally driven to extinction. Another hypothesis, named the Red Queen hypothesis by its originator (van Valen 1973), suggests that parasite pressure can generate a direct selection benefit for individuals with rare or novel genotypes; these genotypes are more readily produced via sexual reproduction, and Jaenike (1978) applies this hypothesis to account for the maintenance of sex within populations. The name ‘Red Queen’ comes from Lewis Carroll’s Through the Looking Glass, where the Red Queen explains to Alice that ‘here, you see, it takes all the running you can do, to keep in the same place’. Organisms have to keep evolving to stay in the same place, or they will become extinct.

In brief, it appears that Weismann’s basic ideas are supported by experimental observations (Burt 2000). Experiments on living organisms which can reproduce asexually or sexually show sexual reproduction accelerates adaptation (e.g. see Goddard et al. 2005, McDonald et al. 2016 and Luijckx et al. 2017). Here we describe why sexual reproduction generates more variation in the progeny organisms.

As previously explained, the ovum contains 23 chromosomes, 22 of them being the autosomes, plus the X chromosome. The spermatozoon also contains 22 autosomes plus either the X or the Y chromosome. In humans, the male carries the XY chromosomes and the female carries the XX chromosomes. Thus sex of the baby is completely determined by the father, not the mother.

Cell division where the number of chromosomes is retained is mitosis (Fig. 2.4). Before a mitotic division, the amount of DNA is doubled, and thus after division, the number of chromosomes per cell remains the same. For example, in the adult intestine, epithelial stem cells undergo mitosis to produce more progenitor epithelial cells, to make up for those epithelial cells which are shed. Another example are the haematopoietic stem cells in the red bone marrow; they undergo mitosis to produce all the mature blood cells. It is important to note that the two daughter cells resulting from a mitotic division contain identical nuclear DNA.
Cell division where the number of chromosomes is halved is meiosis (see Fig. 2.4). In this process, the amount of DNA is also doubled, but the cell undergoes two divisions, meiosis I and meiosis II, at the end of which four haploid cells are produced. Before meiosis I, the homologous chromosomes are paired up, there is crossing-over of the chromatids and recombination of genetic material. Since there is recombination of homologous chromosomes during meiosis I, the four daughter cells all have different DNA sequences in their chromosomes. In the production of male gametes, each primary spermatocyte gives rise to four spermatozoa. In the production of female gametes, each primary ovum gives rise to only one mature ovum; the other three cells resulting from meiosis degenerate into polar bodies.

Note that after meiosis, every haploid cell is slightly different genetically. When haploid cells fuse in fertilisation to give rise to the zygote, the zygote has a genetic make-up different from either the mother cell or the father cell. Note also that, in mitotic divisions, the nuclear DNA of all the daughter cells are identical to the mother cell. Thus reproduction involving meiosis and fusion of haploid cells to form the zygote (sexual reproduction) produces much more variation than mitotic division alone (asexual reproduction). This has profound consequences for evolution.

At first sight, meiosis appears to be a rather complicated method of producing haploid cells. It would seem that a more direct method is to divide a diploid cell into two haploid cells, without replicating the DNA. The evolutionary reasons for meiosis have been explored by Wilkins and Holliday (2009), and these scientists suggest that the meiotic process as it currently exists could have evolved more easily from mitosis, by including only one new process: the pairing together of homologous chromosomes. The machinery to carry out all other meiotic processes can easily be adapted from mitosis. On the other hand, if haploid cells were to be produced by dividing a diploid cell, many more processes would have to be developed for this purpose.

The spermatozoon contains very little cytoplasm. The ovum has cytoplasm and hence mitochondria. Thus the mitochondrion from one’s body is most probably exclusively from
one’s mother (Giles et al. 1980); it is still disputed whether paternal inheritance can take place (Wei and Chinnery 2020).

The male gamete (spermatozoon) and the female gamete (ovum) are of very different sizes. The spermatozoon contains mostly genetic material, whereas the ovum contains genetic material and a large amount of cellular material to sustain the zygote after fertilisation. There is a very big difference in the sizes of these two gametates, a phenomenon called anisogamy. How does this come about?

This question has been considered by Kalmus (1932) and Scudo (1967). Parker et al. (1972) produced a detailed article exploring not only the evolution of anisogamy, but also whether it is a sustainable system in the long term. Although we do not have fossil evidence of the transition from isogamy to anisogamy, there is evidence supporting this theory (Parker 2011).

These scientists considered primaeval living organisms living in an aqueous environment. The cells of these living organisms produced gametes of different sizes: they were released into the aqueous environment and they could fuse with each other without restrictions. Two considerations governed the number and sizes of the gametes. A large gamete would be more likely to provide cellular support for the genetic material, and thus ensure survival of the zygote. Thus two large gametes fusing would give rise to a large zygote with high survival. On the other hand, given the same amount of resources, making a large number of small gametes would increase the probability of the small gametes fusing with another gamete and thus the formation of a zygote. Hence one factor tended to favour a large number of small gametes, whilst another factor tended to favour a small number of large gametes.

Using these reasonable assumptions and elaborating them with other conditions (e.g. the fitness of the zygote was dependent on the size of the zygote), scientists were able to show that two types of gametes, one called the microgamete and the other called the macrogamete, would evolve, and that these populations were stable over at least tens of generations. No gametes of intermediate size would emerge. Scudo (1967) and Parker et al. (1972) also carried out numerical simulations to quantify the evolution of anisogamy and established conditions for its emergence and continued existence. They showed that anisogamy was an evolutionary stable strategy (ESS). Parker et al. (1972) also argued that once anisogamy had evolved, it would be evolutionarily advantageous for the microgametes and macrogametes to lose the ability to fuse with each other; only microgamete-macrogamete fusion would be possible. This probably caused the macrogamete to lose its motility. The motile spermatozoon and the immobile ovum in humans most probably evolved from such an anisogamy system.

There are inevitable biological consequences of anisogamy in humans. The male reproductive system has evolved to produce continuously a very large number of very small and motile cells. The female reproductive system has evolved to nurture a very small number of very large cells and to provide an environment for the embryo and subsequently fetus to develop.

### 2.1.4 Embryology

Fertilisation of the ovum by the spermatozoon usually takes place in the widest part of the uterine tubes. The spermatozoon and the ovum fuse to form a zygote, which is still surrounded by the zona pellucida of the ovum. The zygote divides, and up to about the two- or four-cell stage, the cells are totipotent. This means each of the cells is capable of generating a globally coordinated developmental sequence and becoming an embryo (Condic 2014). The embryo reaches the 16-cell stage after about three days. At this stage, this collection of cells is called a morula, and the cell mass enters the uterus. The cells divide further, the zona pellucida disappears and a fluid-filled cavity forms in the middle of this cell mass; the blastocyst is formed. The blastocyst cells are divided into the inner cell mass or the embryoblast, and the outer cell mass or the trophoblast (Fig. 2.5).
Monozygotic twins develop if the embryo at the two-cell stage divides into two embryos. Twins also develop if the inner cell mass splits into two completely separated groups. In all cases, the nuclear DNA of the embryos are the same. The mitochondrial DNA is also the same, but the proportion of mitochondrial DNA will be different from embryo to embryo; during the division, the nuclear DNA is divided in a tightly controlled manner, but the mitochondrial DNA is not. Different mitochondria contain different DNA; thus, there are different 'types' of mitochondria within a cell. One embryo ends up with a higher proportion of one 'type' of mitochondria, and the other embryo ends up with a lower proportion. Thus it is possible to tell the cells of monozyotic twins apart by examining mitochondrial DNA (Pfeiffer et al. 2004).

About six days post-fertilisation, the tropoblast cells attach to the lining of the uterus, and implant into the uterine endometrium; this is the glandular part of the uterus. By about nine days post-fertilisation, the tropoblast further divides into two parts, the inner part becomes the cytotrophoblast, where the cells are distinct, and the outer part forms the syncytiotrophoblast, where the cells start to fuse, and lacunae form in the syncytiotrophoblast (see Fig. 2.6).

By about 12 days, the syncytiotrophoblastic cells erode into the endothelium of maternal endometrial capillaries, in a manner similar to the invasion of cancer cells (Holtan et al. 2009; Mor et al. 2017; Voss et al. 2000). The lacunae of the syncytiotrophoblast become continuous with the maternal capillary system. More and more blood flows into the trophoblastic system, and the utero-placental circulation is established (see Fig. 2.7).
As the fetus grows, the interface between the mother and the fetus also grows in size and complexity; specialised blood vessels develop in the uterus to supply the utero-placental circulation. There are also changes in the interface between the fetal trophoblast and the maternal capillaries; villi develop from trophoblast cells, and the maternal vessels are eroded to release blood into the intervillous spaces, so that a large and thin area develops for the exchange of gases, nutrients and selected proteins. This specialised organ, formed from maternal and fetal tissue, is the placenta.

The placenta carries out many functions. It allows gaseous exchange to take place, and also carries nutrients to the fetus and waste products to the mother. It secretes hormones and provides an immunological barrier to the fetus. It is at once the lungs, kidney, the immune system and endocrine organ of the fetus. The placenta, together with the fetus, is called the feto-placental unit, to emphasise the fact that the placenta is, in many respects, an extension of the fetus. At term, the placenta weighs about 500 g and receives about 600 ml/min of maternal blood flow. The average cardiac output of an adult is about 5 l/min, so this is about 10% of the maternal cardiac output. This blood flow is made possible by the uterine arteries, which are small when the mother is not pregnant, but grow during pregnancy and can reach large dimensions without rupture. As an aside, men do not possess arteries which can adjust their dimensions to this extent, so one of the challenges of male pregnancy is to provide the feto-placental unit with enough blood.

Concomitant with the development of the placenta is the development of the embryo, or from the eighth week onwards, the fetus. This is an intricate and complex process under genetic control. What has emerged from recent studies is that genes responsible for tissue and organ development cause the secretion of different growth factors in the developing embryo. The concentration gradient of these different growth factors induces tissue and organ development. Unfortunately, it is still not clear how the concentration gradient of these growth factors affect development at the cellular and molecular levels. Sadler (2018) contains more details about these processes. Embryology is a discipline as old as medicine itself, and Needham (1959) is a comprehensive treatise discussing the historical development of the subject up to the nineteenth century. For more modern developments, Gilbert (1994) is a good monograph.

2.2 Assisted Reproductive Technology

The World Health Organisation (WHO) defines assisted reproductive technology (ART) to be ‘all treatments or procedures that include the in vitro handling of both human ova and
sperm or of embryos for the purpose of establishing a pregnancy’. This includes, but is not limited to, in vitro fertilisation (IVF) and embryo transfer, gamete intra-Fallopian transfer (GIFT), zygote intra-Fallopian transfer (ZIFT), tubal embryo transfer, gamete and embryo cryopreservation, ovum and embryo donation and gestational surrogacy. ART does not include assisted insemination (artificial insemination) using sperm from either a woman’s partner or a sperm donor (Zegers-Hochschild et al. 2009). Europe follows this definition, but the US Centers for Disease Control and Prevention use a slightly different definition where assisted insemination is included. The reason for carrying out these procedures is often infertility, which is defined as the inability of a couple to conceive after a year of unprotected sex (Zegers-Hochschild et al. 2009). However, these methods are also applied to reduce the chances of genetic diseases. Assisted reproductive technology is widely used. In the Americas, Australasia, Europe and Japan, over 1.4 million live births in the decade 2004–2013 took place after ART intervention (Kushnir et al. 2017).

We can divide the assisted reproductive technology procedures into the following: procedures which handle spermatozoa, procedures which handle the ova and procedures which handle the fertilisation process.

### 2.2.1 Spermatozoa Handling
In some men, no sperm is found in the ejaculate (azoospermia). Azoospermia can be obstructive or non-obstructive. In the obstructive type, spermatozoa are produced but they are not delivered to the ejaculate, usually because of ductal problems. In the non-obstructive type, there is abnormal sperm production, often because of hormonal abnormalities. The treatment of non-obstructive azoospermia usually includes hormonal stimulation. Moreover, surgical procedures can be carried out to extract the spermatozoa directly from the epididymis or the testis. The reasoning behind this procedure is that the testis of these men often contains focal areas of normal spermatogenesis against a background of germinal cell aplasia. The following procedures can be considered:

1. **Percutaneous sperm retrieval**
   This procedure extracts sperm by needle insertion into the testis, usually under local anaesthesia. It was first described by Obrant and Persson (1965), and has been modified for mapping the spermatogenic areas in the testis for subsequent surgical extraction (Turek et al. 1997). Sometimes the spermatozoa are aspirated from the epididymis.

2. **Surgical sperm retrieval**
   Surgical sperm retrieval includes microsurgical epididymal sperm extraction (MESE), testicular sperm extraction (TESE) and microsurgical testicular sperm extraction (microTESE). Surgical operations are carried out under general anaesthesia: the testis is dissected and spermatozoa are extracted (Janosek-Albright et al. 2015).

### 2.2.2 Ovum Handling
Problems with ovulation and the female reproductive system can lead to infertility in a couple. The underlying cause could be problems with ovulation (primary ovarian failure, thyroid problems or polycystic ovarian syndrome), failure of oocyte to mature, problems with transport of ova (Fallopian tube scarring), problems with the uterus (endometriosis, fibroids, uterine anatomical abnormalities) (Lindsay and Vitrikas 2015). Treatment of these women begins with a proper assessment of the cause(s) of infertility. The underlying causes are defined, and treatment includes correcting the hormonal imbalances and, where appropriate, surgical repair of the female reproductive tract. Ovulation induction can be tried using hormonal stimulation.

### 2.2.3 Fertilisation
Some infertile couples require more extensive treatment to achieve fertility. Intrauterine insemination is used for infertility resulting from scarring of the cervix, low sperm count, low sperm motility and female endometriosis (Kamel 2010). It involves inserting the sperm into the uterus to promote fertilisation, usually the woman having undergone ovarian stimulation (ESHRE Capri Workshop Group 2009). According to the WHO definition (Zegers-Hochschild et al. 2009), intrauterine insemination is not an assisted reproductive technology because no ovum handling takes place.

A more effective method to promote fertilisation is *in vitro* fertilisation (IVF). This procedure was first developed by Steptoe and Edwards (1978), and it involved laparoscopic recovery of the mother’s ova. Fertilisation of an ovum by the father’s spermatozoan was carried out in cell culture media. After two-and-a-half days, when the zygote reached the eight-cell stage, it was re-implanted into the mother’s uterus using a catheter. After 38 weeks and 5 days, the baby was born successfully. *In vitro* fertilisation has since been carried out in many couples all over the world using broadly similar protocols. To improve the success rate, other procedures can be coupled to it: the ovaries can be hyperstimulated to ensure ovulation (Shrestha et al. 2015); luteal support in the form of hormones is administered to the mother after embryo transfer (Xiong et al. 2014). Other variations on the theme include intracytoplasmic sperm injection (ICSI), where the sperm is directly injected into the ovum to overcome problems with defective spermatozoa; assisted hatching, where the zona pellucida around the developing zygote is incised before embryo transfer to aid implantation, and various forms of pre-implantation genetic screening.

A method related to IVF but that, strictly speaking, does not handle the fertilisation process is gamete intra-Fallopian transfer (GIFT). The procedure is similar to IVF, but the gametes are mixed together and then immediately placed in the Fallopian tubes laparoscopically (Asch et al. 1984). Another variation of this method is zygote intra-Fallopian transfer (ZIFT), where the gametes are mixed and then placed in the Fallopian tubes within 24 hours.

### 2.2.4 Pre-implantation Genetic Diagnosis

It is possible to perform genetic analysis on the embryos prior to implantation. This method, called pre-implantation genetic diagnosis (PGD) or screening, was pioneered by Handyside et al. (1990). In those clinical cases, only part of the embryonic genome was tested. Nowadays, a more intensive DNA mapping can be performed to test for any single-gene defect. The testing can also be done at different stages of embryonic development (Traeger-Synodinos 2017).

### Medical and Legal Considerations

The advent of these assisted reproductive technologies has helped a large number of infertile couples to have children. However, IVF and ICSI have been shown to cause complications, both for the mother and for the baby. It used to be thought that this came about because of the high probability of multiple pregnancies (Qin et al. 2017a). However, as IVF/ICSI has improved, more singleton pregnancies have resulted, and these still carry a higher risk of complications such as maternal hypertension, congenital malformations of the baby and prematurity (Chen et al. 2018; Pandey et al. 2012; Qin et al. 2017b; Simpson 2014; Sullivan-Pyke et al. 2017), partly because of sperm DNA damage during the process (Simon et al. 2017). There are also studies which show that assisted reproductive technologies may affect the methylation of DNA of the embryo, thus affecting which allele will be expressed (Uyar and Seli 2014). Thus there are public health implications of assisted reproductive technologies.

The other consideration comes from possible interventions during these procedures. It is possible to use pre-implantation genetic diagnosis or screening to test for genetic defects of the baby, but it is also possible to use the same technology to select for other characteristics before implantation, *e.g.*, the sex of the baby. There have been reports that IVF is used for
Regulation of Pre-implantation Genetic Diagnosis

The Human Fertilisation and Embryology Act 2008 sets out the circumstances in which pre-implantation genetic diagnosis (PGD) is permitted. This includes ‘to establish if an embryo has an abnormality that might affect its capacity to result in a live birth’ and ‘to avoid a serious medical condition’ (Schedule 2, paragraph 1ZA). The HFEA Code of Practice explains that pre-implantation genetic diagnosis (PGD) can be carried out for a heritable condition only in two circumstances:

- Where there is a particular risk that the embryo to be tested may have a genetic, mitochondrial or chromosomal abnormality, and the Authority is satisfied that a person with the abnormality will have or develop a serious disability, illness or medical condition; or
- Where there is a particular risk that any resulting child will have or develop a gender-related serious disability, illness or medical condition. A condition is gender related if the Authority is satisfied that it affects only one sex, or affects one sex significantly more than the other. In the first situation, PGD may be carried out to establish whether the embryo has the suspected abnormality; in the second, PGD may be carried out to establish the sex of the embryo.

The Code makes it clear that where PGD is used, it is not permissible to then select the embryo which is likely to develop a serious physical or mental condition.

The approach of the HFEA is seeking to draw a middle path between the extremes of allowing PGD for any reason at all and not permitting it all. It is worth explaining briefly the arguments for the two extreme views to see why the middle path has attractions.

Supporters of the claim that PGD should be permitted for any condition emphasise the importance of freedom of choice, reproductive autonomy, for a mother (Harris 2016). No one should prevent a woman from selecting her embryos as she chooses, just as no one could interfere with the decisions of a woman to have sexual relations with a ginger-haired man in the hope that the baby born would have ginger hair. There is also an argument that no wrong is done in PGD. An embryo who is not selected has no moral or legal status and so is not harmed if not selected. It is worth noting, before moving on to the arguments against PGD, that these arguments in favour seem to support a permissive attitude towards PGD, but do not explain why the state should fund it.

The argument against PGD is that, if PGD is used against a particular condition, it is sending a message that people with that condition would be ‘better off dead’ or that the world would be better if we did not have people with that condition. This is most powerful in less serious conditions. Imagine it were possible to select against autism; this would send the message that it was better if we had no autistic people in our society. Not only would that be untrue and society would be harmed if the autistic community were removed, it would also be sending a very negative message to autistic people.

In case people think that any condition, no matter how minor, can be a reason for PGD, this is not the case. There is a list of conditions which qualify for PGD, the severity of which varies but which are predominantly those where there is no real expectation nor inherent capacity for the sufferer to have any enjoyment of life. For example, type B molybdenum co-factor deficiency patients will be born normally, but within the first few days of life will become severely irritable, start having epileptic seizures, will never regain consciousness and will have progressive neurodegeneration (they will not swallow and will have to be fed by gastrostomy). They will continue to have seizures and abnormal muscle tone in the first several months of life, until the neurodegeneration is so severe that they lose the capacity to move and fail to have any interaction with the outside world. Ultimately they succumb to an infection and die within a few months to a few years. About 80% of the conditions on the PGD list are similar to type B molybdenum co-factor deficiency in their severity.
Allowing PGD and not implanting the embryo is thus not a simple matter. On the one hand, there is the argument that some conditions allowed on the PGD list are compatible with a reasonable quality of life given an acceptable burden of treatment. Allowing this would send a signal that society does not want people with these conditions. On the other hand, there are some very serious diseases on the list where the patients have no expectation nor capacity to have any enjoyment of life, with no possibility of improvement nor cure with current technology. Moreover, it may be argued that simply giving parents the option to test for a condition is not saying anything about people with that condition. It is generating a choice for parents and is not sending any kind of message as to how parents should exercise that choice.

The list of conditions allowed for PGD is a source of controversy. It is decided by the Statutory Approvals Committee of the Human Fertilisation and Embryology Authority. While it draws on considerable expertise, it primarily deals with the list by responding to application to and conditions to it. This can mean the contents of the list reflect who applies to the HFEA, rather than necessarily representing a complete overview of all conditions that might be included. To some extent this can mean the list lacks coherence, but then it does mean that there is considerable flexibility in adding to it as necessary.

### 2.2.5 Allocation of Parenthood

Currently there is complex legal regulation of parenthood. Whereas in the past a family law textbook would be unlikely to spend more than a page or so explaining who the mother and father of the child was, now it would take a chapter (Herring 2019b). One reason for the complexity is that the law draws a distinction between who is the parent of a child and who has parental responsibility of the child. Having parental responsibility gives you the authority to make day-to-day decisions in relation to the child (e.g. to consent to medical decisions or make decisions about education). Being a parent carries few everyday rights, but gives you a say in matters such as adoption etc. Not all parents have parental responsibility, but most do. A father who is not married to the mother nor on the birth certificate does not have parental responsibility without a court document. Similarly, not all those with parental responsibility are parents, but most are. A step-parent can acquire parental responsibility. Traditionally it was thought that being a parent was essentially a biological fact (one’s gametes produced the child) while having parental responsibility was a social fact (one was performing the role of being a parent). It is now far more complex than that. We will focus on how the law determines who is a parent, because that is the question which has been traditionally seen as a biological one.

In the past the law was relatively straightforward: the genetic mother was the mother and the genetic father, the father. The only real difficulties were to deal with cases where the evidence about this was unclear and what presumptions should apply in such cases. This is not the place to set out in detail the current law, but it is marked by several notable features:

1. The mother is the woman who carries the child (whether or not she is the genetic mother) (section 27(1) of Human Fertilisation and Embryology Act 1990).

   This provision seems influenced by three factors. The first is the policy of not discouraging a woman from donating an egg for fear that they will become a parent and have the additional responsibilities (such as child support) that go with that. We discuss that further, shortly.

   The second is the growing emphasis in family law on the importance of the quality of the social relationship between the child and the putative parent, rather than the blood tie. This is not to say the genetic link is not seen as something important in the law; it is rather that it is disconnected from parenthood. Hence a child may have a right to find out the identity of their sperm donor ‘father’, while it is clear the sperm donor will not be the father in the eyes of the law. Hence the law recognises that the closeness of the relationship between the mother and the child during the pregnancy is of very special
significance. This was revealed in *Re TT v. YY*[2019] EWHC 2384 (Admin), where a trans man who had given birth to a child sought unsuccessfully to be registered as the father. McFarlane P explained why he was the mother:

Being a ‘mother’, whilst hitherto always associated with being female, is the status afforded to a person who undergoes the physical and biological process of carrying a pregnancy and giving birth. It is now medically and legally possible for an individual, whose gender is recognised in law as male, to become pregnant and give birth to their child. Whilst that person’s gender is ‘male’, their parental status, which derives from their biological role in giving birth, is that of ‘mother’.

(Paragraph 279)

While critics might complain the case results in the man being labelled as the mother by the law, even though he would be regarded by the child and others as the father in social terms. The decision recognises that the label mother recognises the particularly important role that the carrying of the child and giving birth conveys, one not captured by the label father. It may also be that the abortion debate has thrown light on the significant impact of pregnancy on the body of the mother as indicating it as something of such importance that it should be recognised in the law. All of this, then, to see parenting as a description of role of someone caring for a child, being in a close relationship with them, rather than being a biological connection.

A third (and allied) point is that the principle that a child’s welfare is the paramount concern in cases involving children, found in section 1, Children Act 1989, has come to dominate family law. Indeed in the United Nations Convention on the Rights of the Child, Article 3.1 states:

In all actions concerning children, whether undertaken by public or private social welfare institutions, courts of law, administrative authorities or legislative bodies, the best interests of the child shall be a primary consideration.

This kind of thinking has led to a downplaying of the importance of adults’ rights in cases involving children, as the focus is on what is best for children. This thinking can be applied to the allocation of parenthood (Herring 2019c). In that case the person with the strongest connection to the child, who has shown most commitment to the child, certainly at the point of birth is the mother.

2. A child can have only one mother and one father

Despite the flexibility shown towards parenting mentioned in the first point above, the law seems still shackled by the concept of the child having one mother and one father. This is most obvious in the provisions designed to recognise both parties to a same-sex relationship seeking assisted reproduction can be a parent. The 2008 Human Fertilisation and Embryology Act recognised this by stating that (in the case of two women) the woman who gives birth is the mother, but her partner is the ‘second parent’, but not mother. This is all the more odd given that if a woman seeks assisted reproduction with a male partner he will be the father (rather than ‘second parent’). It seems this probably reflects the reluctance of the law to break free from the assumption that a child can only have one mother and one father. Alternatively it might demonstrate the law’s commitment to the idea that a mother must be the person who gestates and gives birth to the child.

3. The law seeks to ensure a sperm or egg donor is not at risk of becoming a parent

Clearly a major policy behind the Human Fertilisation and Embryology Acts is to ensure that sperm and egg donors are not discouraged to donate to licenced clinics by fear of having the obligations of parenthood imposed upon them. A notable exception to this is that since 2006, children can obtain identifying information about their ‘sperm donor fathers’. This does not create any legal responsibilities on the sperm donor, but
could create moral or social expectations. We will soon find out what children do with the information they receive and whether it does lead to meaningful relations between donors and their offspring. However, it is clear that no legal obligations flow from that. It must be emphasised that this is only true where the donation takes place in a licenced clinic. Informal sperm donors, done outside the setting of a licenced clinic, are still treated as the father of the children they produce.

Looking to the future we suggest that the law is likely to develop in several ways:

1. **The importance of genetic links will be separated from parenthood.** Increasingly we see the law moving away from attaching weight to the genetic link between a child and adult as the marker of parenting, and instead emphasising the relationship or expected relationship of care between a child and an adult as being the marker of a parent. This is not to say that genetic links will not be seen as important; they will be for medical and social reasons. However, that can be recognised through a right to one’s genetic origins, which can be protected separately from allocation of parenthood.

2. **Equality between different parental forms.** It is increasingly recognised that the law should be neutral between family forms, where there are relationships of care. Obviously, now, same-sex and opposite-sex couples should be treated in the same way. We predict this will mean that the allocation of parental roles will be the same regardless of the sex of the parents. This will mean that the law’s reluctance to recognise more than two mothers or two fathers will need to be set aside. It also means that with increasing rates of separation between parents, a child is likely to experience more than two adults undertaking a parental role during their life (e.g. through having step-parents care for them). The law will need to recognise the different parent figures in a child’s life. More controversially it may mean that in a case of a polyamorous relationship, more than two adults can be recognised as a child’s parents.

### 2.3 Changing the Gametes or the Zygote

#### 2.3.1 Mitochondrial Diseases and the ‘Three-Parent’ Baby

In 2015, Parliament passed the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015. These permit and regulate mitochondrial replacement therapy (MRT). The suggested treatment method aims to help mothers who have mitochondrial diseases.

**Physiological Functions of Mitochondria**

The mitochondrion was first recognised as a cellular inclusion inside the cytoplasm but outside the cell nucleus by Altmann (1881), who called them bioblasts. It is a few microns long and has an elongated shape. The name mitochondrion was coined by Benda (1898), who combined the Greek words for ‘thread’ (mitos) and ‘granule’ (chondros), which referred to the appearance of these structures inside cells undergoing spermatozoon formation.

Mitochondria are indispensable for cellular energy production (Mitchell 1961, 1966). Mitochondrial proteins are coded for partly by the DNA of the cell nucleus, and partly by DNA inside the mitochondria. The complete human mitochondrial DNA has 16,569 base pairs (Anderson et al. 1981), and its inheritance is most probably exclusively maternal (Giles et al. 1980); it is still disputed whether paternal inheritance can take place (Wei and Chinnery 2020). Traditionally, it is considered to contain 37 genes, but recent work shows that mitochondrial genetics is more complex and quite different from that of the rest of the cell (Yen et al. 2013); we are discovering more about how these genes function as research advances.
Mutations of the mitochondrial DNA can cause diseases. They are rare and have a prevalence of at least 9.2 in 100,000 (Schaefer et al. 2008). It used to be thought that mitochondrial diseases only involve energy metabolism, and so replacing the mitochondria would only change the energy metabolism of the individual. However, scientists have found that mitochondria produce a small peptide called humanin, and this molecule is found to protect humans against Alzheimer’s disease (Matsuoka 2011) and cardiovascular diseases (Widmer et al. 2012), and to enhance stress resistance (Yen et al. 2013). Scientists have also found relationships between mitochondrial gene mutations and neurodegenerative diseases (Andalib et al. 2014). In monkeys, mitochondrial morphology in some parts of the brain is correlated to cognitive ability (Hara et al. 2014). In mice, humanin has been shown to be involved in diabetes (Hoang et al. 2010). In addition, mitochondrial DNA also generates a large number of small non-coding RNA molecules. These RNA molecules may well play an important regulatory role in the control of cellular functions (Ro et al. 2013), and thus disease progression in that individual. Lastly, mitochondrial function affects the function of certain immune cells (Konjar et al. 2018).

**Mitochondrial Replacement Therapy (MRT)**

There are currently two main approaches to MRT (see Fig. 2.8):
1. Chromosome-spindle complex transfer

This method was developed by Tachibana et al. (2009). In experiments using rhesus macaque monkey ova, these scientists used micropipettes to extract the chromosomes (strictly speaking, the chromosome-spindle complex) of the ovum, leaving the mitochondria behind. They then placed the chromosomes into enucleated ova using an extract from the Sendai virus. These ova were then fertilised by intracytoplasmic injection of sperm. Fifteen embryos were transferred into the oviducts of nine recipient female rhesus macaque monkeys. This resulted in three pregnant mother monkeys, with healthy baby monkeys born. The scientists also performed various tests on the mitochondrial DNA, and showed that the mitochondrial DNA of these baby monkeys were derived entirely from the enucleated ova.

In 2017, this method was applied to humans for the first time in Mexico (Zhang et al. 2017). A 36-year-old woman underwent ovarian stimulation and the clinicians obtained 29 ova, but 20 of them were not suitable for treatment. Five ova were chosen from the
viable ones, and chromosome-spindle complexes obtained from them. Electrofusion was carried out between the chromosome-spindle complex and the enucleated ovum from the healthy donor; this procedure avoided introducing foreign proteins from the Sendai virus. Each reconstituted ovum was injected with a single spermatozoon from the partner of this woman. One fertilised ovum was chosen and implanted, and this resulted in the birth of a healthy male baby.

2. Pronuclear transplantation This method was developed by Craven et al. (2010). Initial experiments were carried out on abnormal human zygotes. The scientists extracted the pronucleus from an abnormally fertilised human zygote, and placed it inside an enucleated zygote. Experiments showed that the embryos resulting from this procedure contained the nuclear genotype of the extracted pronucleus. This procedure was found not to work with normal human zygotes (Hyslop et al. 2016); thus, these scientists improved the method so that it works on normally fertilised zygotes. They also critically assessed the success rate of pronuclear transplantation to be >98% when it comes to preventing mitochondrial disease in the newborn.

**Permitted Process**

The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 (‘the 2015 Regulations’) set out in detail the circumstances in which eggs and embryos using donated mitochondria can be used in connection with assisted conception under the Human Fertilisation and Embryology Act 1990 (HFEA 1990). Regulations 4–7 set out the process which an egg or embryo must have undergone for the Regulations to apply. This procedure was explained in detail in the previous section. The nuclear DNA is removed from an egg or embryo from the mother (i.e. the woman intended to carry the child) which has ‘abnormal mitochondria’ and placed in a donated egg or embryo which has ‘healthy mitochondria’ and has had its nucleus removed.

There are two points we would highlight about the details of the permitted processes as defined in the 2015 Regulations. First, Regulations 3(c) and 6(c) make it clear that apart from the replacement of the nucleus, no other alternations can be made to the egg or embryo which is produced. The Regulations clearly do not give a green light to extensive genetic manipulation of eggs or embryos.

Secondly, the process can only be used in cases where it is designed to help a woman whose egg has mitochondrial abnormalities, caused by mitochondrial DNA (regulation 5). In Regulation 8, if the technique is used in relation to an embryo, then the embryo must have a significant risk of such abnormalities. The Regulations do not, therefore, allow the use of this procedure for cosmetic or personal reasons. Nor could it be used simply because three people wanted to raise a child who was genetically related to them. Specifically, it could not be used by a lesbian couple who wished to produce a child which was genetically related to both of them.

**Right to Withdraw Consent**

The Regulations deal with the issue of consent to the use of the donated gametes for permitted processes. The Regulations generally adopt the consent provisions in Schedule 3 to the HFEA 1990, which apply to the use and storage of gametes generally. However, Regulation 16 makes an important difference in mitochondrial donation cases. Where a person has consented to the use of their egg or embryo in mitochondrial donation, they cannot withdraw their consent once the nuclear DNA is removed from their embryo or egg and inserted into the mother’s egg or embryo. Indeed once that insertion has taken place, Regulation 17 means that for the purposes of Schedule 3 consent provisions, the material will cease to be regarded as theirs and they have no claims over it. This is in contrast to the position of the sperm donor, whose consent is still required if their sperm has been used to create an embryo. It seems that the limited DNA content of the mitochondrial donor means their claim to the material is regarded as much less important than that of the sperm donor.
Right to Know
Can a child born using MRT seek information about their mitochondrial donor? Section 31ZA of the Human Fertilisation and Embryology Act 1990 will be added by the 2015 Regulations:

(2A) The applicant may request the Authority to give the applicant notice stating whether or not the information contained in the register shows that a person is the applicant’s mitochondrial donor, and if it does show that, giving the applicant the following information contained in the register —

(a) the screening tests carried out on the mitochondrial donor and information on that donor’s personal and family medical history,

(b) matters contained in any description of the mitochondrial donor as a person which that donor has provided, and

(c) any additional matter which the mitochondrial donor has provided with the intention that it be made available to a person who requests information under this section,

but not giving any information which may identify the mitochondrial donor or any person who was or may have been born in consequence of treatment services using genetic material from the applicant’s mitochondrial donor, by itself or in combination with any other information which is in, or is likely to come into, the possession of the applicant.

A person using MRT will not, therefore, be able to find out the identity of the mitochondrial donor. They are, however, entitled to find limited information about the screening tests performed on the donor. The Regulations do permit the donor to provide information to be passed on to the child if they later seek that information. It seems, however, that this cannot include information identifying the donor or child born using the material. Provision is also made for a mitochondrial donor to access limited, non-identifying information about children born from their donation, although the child will not be notified about requests for information.

The Regulations make it clear that a mitochondrial donor and the resulting child are not related so far as the law is concerned, but the provisions in the HFEA allowing for a couple intending to marry or enter a civil partnership to check whether they are biologically related will not apply.

It is the view of the authors that the right to know is not adequate. We do not know as yet the full functions of the cytoplasm which goes with the donor mitochondria in this treatment. At this stage, screening for certain conditions might seem adequate, but as medicine advances, we might be able to know more about what a child has inherited by being born from the mother’s nuclear genes and the donor’s mitochondrial genes. The other parts of the cell which come with the mitochondria could have unforeseen effects. An example, some patients with short stature used to be treated with growth hormone obtained from cadaveric pituitary glands. Some of the dead donors contained prions for Creutzfeldt-Jakob disease. It was not possible at that time to test for this, so many recipients of such growth hormone subsequently contracted Creutzfeldt-Jakob disease (Peden et al. 2007).

We therefore suggest that a small number of somatic cells from the donor be kept in a repository. In case these children born with this method develop rare pathologies, scientists could go back to the cell bank and investigate if this procedure could be the cause of these diseases. The identity of the donor need not be disclosed, but a record should be kept of which children received whose ova, together with a sample of cells from the donor.
Who Is the Parent?

Regulation 18 makes modifications to section 54 of HFEA 2008 to provide that where a child has been born following treatment services, a person who donated mitochondria is not eligible to apply for a parental order on the basis of that donation alone. Regulation 17 inserts into paragraph 22 of Schedule 3 to the HFEA 1990 the following provisions:

(A1) For the purposes of this Schedule, neither of the following is to be treated as a person whose gametes were used to create an embryo (‘embryo E’) -

(a) where embryo E is a permitted embryo by virtue of regulations under section 3ZA(5), the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of embryo E;

(b) where embryo E has been created by the fertilisation of an egg which was a permitted egg by virtue of regulations under section 3ZA(5), the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of that permitted egg.

(3B) For the purposes of this Schedule, in a case where an egg is permitted egg by virtue of regulations under section 3ZA(5) the egg is not to be treated as the egg of the person whose mitochondrial DNA (not nuclear DNA) was used to bring about the creation of that permitted egg.

The effect of these regulations is that the egg produced using MRT will be treated as the egg of the mother and the donor will not be treated as a parent. For the purposes of parenthood they will be in analogous position to that of a person donating sperm for assisted reproduction.

Ethical Issues

The primary argument in favour of permitting MRT is relatively straightforward: it can radically improve the quality of people’s lives. As Savulescu (2015) puts it:

Imagine that there was a law which prevented 150 children a year suffering from a life threatening liver or kidney failure from receiving a transplant. This would be unethical. But this is precisely the current state of affairs for around 150 children every year in the UK suffering from mitochondrial disease, or mitochondrial failure.

This argument assumes that MRT will be effective and the fears of undesirable side effects are unfounded. We will not explore the evidence for these. The HFEA will only authorise the procedure in circumstances when it is reasonably confident such problems will not arise. The issues raised in that debate are essentially the same whenever novel treatments or drugs are created.

Two-Person Input

There may be some who believe there is something essentially good about being related to two people. That is how nature intended things to be. Meddling with the natural two-person link is dangerous. Sommerville (2010), whilst not explicitly considering MRT, wrote:

That the most fundamental human right of all is a child’s right to be born from natural human biological origins ... Children also have a right to be reared within their biological families and to have a mother and a father, unless an exception can be justified as being in the ‘best interest’ of a particular child.

Several responses may be made to such an argument. First, the view that children should be raised by their biological parents would object to donor-assisted conception generally. It
is not a particular argument against MRT, but rather an objection to children being created outside the traditional biological norm. It might readily be rejected on the basis that society has moved well beyond the view that children should be raised by their biological parents. We would argue, as no doubt would many people, that being raised by loving carers is far more important than them having a biological link to you. Indeed relationship breakdown and the child protection law mean that it is now common for children not to be raised by their parents.

Secondly, Sommerville (2010) accepts that it may not be in the best interests of a child to be raised by their biological parents. It may be argued that it would be better for the child to be born without the mitochondrial disease, than with it. It is, therefore, better for the child to be born using MRT and not be raised by their biological parents.

Thirdly, the claim that a process is ‘unnatural’ and therefore wrong must be questioned. After all, the whole of medicine is ‘unnatural’, but does it mean we should abandon all medicine? As Haldane (1924) explained,

The chemical or physical inventor is always a Prometheus. There is no great invention, from fire to flying, which has not been hailed as an insult to some god. But if every physical and chemical invention is a blasphemy, every biological invention is a perversion. There is hardly one which, on first being brought to the notice of an observer from any nation which had not previously heard of their existence, would not appear to him as indecent and unnatural.

A fourth response to Sommerville (2010) is simply to question why it matters at all that we are only biologically connected to two people. After all, there is DNA in our bodies from a wide range of viruses and bacteria which do not come from our parents (see Sect. 5.6). Perhaps more readily understood is the fact that a person may have a transplanted organ, with DNA from a ‘third person’, but that is not seen as particularly harmful or undesirable. Indeed this argument may be taken further and question the extent to which a person’s DNA defines their identity.

As Baylis (2013) puts it, ‘identity is not in the genes but in the world in which we live and the stories we construct and are able to maintain.’ Interestingly, however, she uses this insight to claim that a child born with MRT will have a different identity from the one born without, not because of any significance attached to DNA per se, but rather the absence of the condition which would otherwise form part of their identity. Without the condition they will have a very different life to that they would have with it.

But this brings us to the crux of the issue: not whether it is appropriate to bring a child into the world with DNA from three parties, but whether it is right to manipulate DNA so that the person who comes into the world is different from the one who otherwise would. However, as Palacios-González et al. (2014) argue, the children who would have been born with the condition cannot be said to be harmed because they have never existed. This raises the infamous ‘non-identity problem’ which is much discussed in philosophical literature.

Genetic Identity
A slightly different argument would be that a child born using MRT would suffer from confusion over their genetic identity. Rather than having two genetic origins they would have three. Children are, however, nowadays raised in such a variety of family forms that it is increasingly hard to claim there is a norm and that being raised outside that norm is ‘confusing’.

Germ Line
One argument that is sometimes used against MRT is that it involves ‘germ-line genetic modification’, meaning that it is not just the offspring’s DNA that is modified, but also the DNA of the generations to follow. Nazir-Ali (2015) argues:
The proposed technology will interfere with and change the germ-line forever. This is breaking an international consensus that genetic engineering should not be used to modify human eggs or sperm in such a way as to alter the characteristics of future children.

It is very questionable whether MRT does this. Remember it does not introduce any new mitochondrial genes into the human germ line. Nor does it manipulate any existing genes. It combines the DNA from one egg with the DNA of another, but that does not seem to be any more challenging to the germ line than a sperm and an egg combining.

**Harm to Egg Providers**

Baylis (2013) has argued that MRT carried dangers for the egg donors. They will bear the cost and pain of egg retrieval, with little return. It must be admitted that it is unlikely many women will come forward to donate eggs utterly altruistically. However, it may well be that women will be willing to do this for sisters, relatives or friends. While Baylis (2013) questions whether the emotional benefits of egg donation justify the physical harms, that is surely a question we can leave to individual donors. We know that people are willing to undertake huge levels of care and sacrifice to look after their elderly parents, for example. Parents make substantial sacrifices to care for children. It is not clear that egg donation is significantly worse than any of these things.

A more powerful point is whether it is appropriate to expect these sacrifices for the limited good. A critic may complain that those concerned about passing on genetic conditions can make use of the alternatives of adoption or fostering. Baylis (2013) argues:

> It is unclear why a ‘wish’ for a genetic link on the part of prospective parents should be taken to justify the imposition of health risks on future children and subsequent generations. Family making should be about establishing loving, caring, nurturing relationships and these may or may not include genetic ties.

Is MRT, then, simply pandering to the unjustified wishes of those who wish to have children genetically related to them? This argument is not one against specifically MRT but any assisted reproductive technology used by those seeking to have a child genetically related to them. While we would agree with Baylis (2013) that we should encourage people to see that being a parent is about caring for a child, not about being genetically related to him or her, people do have a strong desire to have genetically related children. Maybe there is a degree of biological programming about that. The debates about the importance of a biological link to parenting will no doubt continue for the foreseeable future. It is not the role of the law to take sides on such a contentious issue. Where a donor is willing to make the sacrifice and where to many people having a child genetically related to them is a clear benefit, the case for the law prohibiting the sacrifice seems weak.

**Summary**

The Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015 mark the next step in expanding the use of reproductive technology. They offer parents concerned about the passing on mitochondrial diseases a way of avoiding that. While critics may be concerned this is a step towards genetic engineering of children, the Regulations clearly restrict its use to avoiding the passing-on of mitochondrial diseases, and as such, it is similar to pre-implantation genetic diagnosis, which is already practiced. The Regulations are also carefully drafted to ensure a child has only one mother and remain wedded to the notion that biology must limit the law, so that a child can have no more than two parents. As technology moves away from that assumption, surely the law will follow in due course and come to recognise that a child can have three parents. And if three, why not more?

**2.3.2 Gene Editing Methods**
Mitochondrial replacement therapy allows us to change the genes of a baby to avoid diseases. However, the changes that are possible using this method are very limited. Scientists have tried to edit specific genes using zinc-finger nucleases (Urnov et al. 2010) or transcription-activator-like effector nucleases (Joung and Sander 2013). However, in order to edit different genes, these proteins have to be re-designed. It is thus a rather inefficient method, as different DNA sequences require proteins of slightly different structure and function.

Recently, a method has been developed that has the potential to allow us to change our genes almost at will, without the need to change the protein every time for a different gene sequence. This method is the CRISPR-Cas9 technology or, more accurately, the CRISPR-Cas9 RNA-guided DNA endonuclease method.

CRISPR stands for clustered regularly interspaced short palindromic repeat. CRISPRs are DNA sequences of between 21 and 38 base pairs found originally in bacteria. Between these sequences are the ‘spacers’, which are DNA sequences of between 26 and 72 base pairs. Viruses which infect bacteria inject their DNA into the bacterial cell, and these viral DNA are processed by the bacteria to form spacers. The long DNA-containing stretches of spacers sandwiched between CRISPRs are transcribed into RNA, and the RNA is recognised by a family of proteins called Cas (CRISPR-associated) proteins. The viral RNA is then destroyed by Cas proteins to defend the bacteria against viral attacks. More details about this bacterial immune system can be found in a review by Rath et al. (2015).

Scientists subsequently recognised that the CRISPR-Cas system can be used to edit genes in human cells (Fig. 2.9). The Cas protein can accept a ‘guide RNA’ molecule which has a sequence complementary to that of the DNA to be edited. The DNA is cut at a specific point in the specified sequence. Endogenous DNA repair mechanisms would then process the cut DNA. If a DNA sequence with homology to the cut sequence is inserted, homology-directed repair (HDR) would cause specified changes to the gene. Or if the gene is to be inactivated, the non-homologous end-joining (NHEJ) repair can be activated to cause insertions and deletions in the wild-type gene. The CRISPR-Cas method is thus a very versatile system; the same protein can be used to edit genes of different sequences, simply by changing the guide RNA sequence (Komor et al. 2017). Not surprisingly, this method has been applied widely to a large number of living organisms (Barrangou and Doudna 2016).

The first human trial involving this new gene-editing procedure took place in October 2016: clinicians in Chengdu, China, delivered cells modified using the CRISPR-Cas method into a lung cancer patient, as part of the treatment for cancer (Cyranoski 2016). Moreover, scientists have built on the success of the CRISPR-Cas method to discover the Cpf1 bacterial protein, which is more efficient than the CRISPR-Cas system. Specifically, it cleaves DNA leaving a staggered double-stranded break, which makes subsequent DNA changes by either NHEJ or HDR easier (Zetsche et al. 2015).
More recently, a more precise method for editing genes called prime-editing (Fig. 2.10) has been developed (Anzalone et al. 2019). It is more specific, and capable of making a larger variety of edits. Most importantly, it does not rely on the cell’s repair system to make the changes, and this method reduces the number of unintended changes.

2.3.3 Gene Editing of Germ-line Cells
The advent of the CRISPR-Cas and associated methods has rendered gene editing feasible, though still difficult (CRISPR yields are low and there are risks with off-target alterations). Gene editing has been used to treat cancer since 2017 (Baylis and McLeod 2017), but the changed genes only stay with the individual. The same technology can be used to change germ-line cells, where the changes will be carried on to future generations. With the appearance of prime-editing, it would not be difficult to envisage a future where ‘designer babies’ are born. The first gene-edited babies were born to Chinese parents in 2019.
(Cyranoski and Ledford 2018). The scientist Jiankui He used CRISPR to alter the CCR5 receptor of twin girls, to render the babies resistant to HIV infections (CCR5Δ32 mutant, where 32 base pairs are missing from the gene, confers resistance to HIV infections). Unfortunately, he could not achieve deletion of the 32 base pairs. One of the babies has a 14-base pair deletion (Wang and Yang 2019), and the other has a 4-base pair deletion with an insertion (Ryder 2018). His actions were universally condemned (Cyranoski and Ledford 2018) and this incident is probably going to lead to an international moratorium on gene editing of germ-line cells (Lander et al. 2019).

Here we would like to consider some aspects of gene editing.

Which Genes to Edit?

One might be tempted to think that one could edit the genes of one’s cells at will to achieve all kinds of effects. The problem is that we often do not know which genes to edit. Take a trait which many parents might like for their children: intelligence. Research shows that this trait is affected by a large number of genes, i.e., the inheritance is polygenic. In the case of intelligence, Davies et al. (2011) found that about 40–51% of intelligence is heritable, and that the inheritable part is controlled by over 100 single-nucleotide polymorphisms (SNPs). By SNP, we mean that there is a difference of only one nucleotide between the different forms of these genes. Some of these base pair changes are found in coding sequences, but others are found in non-coding sequences. With current technology, it is quite difficult to specifically alter over 100 positions in one’s genome.

Even if it becomes technically feasible to alter hundreds of base pairs in one’s genome, one then faces the question: what are the consequences of all these changes? They may well make somebody more intelligent, but are there other consequences? We know that a number of genes are called regulatory genes, and they control the functions of more than one genes. Disruption to regulatory gene functions could have far-reaching consequences (Maston et al. 2006; Vernimmen and Bickmore 2015).

Who Controls One’s Genes?

The deceptively simple answer would be ‘the individual concerned’. A little more thought would show that things are not that simple.

Humans live in a community, and there is a lot of mixing and exchange of bodily material (see Chap. 5 for more details). Marriages and child-bearing entails the mixing of genes in the newborn. One’s genes are usually assumed to ‘belong’ to oneself, but they also have effects on the whole community. A good example would be sickle cell anaemia (SCA).

Sickle cell anaemia (SCA) is a genetic disease, so called because the red blood cells of the patients are sickle in shape. The sickle shape of the red blood cells and associated anaemia were first described by Herrick (1910), and the molecular basis was worked out by Pauling et al. (1949). Normal individuals carry two genes, one from each parent, which code for haemoglobin A (normal haemoglobin). Sickle cell anaemia patients have mutated genes which code for an altered form of haemoglobin, haemoglobin S (Ingram 1956, 1957). The red blood cells with haemoglobin S are less elastic than normal red blood cells, and tend to stick at branching points in blood vessels, leading to haemolysis, vasculo-occlusive crises and associated blood problems. Allison (1954) showed that people who carry one sickle-cell haemoglobin gene and one normal haemoglobin gene (people with the sickle-cell trait) have resistance towards malaria infections.

Homozygotes with the sickle cell gene die early. In an environment where there is no malaria, heterozygotes for SCA die at a younger age. However, in a malaria-infested area, heterozygotes have a survival advantage. It is not difficult to envisage how the environment would change with global warming, so if a cloned cell is heterozygote for SCA, and the parents would like to alter the germ-line cells, should that be allowed? If this can be allowed, and the SCA gene dies out from the human population, is that to the survival advantage of our species? Permitting some people to suffer from SCA for the good of the
human race might be regarded by some as infringing the Kantian imperative against using a person for the good of others.

The legal issues raised here would be twofold. First, there is the question of whether amending genes for sickle cell anaemia would be permitted at all. At the moment gene editing requires a licence under the Human Fertilisation and Embryology Act 2008, and licences for gene editing have been granted. It seems therefore that we are well on the path to undertaking the research so that we could amend genes in relation to sickle cell anaemia. If that produces an effective and safe way of changing the genes, then it is likely to be permitted.

Second, there is question of whether or not we should require parents who are at risk of having a child with sickle cell anaemia to undergo PGD and then have the editing required to remove the condition. At first, this will seem a very intrusive requirement for the law to undertake. However, generally where a child has an illness and treatment is available, which parents refuse, the court will order the treatment regardless of the objections of the parents. We have seen this in the case of parents of Jehovah’s Witness parents who refuse to consent to blood transfusions for their children (An NHS Trust v. Child B and Mr and Mrs B [2014] EWHC 3486 (Fam)) and even order children to receive vaccinations despite the objections of a parent (Re B (A Child: Immunisation) [2018] EWFC 56). However, PGD in relation to sickle cell anaemia would be different for two reasons. First, there is the problem that, unlike the blood transfusion cases, there is no currently existing child whose welfare can be considered by the court. This is a legal problem in that there is no jurisdiction that could be invoked to require an order to be made and it would make new legal precedent to make orders designed to benefit a currently non-existing person. Second, and perhaps more importantly, it is difficult to see how such an order could be given effect without requiring couples who are risk of producing a child who would have sickle cell anaemia from using assisted reproduction. Doing that would be seen as a major interference in their human rights.

2.4 Cloning

Cloning raises high emotions. To some extending the possibilities of human reproduction beyond normal sexual intercourse is terrifying, raising profound questions about our identity. Article 11 of the UNESCO Universal Declaration on the Human Genome and Human Rights (1997) states that ‘practices that are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted’. However, it is unclear to us how human dignity is offended by human cloning, and whose human dignity is involved. To others, cloning provides exciting possibilities of enabling couples to have children who would be unable to have them otherwise and offers the hope for the treatment for or lessening the incidence of certain diseases (Humber and Almeder 1998; Lauritzen 2001; Moffat 1998).

Now that the cloning of many mammals is feasible, and there have been some (dubious) claims that humans have been cloned, prediction about the effects of cloning has moved well beyond the realm of science fiction. But the question of whether or not to clone is one that has attracted much attention and this has led in many cases to a polarisation of views. This section is based on the assumption that, to some extent, human cloning will be permitted. First, we briefly describe the science underlying cloning technology. Then, we consider to what extent human cloning should be lawful. Lastly, we consider the potential impact of human cloning on many of the assumptions that underline family law and the legal regulation of assisted reproduction. The extent to which cloning of humans is permitted is, of course, high controversial.

2.4.1 Cloning Technology

A clone is a group of cells that have identical DNA sequences to the ‘parent’ group of cells, though, in reality, almost all the clones that have been produced so far are not true clones, because their non-chromosomal (mitochondrial) DNA are different from that of the ‘parent’
even though their chromosomal DNA are identical. Currently, there are two methods to create a human clone: one is a method that has been tried and tested in animals, whereas the other method is more speculative and still being researched.

**Somatic Cell Nuclear Transfer (SCNT)**

Currently SCNT is the only technique available for creating a clone. This is a process whereby fertilisation is circumvented, and the ovum is activated not by the nucleus formed from the genetic material from the spermatozoon and the ovum, but by a nucleus introduced externally. This is not a new technology. Briggs and King (1952) extracted cell nuclei from frog blastula, a largely undeveloped embryo, and placed them into frog eggs whose nuclei had been extracted and discarded (enucleated frog eggs). They found that the transplanted nuclei could direct normal development of the frog eggs. The experiment was performed to investigate if the frog egg could re-programme the externally introduced nucleus so that the nucleus could direct normal development of the ovum. This subject has been reviewed by Gurdon et al. (1979).

The nuclei used in the previous work were usually obtained from embryonic cells in various stages of development, and the recipient cells have to be pre-treated so that the donor nuclei and the recipient cells are in a coordinated phase of the cell cycle (Campbell et al. 1996a). Gurdon et al. (1975) showed that, in amphibians, it was possible to use nuclei obtained from non-embryonic cells to activate an ovum. Campbell et al. (1996b) then extended this work to mammalian cultured cell lines, and Wilmut et al. (1997) made an important breakthrough by enabling non-embryonic cell nuclei to be used. In this famous experiment to create Dolly the sheep, the recipient ova came from ewes, but they were enucleated, and the nuclei replaced by those obtained from mammary epithelial cells.

What is so special about using non-embryonic nuclei to activate ova? Embryonic cells up to the two-cell stage or four-cell stage are totipotent; that is, each cell is capable of generating a globally coordinated developmental sequence to yield a human being. Beyond that stage, the embryo cells no longer possess totipotency. Many of these embryonic cells can still develop into different kinds of cells; that is, they are pluripotent; pluripotent cells produce, but do not organise, all or most of the cell types found in a mature individual (Condic 2014). The research of Wilmut et al. (1997) shows that it was possible, at least in one mammalian species, to use adult cell nuclei to activate ova to develop into individuals, or ‘clones’; these individuals have almost the same genetic make-up as that of the original donor individual. As a corollary, it should be noted that totipotency is a property of the cell nucleus and cytoplasm combined. A cell can only be totipotent if the nucleus is ‘programmed’ to generate the coordinated development sequence and the cytoplasm is in a state to participate in this coordinated development. This is the reason why an adult cell nucleus has to be placed in the cytoplasm of the ovum, as the only totipotent cytoplasm is that of the ovum (Condic 2014).

This method has been made famous by its first application to clone Dolly the sheep (Wilmut et al. 1997), and can be modified to treat mitochondrial diseases by pronuclear transfer (Craven et al. 2010; Hyslop et al. 2016), as is explained in Sect. 2.3.1. Ova were obtained from an ewe, and the original nuclei of these ova were extracted and discarded (enucleation). The nucleus of a somatic cell from a sheep is extracted and placed in the ovum. The genetic material in the donor nucleus caused development of the ovum, which was subsequently placed in the uterus of an ewe and a lamb was born. This method, though successful, had a high loss rate: Dolly the sheep was born after nearly 300 eggs were used for SCNT, which created 29 viable embryos, of which only 3 survived until birth, and only 1 survived to adulthood. Note that this method does not exactly result in identical individuals, as the mitochondrial DNA comes from the donor ovum, and is not the same across the post-nuclear transfer ova.

Cloning using SCNT has been successfully applied to 23 mammalian species, and recently this has been applied to macaque monkeys (Liu et al. 2018). However, it is more difficult to clone primates, because nuclei from somatic cells do not work (Mitalipov et al. 2007); they
and the recipient cytoplasm require special prior treatment. Liu et al. (2018) did not use somatic cell nuclei, but nuclei from fetal fibroblasts from aborted monkey fetuses. They created 79 embryos using fetal fibroblast nuclei and enucleated ova, implanted them into 21 surrogate mothers, and only two babies were born.

SCNT has been applied to produce human embryonic stem cells (Tachibana et al. 2013), but human cloning using SCNT or derivatives of SCNT would seem to be very technically difficult, though not impossible. The road is thus open for the possibility of cloning humans for at least two purposes: (a) reproduction for infertile couples or others; (b) to produce an embryo, not for growth as a human being, but for creating replacement organs/body products.

**Induced Pluripotent Stem Cell (iPSC)**

The production of the induced pluripotent stem cell (iPSC) is a probable method to make a human clone. Takahashi and Yamanaka (2006) first induced adult mouse cells to become pluripotent stem cells. Condic (2014) has written a review to clearly explain features of totipotent and pluripotent cells: each totipotent cell is capable of generating a globally coordinated developmental sequence and becoming an embryo, whereas pluripotent cells produce, but do not organise, all or most of the cell types found in a mature individual. Subsequently, Takahashi et al. (2007) and Yu et al. (2007) independently induced human cells to become pluripotent stem cells. None of these cells are totipotent, so they cannot direct a development sequence to produce an embryo. Research efforts have aimed to define the structural and functional differences between totipotent and pluripotent cells (Dang-Nguyen and Torres-Padilla 2015), and to investigate how to generate totipotent cells from pluripotent stem cells.

2.4.2 Legislative Responses to Human Cloning

Here we will examine, by way of example, how some jurisdictions have tackled the issue. This account will demonstrate the difficulties faced in producing a legislative definition which prohibits cloning.

**United Kingdom**

The House of Lords in R (on behalf of Bruno Quintavalle on behalf of Pro-life Alliance) v. the Secretary of State for Health [2002] EWCA Civ 29 held, controversially, that SCNT was not prohibited under section 1 of the Human Fertilisation and Embryology Act 1990. In response to the first-instance decision in that case, which the Court of Appeal had overturned, the government hurriedly passed the Human Reproductive Cloning Act 2001. The core provision in section 1(1) is self-explanatory:

A person who places in a woman a human embryo which has been created otherwise than by fertilisation is guilty of an offence.

The criminal offence carries a maximum sentence of ten years. This legislation does not prohibit the creation of a cloned embryo, but only the placing of such an embryo into a woman.

In a way, the history of British legislation on cloning demonstrates what can go wrong if the legislative body of any country is too reactive on the complex issues involved. It would have been ideal if Parliament could have sat down, worked out the possibilities and potentials offered by the new technology, consulted the public and arrived at laws which are far-sighted and practical. The Human Reproductive Cloning Act 2001 appears straightforward, but as technologies develop, there is little doubt it will need to be reconsidered. There are two issues in particular which in due course will need to develop:

1. The legislation only prohibits the placing of such an embryo in a woman. This appears to permit the placing of such an embryo in an artificial uterine environment (in due course, scientific advances may allow any cell from an adult individual to be de-differentiated
into a totipotent embryonic cell, and then go through all the embryonic and fetal stages in an artificial environment, thus circumventing the need for a surrogate mother, see Sect. 2.5), or even the placing of such an embryo in a male, if ever attempts were made to enable men to provide a gestational base for an embryo. It is not inconceivable in the near future that an embryo will be able to survive to term in such an environment. This would enable an embryo to be created by SCNT and then transferred to the artificial uterus and be ‘born’ after ten months of ‘gestation’.

In the more distant future, it would not be totally outrageous to assume that one can get a somatic cell—any somatic cell—and cause it to de-differentiate to attain, if not totipotency, at least pluripotency. These pluripotent or totipotent cells can then be induced to develop into the organ or tissue that requires replacement, the resultant cells placed in the patient and the diseased cells taken out.

2. There may be some concerns that the legislation prohibits the placing in a woman of an embryo. It is not impossible that a scientist would wish to create from manipulated sperm and eggs a clump of cells that is not an embryo (at least in the sense of being capable of developing into a human). These cells could conceivably grow and provide replacement tissues or organs for therapeutic purposes. The Act may not prohibit the insertion of such a clump of cells into a woman.

3. The Act itself does not prohibit the placing in a woman of a hybrid with mixed human and other animal gametes.

As these examples demonstrate, there are difficulties facing any state which wishes to pass legislation which prohibits human cloning. Technological advances can quickly render legislative attempts to ban cloning outdated. Further, national-based bars will be of little use without an international ban.

**Council of Europe**


Any intervention seeking to create a human being genetically identical to another human being, whether living or dead is prohibited.

This 1997 Council of Europe Convention is the first treaty to absolutely prohibit the cloning of human beings (Somekh 1999). It came into force as binding legislation on December 1, 1999, although 6 of the 35 European states that signed the Convention have yet to ratify it.

**United Nations**

UNESCO’s Universal Declaration on the Human Genome and Human Rights states that the respect for human dignity makes it imperative not to reduce human beings to their genetic characteristics and to respect their uniqueness and diversity. Practices contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted. But it is impossible to reduce human beings to their genetic characteristics, because we are complex beings and are always much more than our genes. Monozygotic twins have identical nuclear DNA, but they are not less dignified human beings. It is also unclear whose human dignity is affected by human cloning: is it the originator human or the cloned human, and if so, how?

The likelihood of an effective UN ban on human cloning is much debated. Certainly there are concerns that unless there is universal agreement which is strictly enforced, such an agreement might rapidly break down (Shanin 2002).
United States
A number of US states have passed legislation prohibiting cloning. For example, the California Health and Safety Code 24185 states:

(a) No person shall clone a human being. (b) No person shall purchase or sell an ovum, zygote, embryo, or fetus for the purpose of cloning a human being. (c) For purposes of this section, ‘clone’ means the practice of creating or attempting to create a human being by transferring the nucleus from a human cell from whatever source into a human egg cell from which the nucleus has been removed for the purpose of, or to implant, the resulting product to initiate a pregnancy that could result in the birth of a human being.

Canada
In Canada, the Assisted Human Reproduction Act 2004 prohibits human cloning and other reproductive technologies.

2.4.3 Options
What options are there for a legal system wishing to address the issue of human cloning?

1. Outright ban on all kinds of human cloning
   One option would be to ban all forms of human cloning. Some commentators argue that an outright ban would be unworkable (Brown 2002). Once scientists have started working on cloning, the technology is known and it may be difficult to ‘close the door on it’. Certainly it would be difficult to encourage further research on the issue if such a plan is developed (Brown 2002). Many commentators take the view that until there has been further research, it is best for the law to adopt a flexible approach.

2. Permitting cloning in certain defined circumstances
   From reading some of the press you could be forgiven for thinking that the reason why couples will use cloning is to produce the ideal baby, with the preferred coloured eyes, hair and skin, and with selected intellectual abilities. There are strong objections to such procedures, and very few professionals working in the area would countenance cloning for these reasons, so what reasons might be permitted? This question is important because it may be that a state would be willing to permit cloning in certain specified circumstances:

   - Permitting cloning as the only way to deal with infertility For some couples cloning would be the only way they would be able to have a child. If a couple wish to produce a child who is genetically related to both of them, but are unable to have a child naturally because, for example, the husband’s sperm is faulty or there is a lesbian couple, then for them cloning would be the only possibility.
     Such an approach could be readily supported by those who see infertility as an illness to which they have a right to treatment. As we provide remedies for some forms of infertility, why should we not provide remedies for all kinds of infertility? The argument has been developed by those arguing that to deny reproductive human cloning would discriminate against same-sex couples. This has led some to suggest that human cloning should be permitted for same-sex couples, for whom this is the only way of having a child, but not available for couples for whom other forms of assisted reproductive technologies would enable them to have a child (Orentlicher 2000).
   - Permitting cloning as the only way to prevent a child being born with genetically inherited illness
     If we allow cloning for infertility, do we allow people to alter the genes? If, for example, there exists an easy test for trisomy 21 (Down’s syndrome), do we test the zygote for it? Under English Law, a mother can request abortion if the fetus is found to be affected with a genetic abnormality. Would such a situation apply to genetically abnormal babies?
to suffer from serious fetal abnormalities. By the use of cloning and genetic manipulation it would be possible to ensure that a child is born without a particular genetic illness (e.g. Huntington’s chorea).

To permit cloning in an attempt to overcome disease may attract public support. There are potential difficulties that would need to be overcome before such an argument could be adopted. First, there is the question of whether it is possible to distinguish between cloning to prevent illness and cloning to ‘perfect’ a child. Is cloning to prevent a genetic predisposition to obesity to be permitted or not under this proposal? What about a predisposition to early hair loss or transsexuality? Supporters of the proposal may accept that the line between preventing illness and enabling perfection may be hard to draw, but that is always true in many issues covering the regulation of medical treatment.

Secondly, the elimination of certain genetically inherited illness is not necessarily desirable for the human race. Consider, for example, sickle cell anaemia (SCA), which has been discussed in Sect. 2.3.3.

3. Regulatory systems

One of the difficulties with a legislative ban on cloning is producing a legislative definition of the activity which is to be prohibited. Such difficulties could be dealt with by a regulatory regime whereby procedures could be licenced on a case-by-case basis (Annas 1994). There might be concerns that if cloning is permitted under some circumstances, then this will be the start of a slippery slope before allowing it for any circumstance (Reiss 2002).

4. Non-legal regulation

Whether or not cloning can be permitted could be left as a matter of clinical judgement, just as abortion is allowed up to 24 weeks, provided two clinicians are willing to sign that the continuation of pregnancy would be detrimental to the physical or psychological health of the mother.

2.4.4 Arguments Against Human Cloning

Here we will examine the arguments that have been made against cloning. It will be emphasised that the arguments are at their strongest against some forms of cloning than others.

Unacceptable Dangers

It is widely accepted that to attempt human cloning in the present state of scientific knowledge would pose unacceptable risks (Caplan 2018; Mitalipov et al. 2007). The rates of miscarriages in attempted cloning and the risk that any child successfully produced would suffer from illnesses or diseases and advanced ageing (Coleman 1999) mean that ethically such experiments would be improper. And yet without such experiments, human cloning technology is unlikely to improve. It is therefore unknown when and how cloning technology will improve to the extent that it is considered safe.

Certainly there are some who take the view that the potential benefits to the human race are so great that concerns about the cloned embryo failures as the technology develops should not overly concern us. It is difficult to see how these experiments could be approved. Currently, human embryo experimentation is allowed up to 14 days or when the primitive streak appears. The primitive streak is considered the starting point of the central nervous system (Sadler 2018). To monitor the development of human clones, scientists need to monitor the development of clones from the earliest stages to at least one or two years of age. This kind of experimentation is unethical and treats the clone as a laboratory animal.

Genetic Diversity
From an evolutionary perspective it is possible to argue that women who cannot have children probably have adaptive reasons for being so, and artificial attempts to make them conceive will involve the propagation of ‘bad’ genes. Although cloning might involve a small number of cases initially, this may multiply over time. Current evidence suggests that children born using assisted reproductive technologies have a higher incidence of health problems, ranging from paediatric cancers to obesity and cardiovascular disease in adult life (Chen and Heilbronn 2017). Such arguments are, however, arguments against all forms of infertility treatment, not specifically against human cloning. Indeed there are concerns that such arguments could be used to prohibit the reproduction of all people with certain diseases.

Perhaps a more moderate form of this argument is the more general concern that the diversity in the human gene pool will be diminished by widespread human cloning. In reality unless cloning becomes a very common method of reproduction, it is hard to see that the challenge to the gene pool will be very great (Foley 2002). There are those who are concerned that the using of cloning for therapeutic purposes will mean that there are fewer ‘outsiders’; that a standard norm of the ideal person will be used to which everyone will aspire (Wang 2001).

**A Right to One’s Own Unique Identity**

Some commentators have claimed that one has a right to be genetically unique (Williamson 1999). The argument is that each person has a right to have their own genetic make-up, which is independent of others. This is because our genetic make-up is regarded as the core to our humanity (Kass 1998; Rao 2002). To ensure an individual’s unique status and separateness from their parents, it is crucial that the child is a combination of genetic material from both parents. The distinction between the child’s and the parents’ genetic make-up also reminds the parents of the fact they must recognise the individuality of their child. Cloning creates the danger of encouraging parents to think they can design and influence improperly their child’s development (Kaveny 1999).

To some commentators, however, such a claimed right to genetic uniqueness is hard to justify in relation to prohibiting cloning:

1. Nature itself permits individuals to share DNA: monozygotic twins share the same nuclear DNA, but the proportion of their mitochondrial DNA is different (see Sect. 2.1.4). Even where DNA is shared, the effect of personal, environmental and social experiences will mean that the individuals will neither appear identical, nor share personalities. It is, therefore, possible to have a unique identity, personality and character, even where the DNA is shared (Roberts 1999). However, it can be replied that each twin still draws their genetic basis from two parents. It could also be argued that the cloned child could trace two sources of genetic material from their grandparents, not from the parents.

2. As explained in Sect. 2.3.1, with the current method of cloning using SCNT or variants thereof, the clone will not share mitochondrial DNA. This may change in the future, if methods are devised to copy even mitochondrial DNA over.

3. The parent of a cloned child may be even more sensitive than the parent of a child born of normal sexual reproduction to ensure that the child is aware of their unique identity (Silver 2000).

In response to these arguments, the genetic identity argument could be rephrased. Rose (1999) has expressed concern that cloning ‘confuses the intergenerational structure of the family’. The House of Lords Select Committee on Stem Cell Research (appendix 6, paragraph 6, page 200) put it this way:
If the cell nucleus from the father were used, for example, the child would be the
genetic son of its grandparents, the genetic sibling of its uncles and aunts and the
genetic uncle of its cousins. The range of ambiguities introduced into family
relationships by cloning from a close relative would be large and the possibility for
emotional confusion and uncertainty, not only on the part of the cloned child,
considerable.

As the Committee notes, these concerns may be lessened if the clone was not a family
member, but the most likely circumstances in which cloning would be used are those where
a couple or an individual wants a child genetically related to them.

A slightly different point is that cloning creates the possibility of a ‘fatherless’ child: a
child genetically related to only the mother. To some that creates an unacceptable position
to put a child in (Nelson 1998).

Nevertheless, against all these arguments, one still would like to ask if a unique genetic
identity is part of ‘human dignity’. Genes determine our abilities, but genes do not determine
our destinies. Our personal identity comes not only from our genes, but also from our
environment, our relationships and what we decide to do with our lives. To some people, it is
unclear why human cloning offends human dignity.

**A Right to an Open Future**

Some have argued that children have the right to choose an open future (Raz 1988). Even if
there is no biological reason for this, a cloned person may believe that they are genetically
pre-ordained to be like their clone. In reply it might be said that there may be a sense that
even a child born using normal reproduction may feel destined to have some of their
parents’ characteristics (Kass and Wilson 1998; Kaveny 1999). The assumption will be that
the child will follow their parent, rather than there being delight (or disappointment) when
they do so (Kaveny 1999). Supporters of cloning suggest that such concerns are speculative
(Orentlicher 1999; Robertson 2000); notably there are no such concerns with twins. It has
even been argued that whatever such harms may be, claims of diminished individuality are
more preferable to not being born at all (Orentlicher 1999).

**Religious Objection**

Some have argued that there are religious objections to cloning of humans (Campbell 1998;
Dorff 1998; House of Lords 2002). It is clear that writers claiming to present a religious
perspective have not agreed over whether all uses of human cloning should be forbidden
(Campbell 1998). The religious arguments against cloning have been that the child of a co-
operative procreative union between two people is an embodied symbol of the couple’s
mutual love and a gift of their intimacy (Campbell 1998; Richardson 1998). Further, it has
been argued that each person has been created as an individual as part of God’s creation
(Fadel 2002). By contrast the child of technology was a ‘product’ of human will and design
(Ramsey 1966). In part this is a debate between those who believe that humans have been
given by God dominion over the earth and those who believe that people should not ‘play
God’ in areas that are inappropriate for human intervention.

**Money Concerns**

There are concerns that cloning will be available only to the wealthy. Such concerns can,
however, be raised about almost any form of medical treatment.

**Harm to the Position of Women**

Some suggest that cloning is likely to work against the position of women (Mahowald
2000b). The argument tends to be that cloning is likely to be particularly attractive for men
who cannot have children (Mahowald 2000a). The risks, pains and discomfort of ovarian
stimulation, ova retrieval and embryo transfer will all fall on women, not to mention, of
course, of the experiences of gestation and childbirth. It has been claimed that for each
human cloning attempt, there will be a need for several hundred ova, and there is a high risk of late fetal deaths in cloned embryos, which carries with it risks of physical and emotional harm (Smolin 2001). All of these will impose burdens on women. There are also wider concerns that reproductive technologies such as cloning increase and perpetuate the exercise of medical and patriarchal power over women’s bodies (Petchesky 1980; Ryan 1998).

The idea of the ‘infertile man’ (Mahowald 2000a) is medically unsound; in medicine, we talk about an infertile couple, as an individual is always infertile by definition. Moreover, the feminist standpoint of Mahowald (2000b) has been criticised for resting on questionable assumptions, e.g., the view that nondominant groups in society have a superior perspective simply because of their nondominant position is presented uncritically. She also tends to accept claims uncritically; e.g., she claims that women are under-represented in clinical trials, which is untrue (Stolba and Satel 2000). Lastly, concerns that cloning would disproportionately impose burdens on women must be weighed against the strong desire for women to have children for whom cloning will be the only option, such as lesbian couples. These concerns, it is submitted, may call for regulation to ensure that women do not become only ‘vessels’ in the hand of medical professionals, but there is nothing in the nature of human cloning which necessarily demeans women.

**Parenthood/Natural Parenthood**

There are some who are concerned that cloning will undermine the very concept of parenthood (Annas 1994). Rao (2002) puts it this way: cloning frees individuals from the need to connect with others and engage in marriage or any kind of intimate relationship in order to have children. In so doing, cloning could be viewed as radically individualistic and ultimately antisocial or even alienating, the paradigm right of isolated individuals. Ryan (1998) draws a distinction between acquiring children and having children. This ties in with some of the arguments that children should be regarded as a gift. She argues that the nature of acquiring a child is destructive to the child’s interests.

Some reject these arguments. Step-parents and adoptive parents are no less parents because they lack the genetic link (Silver 2000). Is not parenthood about the love, support, work and care for a child, rather than the genetic link? Indeed research on ‘non-traditional’ families shows that the quality of family relationships and the wider social environment are much more important in children’s psychological development than the number, gender, sexual orientation or biological relatedness of their parents (Golombok 2017).

**Asexual Reproduction as Abnormality or Is ‘Repugnant’**

There are those who claim that human cloning is abnormal (Annas 1998). More specifically, cloning would render men obsolete in the reproductive process (Hackett 1998). It severs the link between love, sex and reproduction (Kass 1998). The intimate connection required in sexual reproduction is seen by some as a key element in what it is to be human (Davis 1999; Rao 2002). However, one must weigh these factors against the desire to produce a child, which can be a profound one for some adults (Silver 2000).

Kass (1998) has argued that society’s natural repugnance of cloning reflects a sound intuition of the profound principles of things that people hold dear. Other have questions whether merely feelings of disgust per se are sufficient to justify outlawing an activity (Sunstein 2002). Feelings of repugnance which are not supported by moral arguments should not form the basis of law (Rao 2002; Tribe 1998). Others go so far as to suggest that repugnance is defined as an inexplicable loathing of which we should be highly suspicious. We should seek to overcome our repugnance, not exalt it to the status of a legal principle (Kunich 2002). In a way, this is system 1 thinking against system 2 thinking (see Sect. 3.3.3). For complex legal matters, we should aim to use system 2 thinking and should not use repugnance as a reason to legislate.

**Not Pro-child**
Some object to cloning on the basis of the harm to the child. Some of these reasons have already been mentioned: concerns that the child will feel or be regarded as being predestined to follow his or her clone’s shoes. Annas (1998) has been willing to go so far as to say that ‘cloning would, however, fit well in a list of things that should never be done to children, including female genital mutilation, forced labour, nonconsensual reproduction, and sterilisation. For children, it is a form of child abuse, asexual child abuse’, although it is unclear to us how the cloned child is ‘abused’ by virtue of his or her being cloned. If children are acquired and even to be designed, there are concerns that children will end up being treated like property (Garavaglia 2002). As Finnis (1998) puts it, children have the right not to be treated like a product.

It does not necessarily follow that a clone is predestined to follow the original’s shoes: we are partly determined by our genes, but also partly by our environment. Several defenders of cloning argue that such harms are purely speculation (Moffat 1998). Even if there is evidence of such harms, these need to be balanced against the benefit of coming into existence. Burley and Harris (1999) suggest that only if the harm could be said to blight the life of the child could a cloning ban be justified.

Against the viewpoint of treating children like a ‘product’ or property, one could argue that, before cloning is even possible, children have been treated like a product or property historically and still are in some societies (Lancy 2008). Lancy explains that, in some societies, the child contributes to the household: this is called the ‘chattel’ prototype. The ‘cherub’ prototype, where the child is valued for his or her sake, is seen in Western, educated, industrialised, rich and democratic (WEIRD) countries. We are not here to assess the different ways of treating children, but we would like to emphasise that cloning cannot be responsible for treating children like a ‘product’ or property; these viewpoints have been around for a long time.

**Involuntary Parenthood**

Some commentators are concerned that permitting cloning will too easily enable a person’s DNA to be used without their consent, thereby rendering a person a parent involuntarily. All that would be needed to create a child would be someone’s hair, saliva or other material (Orentlicher 1999). The obvious solution would be to outlaw cloning without the consent of all those whose genetic material is involved. The answer to this should be sensible legislation and effective enforcement against the misuse and abuse of DNA. Even without human cloning, DNA can be used for identity theft, so problems with DNA misuse are not peculiar to human cloning.

### 2.4.5 Arguments for Human Cloning

We now examine the reasons for allowing human cloning.

**Enable Couples to Have Children**

Quite simply, cloning enables people to have children who otherwise would not be able to, in particular those couples who are infertile due to gametic insufficiency, either because the woman does not produce effective ova or because the man lacks effective sperm. The benefit of cloning over forms of assisted reproduction is that the couple need not use a third party into their relationships (Orentlicher 1999). Also for those women who want to have a child but do not want to involve a man, cloning now enables them to have a child.

As a corollary, there has been much debate over whether or not there is a right to procreate. If such a right is recognised, then the state is only permitted to interfere in such a right by barring cloning if there is the strongest of justifications. Robertson (1994) is perhaps the leading proponent of such a view: the genetic link is seen as fundamental to what it is to be human. Critics of Robertson (1994) argue that the right to reproduce has been separated from the normal understanding of reproduction. A concern is that the right is interpreted in line with the parents’ wishes and designs (Kaveny 1999; Massie 1995).
Even if there is a right to reproduce, it does not necessarily follow that it is a right to insist on a genetic link with any child produced (Annas et al. 2002).

One argument is that cloning could ensure that there is no discrimination on the basis of sexual orientation, ‘Gay couples could become as fertile as heterosexual couples’ (Orentlicher 2000). Now that an increasing number of jurisdictions, including England, permit same-sex marriage (Marriage (Same Sex Couples) Act 2013) and support the principle of outlawing discrimination against people on the basis of sexual orientation (Equality Act 2010), there is a strong case for saying that the state should not seek to prevent same-sex couples from having the same access to treatments that enable them to have a child together. At least there need to be strong arguments to deny them access to those treatments.

**Rights of Scientist**

Some have seen the rights of the scientists as being a significant factor in the debate. Scientists have the right to carry out research that they wish unless there are convincing reasons to prevent them (Reiss 2000).

**Disease**

Reproductive cloning can be justified on the basis that it provides a means for continuing the human race if all men were rendered sterile by some catastrophic event (Annas et al. 2002). Therapeutic cloning also offers the possibility of cloned embryos providing self-compatible cells or tissues for medical uses, especially transplantation. However, pioneering work shows that somatic cells can be induced to become pluripotent stem cells (Takahashi et al. 2007; Yu et al. 2007), so there is much less need to create a whole embryo. Self-compatible cells can be generated by inducing one’s somatic cells to become pluripotent stem cells and dictating the differentiation of these stem cells.

**Assisted Reproduction Without Third Party**

Cloning offers some advantages over assisted reproduction in that no donation or third parties are involved. This may be preferred by most couples and may also cause the child less confusion over his or her genetic origins later in life (Orentlicher 2000).

**2.4.6 Conclusion**

We do not see any convincing argument why human cloning is an affront to human dignity. Certainly there is no a priori reason why it should be banned outright. Of much greater concern to us is that cloning carries a big risk of producing human beings who are less healthy. Children born of assisted reproduction have a higher incidence of health problems, ranging from paediatric cancers to obesity and cardiovascular disease in adult life (Chen and Heilbronn 2017). Assisted reproductive technology is already less intrusive than cloning, and if the former poses a health risk to the child, cloning would probably be of a greater health risk. Until and unless these obstacles can be obviated, human cloning will remain an extremely risky procedure. And yet to perfect human cloning technology, unethical experiments need to be performed, and thus we do not see how human cloning can be made safe.

One’s genetic identity is not the only identity of oneself. Kamm (2000) writes:

[I]image you are under a massive delusion about the way in which you were actually produced. Everything about you remains as you are now, except that you are not the product of sexual reproduction, but of mono-parental cloning. Would you think that your rights changed dramatically? I do not think you would. The question of the historical process of events that leads to the existence of a certain sort of being can, for the most part, be distinguished from the value of the entity that is produced and what gives it value. And that is one of the most important things to remember in this area.
She adds that no one is able to replace themselves. We feel that these ideas almost fully encapsulate ideas surrounding cloning and unique genetic identity. We are much more than our genes; we are what we can do.

### 2.5 Ectogenesis

Readers will be relieved to know that this section will not attempt to seek to resolve the fierce debates over abortion and the regulation of pregnancy. Rather it will set itself a narrower task. That is, to consider how ectogenesis or ‘artificial wombs’ will alter our understanding of fetal status, pregnancy and abortion. Some have claimed that ectogenesis will ‘end the abortion debate’. That would be optimistic. But as we shall see, it may impact on some of the arguments used and create some new issues around the regulation of pregnancy.

From Sect. 2.1, we know that to develop an artificial uterus, there are two ingredients. The artificial uterus must provide a protective environment for the fetus to develop; in natural pregnancies, this is provided physically by the uterus. In addition, the artificial uterus must also provide the placental function; it must allow the exchange of gases, nutrients and proteins to take place. Historically, the placental part of the artificial uterus was first developed. The environmental function of the artificial uterus was developed much later. There has been no attempt to merge these two functions in a single artificial uterus, so a large number of technical problems have to be overcome before an artificial uterus combining both the protective and placental functions is made available.

The idea of an artificial placenta was first suggested by Westin et al. (1958) over half a century ago. They developed a method to oxygenate fetal blood, and constructed a constant-temperature, constant-volume incubator to place the fetus in. The fetus was placed in a glucose solution and its umbilical blood vessels were connected to catheters. The deoxygenated blood of the fetus came out of the umbilical artery, was oxygenated by the perfusion equipment and then entered the fetus via the umbilical vein. Monitoring equipment for the electrocardiogram, blood pressure and blood flow were attached to this perfusion apparatus. Westin et al. (1958) performed experiments on seven pre-viable fetuses (i.e. fetuses who cannot survive outside the mother’s body) obtained from spontaneous and legally induced abortions, and were able to keep these fetuses alive for up to 11 hours; during this period, fetal limb movements were observed.

The perfusion apparatus of Westin et al. (1958) represented a revolutionary method to keep premature babies alive, but it possessed no metabolic function. A similar instrument, developed by Callaghan et al. (1962) around the same time, suffered from a similar drawback. Non-gaseous products of metabolism could not be removed from fetal blood in either machine. Independently, Lawn and McCance (1962) developed a similar perfusion apparatus, with a gas exchanger and a dialyser attached, so non-gaseous waste products could be removed using the dialyser. Blood gases were exchanged in an open system, and blood returned to the fetus by gravity. Lawn and McCance (1962) used pig fetuses for their experiments, and were able to keep them alive for 7 hours. The final death of the fetus resulted from engorgement and oedema.

These scientists then constructed an improved version where the blood circulated in a closed system and blood gases were exchanged through sintered nickel plates, and so the rate of circulation was controlled by the fetal heart (Lawn and McCance 1964). Engorgement and oedema were avoided, but since the volume of blood in the circulation was small, plasma had to be added periodically to maintain the circulation volume (Lawn and McCance 1967).

Subsequent developments of the artificial placenta followed the principles of Westin et al. (1958) and of Lawn and McCance (1967), but curiously, not all scientists coupled the gas exchanger to a dialyser. Alexander et al. (1968) were able to keep lamb fetuses alive for about a day on a gas exchanger. Zapol et al. (1969) used only a gas exchanger and infused heparin nutrients, but did not use a dialyser, and extended the survival of lamb fetuses to
two days. Kuwabara et al. (1989) linked the goat fetus to a gas exchanger and a dialyser, and managed to keep the fetus alive about ten days; this research group subsequently extended the survival time to three weeks using a system without a dialyser (Unno et al. 1993). Different methods of controlling fetal blood flow were also tried (Gray et al. 2012; Sakata et al. 1998; Unno et al. 1997).

Currently, the longest survival time for goat fetuses is about three weeks (Unno et al. 1993). For lamb fetuses, it is at least one week (Bryner et al. 2015). None of these methods used a dialyser, so they cannot really be viewed as true artificial placentae, but only extracorporeal gas exchangers. They are also all made up of inorganic material.

Some scientists have attempted to make a truly artificial uterus by tissue engineering. A number of research groups in the world have first built a scaffold and then seeded it with uterine cells at different stages; one of the models was able to support pregnancy in rats (see Campo et al. 2017 for a review). An alternative approach is to use three-dimensional printers to print the organ required (Vijayavenkataraman et al. 2018). Note, however, that a fabricated uterus is only suitable for implantation of embryos of a few days’ old, before the utero-placental circulation is established. Once the utero-placental circulation is established, it would be extremely difficult to tear the feto-placental unit away without excessive bleeding. There are at least two ways to create an artificial uterus for a fetus:

1. The feto-placental unit of the fetus is separated from the maternal circulation and linked to the circulation of the artificial uterus. It is difficult to devise a method to do this, as it will inevitably lead to massive maternal bleeding.

2. The fetus is separated from the placenta, and linked to the artificial uterus, which contains a placenta. The difficulty here is to ensure that the placenta is compatible with the fetus, and also to enable the artificial placenta to carry out all the functions of a natural placenta.

These are both technically challenging, and no easy solutions are forthcoming. Further research is needed to devise solutions to these problems.

### 2.5.1 Use of Ectogenesis

Supporters of ectogenesis (Singer and Wells 1984) have claimed a range of uses to which it could be put. First, it could assist couples who might not otherwise have children. It offers, in this sense, an alternative to surrogacy, avoiding some of the disadvantages that may be attached to it. Second, it offers women the opportunity of avoiding the dangers and inconveniences of pregnancy. As we shall see, some regard it to offer an important opportunity to equalise the position of men and women. Third, for women with moral objections to abortion, it might offer a route to end responsibility for a fetus without ending its life. Fourth, it might provide hope for fetuses that cannot for medical reasons survive in the human womb. Fifth, it might provide benefits in terms of general research into pregnancy-related issues and even in terms of producing organs that might be used for transplantation. Gosden (2000) argues:

Ectogenesis would provide a great opportunity to increase knowledge of what is one of nature’s last great secrets, and it would greatly benefit fetal medicine in general. There is perhaps no subject in biology that fills us with greater awe or of which we are more ignorant than the molding of a baby in the womb. Some people may prefer us to leave nature alone, as they did when antiserum and organ transplants first became available for treating ailing children and adults, but the chance to at last understand the most tender period of existence and, even more important, to cure diseases and help with the creation of life will surely prove irresistible.
The primary intended use of ectogenesis is a response to infertility. It might provide a way for women unable to carry a pregnancy to term, or prone to miscarriage, to have a child. It would also provide a way for a same-sex male couple or indeed a single man to have a child without relying on some of the difficulties involved in using surrogacy.

In the discussions that follow, we consider the legal and ethical issues that might arise in relation to ectogenesis. Currently, English law allows registered institutions to experiment with human embryos up to 14 days. After 14 days, current laws and regulations do not allow the embryo to be kept alive. If ectogenesis is to be made legal, exceptions would need to be made to that rule to allow human embryos to be maintained alive outside a person beyond 14 days. It would also raise a host of difficult legal and ethical issues. We will discuss these now, but we should emphasise that an important distinction can be drawn between cases where a ‘normal’ pregnancy has started but the fetus is transferred from the woman to the artificial womb, and cases where the embryo is created using assisted reproduction outside the woman and immediately placed into the artificial environment.

### 2.5.2 Impact of Ectogenesis: The Status of the Fetus

Ectogenesis is unlikely to have much effect on the debates around fetal status for most people, but it may well require important changes in the law. As is well known, there has been lively debate over what the correct moral status of the fetus is. We will not attempt to determine the correctness of these views, but rather focus on the impact of ectogenesis on the arguments. But before looking at these arguments, a brief overview of the biology of fetal development and an explanation of the concept of personhood are helpful.

Conception takes place when the spermatozoon fuses with the ovum. Fertilisation actually takes place some time later (up to 24 hours later). The conceptus then moves from the Fallopian tube into the uterus and attaches to the uterine lining. This is known as ‘implantation’ and takes place 6–12 days post-fertilisation (see Sect. 2.1.4). The next point of significance occurs about 14 days after conception and is the appearance of the ‘primitive streak’, which is the precursor to the nervous system. This is an important milestone; in human embryo experiments, embryos with a primitive streak or beyond 14 days of age have to be discarded. Another time of significance is viability. This is when the fetus is capable of living outside of the mother. This, with present technology, is 22–24 weeks (Wilkinson et al. 2018). Birth normally occurs about 38 weeks after conception.

In terms of ethical writing, most theories about fetal status depend on the assessment of the individual characteristics of the fetus: is it sentient, can it feel pain, is it capable of independent existence and such matters (Herring 2020)? These will be unlikely to be impacted by ectogenesis. Those who believe that fetal life begins at conception will argue that it makes no difference whether traditional pregnancy or ectogenesis is used. Similarly, those who claim that until a fetus/baby has consciousness and self-awareness it is not a person, will apply that view whatever method of child production is used. For most theories of moral status, if the fetus has morally relevant characteristics, then it begins to acquire moral status. These approaches depend on the individual assessment of the ability of the fetus and ectogenesis is unlikely to have any effect on the application of these. However, there are two reasons why it might impact on the fetal status debate.

The first is for those who hold a relational point of view and claim that the fetus acquires moral status through its relationship with mother (Herring 2020; Seymour 1990). Under this view, if the fetus has been entirely gestated in an artificial environment, then people other than the ‘mother’ could provide the caring relationship that would generate the moral status, such as the father or even the medical professional. However, it is not clear that anyone would necessarily have a relationship with the fetus. That might mean a difficulty for the relational view. It might be argued, however, that inevitably there must be someone providing the energy and nutrients an artificial womb provides and so there is some kind of caring relationship there.
The second is a more significant point; that is, for law, birth is defined as the time at which the fetus becomes a legal person and is entitled to human rights (Herring 2019a). This is picked by the law primarily for pragmatic reasons: it is a readily observable and provable event. While it might be argued that birth itself has moral significance for the moral status of the fetus (Burin 2014), many lawyers will accept that birth is a convenient ‘bright line’ (similar to gaining adulthood at the age of 18). For the law it will be necessary to find an alternative date at which legal personhood begins. One option may be to use an age, perhaps corresponding to the average length of a pregnancy, say 38 weeks. The difficulty is in calculating the date when the ‘fetus’ starts. Where assisted reproductive medicine is used and the fetus is implanted into the woman or placed directly into the ectogenesis machine, then that date can be used as the start point. It would be harder in the case of a natural pregnancy, as the date of conception is never known for certain. In such a case, it may be necessary to create some kind of legal presumption about the start of conception based on a medical assessment given the size of the fetus. The alternative would be to explicitly rely on the moment when the fetus acquires certain characteristics, such as independence from the machine. However, this could be problematic in the case of disabled children who may be dependent on mechanical support. We certainly would not want to be in a position where, say, a three-year-old child dependent on artificial support is not yet a person. It is likely, therefore, that the age approach will be seen as more certain and less discriminatory, and therefore preferable.

2.5.3 Impact of Ectogenesis: Regulation of Termination

Regulation would also be required to deal with a case where the parents wish to switch off an ‘artificial womb’ in a way which would ‘kill the fetus’. We will look at cases where there is a dispute between parents shortly, but here we will focus on cases where there is agreement. The current law on abortion requires the doctor to be satisfied that one of the grounds in the Abortion Act 1967 be made out and that the mother consents. There is no need to obtain the consent of the father, nor anyone else. One option would simply be to transplant this same model over to ectogenesis. However, it might be argued that this is inappropriate.

One major line of argument in favour of the legality of abortion is that to require a woman to continue with a pregnancy and undergo labour against her wishes is a major interference in her bodily integrity (Herring 2019b). There are no other circumstances in which a person would be required to undergo the bodily interference involved in pregnancy or birth, even if necessary to save the life of someone else. However, in the case of an ectogenesis machine, if a woman wants that switched off but her view is overridden, then this would not result in an interference in her bodily integrity. Similarly, although under the abortion debate, the woman’s right to bodily integrity readily trumps the rights of the father or any claim based on the status of the fetus, in the case of ectogenesis, these interests come back into play. We will discuss shortly cases where the parents disagree.

Where the parents agree the machine should be switched off, the status of the fetus becomes the primary issue here. The fetus is not a person under English law, but it is possible to argue that if the fetus has some moral status, especially once outside the mother, then switching off artificial gestation will be euthanasia or at least withdrawal of life support (Simonstein 2006). While generally withdrawal of life support can be lawful, that is only where the treatment is no longer providing a benefit to the patient, and unless there is reason to believe continued life will be painful to the fetus, it is hard to see how that will be so. If, however, the fetus is seen as not having the attributes necessarily to acquire moral status, then the parents are likely to be seen as having control over what happens, as we do, for example, for owners of pets.

2.5.4 Impact of Ectogenesis: Disputes over the Fetus
In traditional pregnancy it is impossible for the father to acquire the depth of relationship or degree of bodily interconnection that a mother has. Hence attempts by fathers to prevent abortions or require abortions have failed (e.g. Paton v. British Pregnancy Advisory Service [1979] QB 276). Whatever claims a father may seek to raise over the fetus, they are trumped by the woman’s rights of bodily integrity. However, this all changes in the case of ectogenesis, certainly once the fetus has been transferred into the ectogenesis machine. If there is a dispute over what happens to the fetus in the machine (e.g. whether it should be removed from the machine), then it is not clear whether the mother’s interests should trump the rights of the father.

Where the fetus was conceived in a laboratory and then placed directly into the machine, the genetic contribution of the mother and the father is almost equal (the 37 mitochondrial genes usually come from the mother Anderson et al. 1981). If a dispute arises, then two routes could be open to resolve that. In Evans v. UK ([2007] 43 EHRR 21), where a dispute arose over whether a frozen embryo should be destroyed, the English courts’ decisions, approved by the European Court of Human Rights, relied on the legislative scheme set out in the Human Fertilisation and Embryology Act 1990 and emphasised the importance of consent and agreement. The embryo could only be stored if both parties consented to that. In that case the father had withdrawn his consent and so it should be destroyed. Notably in that case, the dispute involved frozen embryos and they were held to have no legally relevant rights. It might be argued that the fetus in an ectogenesis machine, even if not having rights, would have some kind of legally protected interests. An alternative analysis would be to compare the right to be a parent (of the parent who wanted the fetus to remain in the machine) with the right not to be a parent (of the parent who wanted the fetus removed). It might be argued these rights cancel each other out. Alternatively, that, if they lose the argument, the harm to the life plans of the parent who wants to produce and raise the child is greater than the harm to the life plans of the parents who does not want to produce the child. That might lead to an argument that in these cases, the right to be a parent carries more weight than the right not to be a parent (although presumably in such a case there would need to be arrangements so that the parent who did not want the child to be produced would not be liable for child support payments).

An alternative approach would be to draw an analogy with disputes over a born child. Here the court will pay particular attention to the parent who has the closest relationship with the child and has undertaken the greatest commitment to the child. Where the fetus has been created in a laboratory and placed into the machine, the court would then focus on who has spent the most time with the fetus. One can imagine a case of ectogenesis where it is the genetic father who takes on the primary role of visiting the child and ensuring the artificial uterine environment is working appropriately and interacting with the child as it grows. Indeed the genetic mother may play no role at all. This approach would be open to acknowledging that a father (or indeed anyone) could, through their care of the fetus in the artificial womb, establish a sufficiently close caring relationship that it receives the protection of the law. Indeed one could imagine a case where a range of people might be able to provide sufficient levels of care to establish a caring relationship deserving of protection.

The issue may be harder where the fetus was conceived or implanted into the woman before being transferred into a machine. Here the woman may argue that the role she has played in nurturing the child in the early stages of life is more significant than subsequent care by anyone else. The difficulty is whether this claim will trump those of, say, a father, who is willing to take on the subsequent care of the fetus, in a role which will not require any bodily involvement of the woman. The resolution may depend a bit on whether the fetus is seen as having moral value in its own right. If it is, then arguably if there is a person willing to nurture the fetus going forward, that course should be pursued. If the fetus is of no interest and seen as simply a collection of biological material, then the mother’s labour in that product could be greater. Such an approach would be seeing the fetus as essentially property to which the mother has made the most significant contribution in terms of labour
(Ford 2005). However, to see the fetus as mere property does not capture how we see fetuses. Leaving aside any fetal rights, we would suggest that in weighing up a clash between a wish to be a parent and a wish not to be a parent, the wish to be a parent should be greater (Steiger 2010). That is because the idea of autonomy is about developing a vision for a good life. One could imagine that not being permitted to raise a child of yours would be a major interference in one’s autonomy/family life. That is why the courts use child protection orders only where absolutely necessary. However, there being a child in the world you do not want to be involved with is no going to stop you from doing anything you want. It is not going to crush any major goals, but not having a child would. In short, in the case of a dispute over whether the fetus should be removed from the machine, the presumption should be that it should remain in the machine.

2.5.5 Impact of Ectogenesis: Allocation of Parenthood

Currently section 27(1) of the Human Fertilisation and Embryology Act 1990 defines a mother in the following way:

The woman who is carrying or has carried a child as a result of the placing in her of an embryo or of sperm and eggs, and no other woman, is to be treated as the mother of the child.

This definition could still be used if the fetus has spent some time in a woman’s body before being transferred to the ‘artificial womb’. The mother would be the woman who, for a time, carried the child. However, first, that still does not deal with the case where the fetus is never carried by a woman. Second, it might be argued that if artificial wombs are to be used as an alternative to abortion for those with conscientious objections to abortion, then it will be more attractive if the woman is not said to be the mother, with the legal and moral responsibilities that flow from that status.

One way of dealing with these cases is to legislate that the person who is intended to be the child’s mother (or child’s parent) will be the parent of the child. This would be in line with the general policy of the Human Fertilisation and Embryology Act 1990, which in its assignment of parenthood seeks to avoid giving parenthood to those who are not intended to be the parents of the child (e.g. gamete donors, see Human Fertilisation and Embryology Act 2008, sections 33–48). It also seeks to ensure that those who are intended to be parents (e.g. the partners of the mother) are granted a parental status. To ensure clarity it would be appropriate to use the scheme used by the 1990 Act of forms being completed to record the intended parental status in relation to the child. One potentially attractive response to this is that if a gay couple were to produce a child and rely on ectogenesis and both be heavily involved in the gestation, then both be recognised as equal parents.

The one issue which might prove problematic with this regime are cases where no one is willing to be the parent of the child. This is most likely to arise where a woman is not willing to continue with the pregnancy but prefers ectogenesis to abortion. There seem to be two options here. One would be to treat the case as similar to any situation where a parent no longer wishes to be responsible for the child, for the court to permit adoption, fostering or special guardianship of the child in an artificial womb. This is likely to resolve most cases, although there would still be situations where this might not be possible. In such a case the child could simply become the responsibility of the local authority to provide the appropriate care, as occurs when a child is orphaned and there are no relatives available to care for the child.

We should also add in passing that there are serious costs issues involved if ectogenesis were to replace abortion. The number of fetuses could be considerable. There were 200,608 abortions in England and Wales in 2018 (Department of Health 2020). If ectogenesis was used in all those cases, there would be considerable cost involved in that provision and for the care of babies when they survived, assuming most of their parents would not want to undertake their care.
2.6 Newborn Screening

Newborn screening is the perinatal testing, typically performed on day 2 or day 5 of life, for genetically inherited diseases. A variety of testing methods are available, depending on the condition screened, but most typically initial testing is a simple biochemical test, which is subsequently followed up by a more definitive second titre test. The inaugural and still most effective example of a newborn screening programme was piloted in the mid-to-late 1960s for the inherited defect in amino acid catabolism, phenylketonuria (Guthrie 1992).

Here perinatal testing of phenylamine levels obtained from a heel prick blood spot allowed for the timely establishment of an exclusion/low phenylamine diet. The early institution of this diet results in the potential for normal intellectual outcomes in a disease where universal mental retardation, epilepsy and dependence on the state for life support had been the norm. The recognition of this as a potential paradigm for the management of other genetic diseases led to calls for national guidance on the selection of other genetic diseases. The resultant criteria (Wilson and Jungner 1968) still provide much of the underpinning of discourse today. In particular four key criteria have remained at the heart of decision making today. These are as follows:

1. An acceptable treatment protocol should be in place that changes the outcome for patients diagnosed early with the disease.
2. There should be an understanding of the condition’s natural history.
3. There should be an understanding about who will be treated as a patient.
4. There should be a screening test that is reliable for both affected and unaffected patients and is acceptable to the public.

While the above criteria have, to a lesser or greater extent, been adopted by many national newborn screening programmes, their interpretation is far from uniform. When these variances in interpretation are combined with local variances in disease incidence and financial and social considerations, it is perhaps unsurprising that adoption varies widely globally. Even within first-world nations the variance is extreme, with California currently hosting a mandated programme incorporating 80 inherited diseases while France screens for only 6.

While it might be argued that extending newborn screening empowers both families and society in general to better care for affected children, it must be remembered that all tests trade sensitivity (the proportion of actual positives that are correctly identified) against specificity (the proportion of actual negatives that are correctly identified). While an ideal test would be 100% sensitive and 100% specific, in reality the more sensitive a test is made, the less specific it becomes. Thus, a trade-off between the false positives (those identified as positive that are not affected) and the false negatives (those positive for the condition that are missed) ensues.

An example of all these difficulties is provided by experience in Pompe disease (glucosidase deficiency) (Bodamer et al. 2017). This disease has various phenotypes, traditionally being divided into (1) a classical neonatal onset form, where patients, unless treated, die from cardiorespiratory failure by one year of age, and (2) a more indolent form, where, in the majority of patients, muscle weakness may not manifest until late middle age. An ideal newborn screening test would be able to separate these differing phenotypes to enable appropriate advice and follow-up to be provided. The newborn screening technology so far adopted has been based on an assay of the glucosidase enzyme activity. However, not only is there an overlap enzymatically between the two phenotypes, but a common genetically derived pseudo-deficiency (a mutation which results in lower-than-expected enzymic levels but no disease) also exists. Second-tier testing is typically genetic, which,
while generally very informative in determining the potential pathogenicity and phenotype of the disease, is far from perfect given the number of novel variants that occur. Thus, Taiwan, the most extensive adopter of newborn screening for Pompe disease, showed 28 true positives (9 infantile cases and 19 adult cases) and 222 false positives in the first 473,738 cases (Chiang et al. 2012). This means that the true positive rate, i.e., the likelihood of having the disease when identified with the disease, was just 10%, i.e., one true case for every nine falsely identified. Furthermore, for two-third of the patients, lifelong medicalisation and regular monitoring has been instituted for a disease that may not manifest until late middle age. Thus, while for the nine infantile patients, identified screening has been life-saving, this has to be balanced against the emotional and financial cost for the wider society.

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Footnotes

3 Section 4A(3) of the Human Fertilisation and Embryology Act 1990.

4 Human Fertilisation and Embryology Act 1990, section 4A.


6 CP (A Child) v. First-Tier Tribunal (Criminal Injuries Compensation) [2014] EWCA Civ 1554.
3. Brain

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3.1 Introduction

Science has been trying to help us understand how we think and how we act. Scientific brain studies have always been difficult because it is not easy to perform experiments on human subjects ethically. Our understanding of how the brain functions historically comes from studies where the human subjects have been injured by accident or in war, or have been born with brain abnormalities. It is only recently that we have been able to investigate brain function non-invasively. Over the years, scientists and clinicians have been able to gradually piece together what different parts of the brain do.

It would be beyond the scope of this book to give a historical account of neurosciences and clinical neurology. The interested reader is invited to consult monographs on this topic such as Finger (1994). Briefly, the brain is anatomically divided into different parts; around the eighteenth century, scientists and clinicians began to realise that the nervous system was responsible for sensation, control of movements and thinking. The assignment of different parts of the brain to different functions started in the nineteenth century (see Figs. 3.1, 3.2 and 3.3). It started with rather gross divisions; for example, Broca identified the lateral part of the frontal lobe as responsible for the production of speech (Broca 1861a, b), but the division became finer under the light microscope. Anatomists divide the brain into white matter and grey matter: grey matter consists of bodies of nerve cells, and white matter consists of myelinated axons. An axon is the elongated part of the nerve cell that helps to transmit the signal, and myelin is a sheath around the axon to help accelerate nervous signal transmission. This division between nerve cell bodies and myelinated axons became more refined when Brodmann (1909) studied the cellular structure of the brain, and divided it into 50 areas for the human (Fig. 3.4). Over time, the subdivision became very fine-grained; for example, the lateral geniculate body receives input from both eyes, and Minkowski showed that layers 1, 4 and 6 of the lateral geniculate body receive input from the eye on the same side (the ipsilateral eye), and layers 2, 3 and 5 receive input from the eye on the other side (the contralateral eye) (Minkowski 1912). Closer to our time, a review describes the use of single-neuron recordings and how they can be used scientifically and clinically (Engel et al. 2005).
**Fig. 3.1** Diagram showing the brain from the left side. The numbers after some areas denote their Brodmann area number. Taken from Strominger et al. (2012)

**Fig. 3.2** Diagram showing the sagittal section of the brain. Taken from Strominger et al. (2012)
Fig. 3.3 Diagram showing the gross divisions of the cerebral cortices of the brain into lobes. The division between the frontal lobe and the parietal lobe is the central sulcus of Rolando, and the lateral sulcus is the division between the temporal lobe and the frontal and parietal lobes. Taken from Graziano (2001)
Observations from patients with brain injury, and treatments for patients with brain problems, have led to a greater understanding of brain function. For example, our knowledge of sleep-wakefulness pathways began with the work of von Economo, who observed the sleep-wakefulness states of brain-damaged patients of encephalitis lethargica during World War I (von Economo 1917). He noted that lesions of the posterior hypothalamus and rostral midbrain led to a state of prolonged sleepiness, whilst lesions of the pre-optic area and basal forebrain led to prolonged insomnia. He therefore suggested that the region of the hypothalamus near the optic chiasma contained sleep-promoting neurons, but posterior hypothalamus contained neurons which promote the wakeful state (von Economo 1929).

Over the years, his theory has been shown to stand up reasonably well to scrutiny. The last few decades have seen the discovery of the neuronal circuitry which is responsible for sleep-wakefulness (Rosenwasser 2009; Saper et al. 2001). Put simply, there are two main pathways in determining the sleep-wakefulness state (Fig. 3.5). The ascending arousal

Fig. 3.4 Diagram showing the cerebral cortex areas as originally defined by Brodmann (1909)
pathway includes the pedunculo-pontine and latero-dorsal tegmental nuclei, which send projections to the thalamus, which are relayed and sent to the cerebral cortices; this pathway also includes ascending projections from the locus coeruleus, the raphé and the tuberomammillary nucleus. The descending sleep pathway includes projections from the ventro-lateral pre-optic nucleus and the lateral hypothalamic orexinergic neurons (neurons secreting orexin) to the tuberomammillary nucleus, the raphé, the locus coeruleus and the pedunculo-pontine and latero-dorsal tegmental nuclei; in addition, lateral hypothalamic neurons which release orexin also innervate the cerebral cortices and the basal forebrain.

Another pioneer in human brain research is Wilder Penfield. Penfield was a Montreal surgeon who treated epilepsy patients by ablating the epileptic foci. In order to identify those epileptic foci, he would anaesthetise the patient under regional anaesthesia, open up their skulls and stimulate different parts of the cerebral cortex using electrodes to identify the area responsible for starting epilepsy (brain tissue is devoid of sensory nerve endings, so the patient would not feel any discomfort nor pain for the duration of this process). During these procedures, Penfield would ask the conscious patients what they sensed, and observe their motor responses. Penfield and Rasmussen (1950) and Penfield and Jasper (1954) detail
many of these surgical cases. For example, in the patient M.Dr., stimulation of an area anterior to the central gyrus in the more caudal region caused the patient to note that there was a shiver in the left arm (ibid., p.84). In patient P.Ge., electrical stimulation of Heschl’s gyrus 2–3 cm below the surface caused the patient to report that he heard a ‘boom, boom, boom’ sound like ‘two motors running’ (ibid., p.115). In another patient, K.H., stimulation of an area near the fissure of Rolando caused the patient to repeatedly say, ‘da, da, da’ (ibid., p.97).

Prior to Penfield’s research, previous work had identified a ‘map’ of the cortical area responsible for movement and sensation, respectively called the motor cortex and the sensory cortex (Fig. 3.6). Penfield was able to draw a more detailed map of the sensory and motor cortices and their connections to different parts of the body (Fig. 3.7). This ‘map’, called a homunculus, is still used in clinical medicine.

**Fig. 3.6** Diagram showing the sensory and motor cortices. The upper panel shows the left cerebral hemisphere and the lower panel shows the right cerebral hemisphere. On the sensory and motor cortices, letters denote the represented body part: H = head, UE = upper extremities, T = trunk and LE = lower extremities. The numbers in brackets denote the Brodmann area number. Taken from Strominger et al. (2012)
Fig. 3.7 Diagram showing the somatosensory homunculus (left) and the motor homunculus (right). Taken from Malinowski (2019)

Penfield’s work was not limited to simple sensory and motor functions; he also discovered which parts of the brain were responsible for language. For example, in the patient C.H., stimulation of an area on the left Rolandic cortex caused him to forget words. When shown a tree, he would not be able to name it, but he said, ‘I know what it is.’ On withdrawal of electrical stimulation, he said ‘Tree’ immediately (ibid., p.112).

These ‘invasive’ investigations were gradually replaced by non-invasive investigations with the advent of investigative techniques such as the positron emission tomography (PET) scan, the functional nuclear magnetic resonance (NMR) scan and electroencephalography. These methods differ in their mode of action.

3.2 Looking Inside the Brain
3.2.1 Electroencephalography
Electroencephalography (EEG) was invented by Hans Berger in 1924, but he did not publish his findings till 1929 (Berger 1929). His original recordings were done by opening the skull and putting the electrodes on the dura of the brain, and recording the changes in electrical potential. Later he discovered that he could do it with pad electrodes on the scalp, in a completely non-invasive manner. Adrian and Matthews subsequently defined the electrophysiology of these recordings (Adrian and Matthews 1934), and put this method on a firm scientific basis.

In EEG, the electrical activity measured was an average of all the surface electrical activity of the brain. The spatial resolution was gradually improved by using more electrodes. However, the electrical activity measured is still limited to the cortical surface; it is impossible to measure electrical activity deeper inside. The spatial resolution of the EEG is 2.5 cm for a 64-electrode configuration, and 1.4 cm for a 128-electrode configuration (Vatta et al. 2002); it can be further improved by using more electrodes, and 256 electrodes have been used in some studies (e.g. see Chang et al. 2014, and Pisarenco et al. 2014). Other developments for EEG include localising the electrical activity in the brain using low-resolution electromagnetic tomography (Pascual-Marqui et al. 1994), or increasing the resolution in the frequency domain by variable-resolution electromagnetic
tomography (Bosch-Bayard et al. 2001). The greatest strength of EEG is its fast temporal response, of the order of milliseconds (Gevins et al. 1995).

3.2.2 X-Ray Computed Tomography (CT Scan)

Plain X-radiography can only give an outline of the skull, and cannot see into the brain. Moreover, it only gives a two-dimensional picture of the head without any depth appreciation. Tomography consists of making detailed pictures of a plane with a revolving camera and then making repeated pictures to build up a three-dimensional representation of the brain. The mathematics behind this was developed by Cormack (1963, 1964). Hounsfield (1973) subsequently built a computerised X-ray machine to realise those ideas, and the first X-ray computed tomography was performed in 1971 on a patient with a brain cyst in the frontal lobe. The X-ray computed tomography scan, or CT scan as it has come to be known in the clinical community, has found great use in diagnosing brain injuries (Maas et al. 2005) and cerebrovascular accidents ('strokes') (Cala 2016), but is not often used to study brain function on its own. However, it is often combined with other methods, especially positron emission tomography, for the latter purposes. The mathematical methods developed in re-creating a three-dimensional object from two-dimensional brain slices have also found wide use in body scanning techniques.

3.2.3 Positron Emission Tomography

Positron emission is a process by which radioactive isotopes give out positrons. The positron is anti-matter (Anderson 1933; Dirac 1928, 1931), so it travels for a very short distance of about 1 mm before it is annihilated when it meets an electron (Dirac 1930); two photons, very occasionally three (Ore and Powell 1949), are then emitted. By registering these photons, scientists and clinicians can hope to localise the position of the radioactive isotopes inside the body.

[^{64}\text{Cu}]tetrasulphonated copper phthalocyanine emits positrons, and these positrons meet electrons to give out \(\gamma\)-radiation. The first clinical study using positron emission was to localise brain tumours using \[^{64}\text{Cu}]tetrasulphonated copper phthalocyanine with a simple \(\gamma\)-ray photon detector (Wrenn et al. 1951). With the development of tomography by Hounsfield (1973) and Cormack (1963, 1964), the positron emission tomography (PET) scan was developed in the mid-1970s (Kuhl et al. 1976; Ter-Pogossian et al. 1975). PET scans use radioactive material to localise the emission of positrons, but combine it with tomography to compute a three-dimensional picture of where the positrons are with respect to the body.

Regions of high neuronal activity have higher metabolism. Since the brain metabolises almost exclusively glucose as its energy source (Erbslöh et al. 1958), the utilisation of glucose can be used as an indicator of brain activity. This has been demonstrated in animals using non-metabolisable analogues of glucose which emit positrons, and observing their accumulation in active cells (Kadekarlo et al. 1985; Kennedy et al. 1976).

Regions of high neuronal activity also have higher blood flow. This was first suggested by Angelo Mosso (Mosso 1881), who observed patients with defects in their skull. He noticed that the outer covering of the brain pulsed, and he developed an instrument to measure the speed and magnitude of pulsation. Then he asked the patient to perform mentally taxing tasks or do nothing, and showed that mental effort increased the speed and magnitude of pulsation (ibid., p.42 figure 1). This correlation between mental effort and brain blood flow was experimentally confirmed (Roy and Sherrington 1890). So in PET scans, either the amount of blood (usually indicated by radioactive water H\(_2\)\[^{15}\text{O}\]) or the amount of non-metabolisable glucose analogues is used as an indicator of local neuronal activity. The first PET scan which assessed brain activity using local glucose usage was performed in 1983 (Dichiro et al. 1983), followed by the first PET scan of the brain that shows which parts were more active, and used the flow of H\(_2\)\[^{15}\text{O}\] as a marker for blood flow (Fox and Raichle 1984). By using different tracers, scientists have used PET scans to study brain ageing and
neurodegenerative diseases, sometimes even tracing the neural pathways involved (Eisenmenger et al. 2016).

3.2.4 Nuclear Magnetic Resonance Scans

Nuclear magnetic resonance (NMR) was first developed by Bloch (1946) and Purcell et al. (1946); they developed this method to detect nuclear spins in bulk matter (‘spin’ in subatomic particles does not mean that the particles rotate; it is a property of these subatomic particles described by quantum physics (Uhlenbeck and Goudsmit 1926)). This method turned out to be of great importance to chemistry, because atomic nuclei change spin with high sensitivity to local electromagnetic fields, and thus they can be used to report on the environment around these nuclei. Subsequently, scientist began applying NMR to living matter, and found that NMR signals from these experiments come largely from the hydrogen nuclei in water and these signals depend on the local environment of these nuclei; healthy and diseased tissues would give out different NMR signals.

In 1973, Lauterbur showed that these NMR signals could be used to form images (Lauterbur 1973). Although this method was valuable, it took minutes to take a small image using NMR. This process was greatly accelerated by the work of Mansfield (Chapman and Mansfield 1986; Mansfield 1977; Mansfield and Chapman 1986) which improved the equipment. It was further improved by the development of a novel image encoding method (Kumar et al. 1975). These developments enabled scientists and clinicians to see human tissue based on the NMR signal, but the images could not inform on the functioning of the tissues and cells. Ogawa and his colleagues showed that deoxyhaemoglobin could be used as a contrast agent, i.e., an agent which shows up different tissues. Using a special NMR technique called gradient-echo NMR, they measured the blood oxygen levels in even small blood vessels using NMR imaging (Ogawa et al. 1990), and obtained clinically useful images.

The brain scans all serve to highlight areas of the brain with high blood flow; the inference is that these brain areas are undergoing high metabolism, and are thus more active. Brain scans tend to have very high spatial resolution, of the order of millimetres. EEG detects electrical activity of the brain cells directly, but since the electrical activity of all the brain cells is summed up, it provides a low spatial resolution of brain activity, even when multiple electrodes are used. However, EEG has a much higher temporal resolution than either the PET or the NMR scan. PET scans measuring glucose metabolism represent a summation of 30–60 min of cerebral glucose metabolism fluctuation (Scheinin et al. 2018). So different methods are used for obtaining different information, and are sometimes combined to gain a fuller picture of brain function (Iannetti et al. 2005). Smith (2012) has also detailed how NMR scanning should develop in the future.

3.2.5 Optogenetics

Optogenetics is strictly speaking not a passive imaging method, but an active intervention. It allows scientists to determine if specific nerve cells are necessary and sufficient for the behaviour under study. This method was developed by Zemelman et al. (2002). These scientists inserted Drosophila (the fruit fly) photoreceptors into vertebrate cells using genetic engineering. By shining a light on mixed cells, some with this photoreceptor and others without, they elicited activity only in neurons with photoreceptors. A few years later, Lima and Miesenböck (2005) inserted photoreceptor proteins to the giant fibre system cells of Drosophila, and by photostimulation of these cells, they elicited escape behaviour characteristic of the fruit fly.

By engineering photoreceptors to specific cells in the nervous system, and by activating them using light, scientists were able to deduce the role of different components of the nervous system of animals such as the zebrafish and the mouse (Fiala et al. 2010). Different control systems are also possible: scientists can now engineer a feedback loop whereby the optogenetic stimulation is dependent on simultaneous observation of a certain behaviour (Groenink et al. 2015). The use of this method is still limited to experimental animals (Allen
et al. 2015), but it is not inconceivable that it will find uses in humans in the future. A recent review explains its use in neuroscience research (Kim et al. 2017).

Optogenetics also allows us to influence one’s behaviour by activating specific neurons in the brain. Experimentally, it has been used to alter the feeding behaviour in rats (Calu et al. 2013), or the addiction for cocaine also in rats (Larson et al. 2015). It has been used to manage psychiatric illness by changing the behaviour of animal models with conditions such as depression, anxiety, addiction (Touriño et al. 2013) and even schizophrenia (McDevitt et al. 2014). In the future, it can conceivably be used to manage these conditions in humans, and also the symptoms of human neurological diseases such as epilepsy (Bentley et al. 2013; Krook-Magnuson et al. 2013) and Parkinson’s disease (Kravitz et al. 2010; Yoon et al. 2014).

This technique brings with it potentials and problems. Its use is not limited to the treatment of diseases involving the brain, but also other parts of the body; for example, it can be used to control abnormal heart activity (Bingen et al. 2014). However, it can greatly interfere with an individual’s brain function. Currently, this method is highly invasive so cannot justifiably be used on humans.

In the future, if this method becomes less invasive, then it would be possible to apply it to humans; e.g., we can use it on the brains of criminals to turn off their criminal tendencies. Whilst this might have benefits for society, it has enormous repercussions for human rights and personal freedom. To what extent can the law act to prevent a crime that is only a possibility? It can conceivably be used by criminals to control innocent people to commit crime. This would have important repercussions on criminal law, as the defence of automatism could be invoked. The law then will have to test if such people under the control of the criminal are conscious of what they are doing.

3.2.6 Transcranial Magnetic and Electrical Stimulation

These are two distinct methods, transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (tES). Like optogenetics, they are more interventional than PET or NMR scans. In tES, the electrical current used can be a direct current, an alternating current or a varying current. Direct current stimulation is most commonly used: two electrodes are put on the brain and linked to an electrical wire, and this causes electrical currents to flow from the anode to the cathode. By taking the wire off the surface of the skull and shaping it into a coil, a magnetic field can be generated locally which would penetrate into the brain; this magnetic field will in turn induce an electrical current in the brain. The net effect is that both methods are similar in that they induce electrical currents in the brain. Both these methods examine the reaction of brain cells to changing magnetic or electrical stimulation.

TMS was first developed to activate muscles directly rather than through nerves (Merton and Morton 1980). The scientists found that, by passing an electric shock over the motor cortex, they were able to elicit synchronous muscle contractions and observed a motor-evoked potential in the primary motor cortex. Unfortunately, the process was rather painful. Barker et al. (1985) improved on this work, and produced a painless stimulator for the human brain. A coil is applied to the surface of the scalp, and this generates a brief but strong magnetic pulse to the brain. The magnetic field induces current flow in the tissue, and this affects the underlying neurons and causes a change in electrical potential, the motor-evoked potential (MEP). TMS has been applied in many human neurophysiological studies. For example, the reading span test (Daneman and Carpenter 1980) involves asking the test subject to read two sentences and to remember the last word of each sentence. This is then repeated with more sentences until the subject fails the recall three times. This test measures the ability of the subject to perform a dual task. TMS over the dorsolateral prefrontal cortex, which contributes to working memory, reduces the mean accuracy of subjects performing this test (Osaka et al. 2007).

TMS has also found clinical uses. Trompetto et al. (2000) examined 21 patients with acute stroke on one side, and they found that the TMS response correlated with subsequent...
recovery: patients with MEPs in response to TMS made better recoveries than patients who did not. These findings were subsequently confirmed by Delvaux et al. (2003), who followed 31 stroke patients for a year. TMS has also been used in the diagnosis of disorders of consciousness (Lapitskaya et al. 2009), and combined with EEG to assess consciousness levels (Grosseries et al. 2014). Most interesting is the use of TMS to disrupt the right temporoparietal junction, a region of the brain thought to be involved in moral judgements. The authors found that TMS disruption interferes with the moral judgements of the subjects (Young et al. 2010). A recent review discusses the scientific and clinical uses of the TMS method (Valero-Cabre et al. 2017).

The commonest type of tES used applies direct current and is called transcranial direct current stimulation (tDCS). It is mainly used to facilitate or disrupt brain function locally and to study the communication between local and distant sites across the brain. For example, when the dorsolateral prefrontal cortex is stimulated with low-frequency electrical currents (0.75 Hz), memory retention is enhanced, whether this process is carried out in sleep (Marshall et al. 2004) or during wakefulness (Kirov et al. 2009). This method complements other methods in showing the importance of the prefrontal cortex in learning; tDCS provides us with an avenue to intervene in the process. A recent review article has summarised research performed using tES (Yavari et al. 2018).

### 3.3 How Does the Brain Function?

We can view the functions of the brain from an evolutionary point of view. The ‘oldest’ part of our brain is the brain stem or hindbrain, which is situated at the base of the brain, and joins the spinal cord on the caudal side. The ‘newer’ part of the brain is the neo-mammalian brain, or the diencephalon, which consists of a collection of structures between the cortices and the brain stem. The ‘newest’ part of the brain is the neocortex, which consists mainly of the cerebral cortices (Fig. 3.8).
The motor and sensory connections from the rest of the brain to the spinal cord pass through the brain stem, so it is an important conduit of communication. In addition, the brain stem also contributes to the control of essential functions such as breathing, heart rate and the sleep-wakefulness cycle. The cerebellum, also part of the brain stem, contributes to the fine coordination and timing of movements.

The diencephalon consists of the thalamus, the hypothalamus and a number of structures around it. It is important in the determination of various instinctive functions such as emotion, memory, spatial coding, hunger and thirst. The thalamus is an important centre of connections, for it coordinates the signalling between different parts of the brain.

The neocortex covers most of the brain, and is generally divided into four lobes on each hemisphere (Fig. 3.3). They process sensory function, initiate motor movements, and provide a higher layer of control over the limbic system. The limbic system consists of a number of structures in the neocortex, the thalamus and the hypothalamus, and is responsible for memory, learning, emotions, hunger, thirst and neuroendocrine functions (see Fig. 3.9). The neocortex also allow us to process language, recognise faces and voices, and carry out long-term planning. The frontal lobes are responsible for processing some of our emotions.

Next we discuss some important aspects of brain function.

### 3.3.1 Consciousness

Consciousness consists of three components: a state of wakefulness, attention or awareness, and conscious access, the last meaning some of the attended information enters our awareness (Dehaene 2014). In most people, these components work together seamlessly to give us an understanding of the external world. However, in some people, trauma or disease injures part of the brain and disorders of consciousness arise.

In trying to understand these disorders of consciousness, it is useful to examine two independent aspects of the problem: is the subject awake, and is the subject aware (Laureys 2005)? A normal person who is awake is awake and aware. A person in a coma, or sleeping without dreams, is neither awake nor aware, but a person dreaming is not awake but aware. Conversely, patients undergoing some kinds of epilepsy called absence seizures are awake but have little awareness. Figure 3.10 illustrates these different states.
Patients in a coma are those who are neither awake nor aware. Patients in the vegetative state or the unresponsive wakefulness state have a sleep-wakefulness cycle, but are not aware. They open their eyes when they are awake, but their motor responses are only reflexive; as far as we can tell, they are not aware. Patients who are in a vegetative state for a prolonged period of time are in a persistent vegetative state (PVS). The minimally conscious state encompasses a broad range of conditions, but they all share the feature that the subjects are awake and show some degree of purposeful behaviour. The locked-in state is not a disorder of consciousness, but a pure motor disorder where the patient has lost all motor control except for a few muscles, but the patient is awake and aware.

One of the greatest difficulties facing clinicians is to determine the status of patients with disorders of consciousness: are the patients awake and/or aware? The first set of clinical diagnostic criteria used to determine the state of consciousness of patients is the Glasgow Coma Scale (Teasdale and Jennett 1974). In this scale, the clinician assesses the patient’s eye opening, best verbal response and best motor response. Each aspect is assigned a mark. Subsequently, a large number of such assessment scales have been devised to determine a patient’s consciousness at the bedside; a recent review has made a critical review of such methods (American Congress of Rehabilitation Medicine, Brain Injury-Interdisciplinary Special Interest Group, Disorders of Consciousness Task Force 2010). Their recommendation is that the best assessment scale is the Coma Recovery Scale-Revised (Giacino et al. 2004), which can be used with minor reservations.

Nevertheless, all these assessment scales based on clinical observations have inherent drawbacks, and their accuracy rate is of the order of 60% (Andrews et al. 1996; Childs et al. 1993; Schnakers et al. 2009). If a patient is unresponsive, is it because the patient is asleep or the patient is in a coma? If the patient is awake, but does not show purposeful behaviour, is it because the patient is in a vegetative state, or does not understand the clinician’s requests (aphasia, or loss of the ability to process language, subsequent to brain damage), or if the patient understands the requests, are there motor deficits which prevent the patient from carrying out those requests? It is becoming clear that diagnosis of these disorders of consciousness cannot depend on behavioural tests alone.

Brain scans and electrophysiological techniques are emerging in importance in determining the consciousness state of a subject. There are distinct differences between patients in coma, the vegetative state, the minimally conscious state and the normal state. For example, PET studies show that, PVS patients exhibit a much lower level of cerebral glucose metabolism, with a reduction of over 50% in most areas (Beuthien-Baumann et al. 2003). In response to noxious or auditory stimuli, in patients in the vegetative state, only the relevant sensory cortices show increased metabolism. Patients in

![Diagram showing different levels of awareness and wakefulness in different states. Adapted from Laureys (2005)](image)
the minimally conscious state preserved activation of higher-order areas of activation such as the frontoparietal cortices; this is similar to healthy controls (Boly et al. 2005).

NMR studies were performed by asking the patient to modify his/her brain activity, and to observe if activity in different parts of the brain is observed. In a pioneering study, Owen et al. (2006) asked a 23-year-old subject in the vegetative state to imagine herself playing tennis, or to imagine herself visiting all the rooms in her house, depending on whether she would like to answer ‘yes’ or ‘no’. In normal alert subjects, imagining playing tennis would activate the supplementary motor area, whilst imagining navigating the house would activate the parahippocampal gyrus (PPA) (Fig. 3.11). When asked questions with known answers (‘Is your name XXX?’ ‘Do you come from YYY?’), the subject was observed to imagine the scenario that gives the appropriate response on the NMR. Though this patient fulfilled the diagnostic criteria for the vegetative state, she retained enough consciousness to carry out requested tasks and display clear acts of intention. Thus the clinicians were able to carry out a ‘conversation’ with the subject through the NMR scans, although the subject could only answer ‘yes’ or ‘no’.

![Fig. 3.11](image)

Activity in the supplementary motor area (SMA) was observed when the patient and control subjects were asked to imagine themselves playing tennis. When the patient and the control subjects were asked to imagine navigating around a house, activity was observed in the parahippocampal gyrus (PPA), the posterior parietal lobe (PPC) and the lateral premotor cortex (PMC). The X-values at the bottom refer to the distance in millimetres from the midline in stereotaxic space. Taken from Owen et al. (2006) by kind permission of the American Association for the Advancement of Science

In a later study of 54 patients, scientists asked the patients to perform these two imaginary tasks inside the NMR scanner (Monti et al. 2010). In this study, only five patients were able to modulate their brain activity. Whilst this study shows the potential of using NMR scans for diagnosing a patient’s state of consciousness, it also shows the weaknesses: non-responsive patients might not be awake at the time of the experiment; they might have other brain injuries leading to aphasia or difficulty in hearing.

Scientists look for more passive NMR scanning methods to assess a patient’s state of consciousness, methods where active participation of the patient is not required. For example, it has been shown that normal humans exhibit ten resting state networks of cognitive relevance. In vegetative state and minimally conscious state subjects, there are fewer neurons in each network (Demertzi et al. 2014). The degree of connectivity between different regions of the brain is reduced in the vegetative state and the minimally conscious state.
state, compared to healthy subjects (Di Perri et al. 2014; Kotchoubey et al. 2013; Tsai et al. 2014). Electroencephalography has also been used to detect differences in the brain activity of patients suffering from different disorders of consciousness (Schiff et al. 2014; Sitt et al. 2014). This method was combined with transcranial magnetic stimulation, where EEG was used to assess the brain response to stimulation and allowed the researchers to determine the consciousness state of the subjects (Grosserries et al. 2014). There have also been attempts to treat patients in the vegetative state using deep brain stimulation (Yamamoto et al. 2010) with varying degrees of success. More recently, Naci et al. (2014) showed subjects a film directed by Alfred Hitchcock, and examined the NMR scans of their brain. They were able to develop a neural index that reliably predicted healthy individuals’ similar conscious experience in response to real-life events over time. They applied this method to a brain-injured patient who appeared to be in a persistent vegetative state, but the brain scan results showed that this patient most probably had conscious experience without any behaviour.

From all these studies, we can conclude that consciousness depends on parts of the brain, notably the cortical areas, functioning normally. This, in turn, depends on parts of the hypothalamus, the pons and the brain stem providing the necessary stimulation to the cortical areas. To some extent, we can determine the functioning of these parts of the brain using different kinds of scans. These results show us that a clinical examination is often inadequate to decide if a patient is suffering from disorders of consciousness, and if so, what kind. In the future, brain scans should be performed if there is any doubt.

These studies raise an important question: if we discover that a patient thought to be in a vegetative state is actually cognisant of his/her surroundings, and can interact with others through these technologies, what do we do with his/her wishes? Are they considered to be mentally competent to dispose of their property, spend money and make or alter their wills? How are we to assess their mental competence? If such patients ask the clinicians to end their lives, what should the doctors do? Can one reliably determine a patient’s consciousness status from question-and-answer sessions via NMR scans, where the patient can answer only ‘yes’ or ‘no’?

These data also raise the question of the ‘best interest’ argument. For a long time, the treatment of these patients has been based on what is in their best interests, without really asking them what they themselves would like. This could conceivably change in the future, with the new methods and findings. For example, we would suggest that clinicians locate a third task which would activate a third area of the brain, so that the subject could use that task to answer, ‘I do not know.’

The legal implications of these discoveries are wide ranging. We could now ‘talk’ to a group of patients who could not express themselves before. We could even ask them if they would like to change their wills. We would first have to establish a set of criteria that the subjects are of ‘sound mind’ using appropriate NMR scans, and then perform a series of NMR brain scans in response to different questions to ascertain their wishes. It is a legal challenge to make this fair and just so that the wishes of these people are respected, and that this method is not abused. The Mental Capacity Act 2005, section 3(1) sets out the test for capacity:

a person is unable to make a decision for himself if he is unable–

(a) to understand the information relevant to the decision,
(b) to retain that information,
(c) to use or weigh that information as part of the process of making the decision, or
(d) to communicate his decision (whether by talking, using sign language or any other means).
So a person in a persistent vegetative state who was able to weigh up the information and make a decision would lack mental capacity if they were unable to communicate their decision. Therefore, decisions would be made by others based on what is in the patient’s best interests. The potential for communication with those with PVS is therefore significant. It would enable patients with PVS to make decisions about their lives.

### 3.3.2 Memory and Learning

As is the case with most neurological discoveries, the brain structures responsible for memory were discovered by accident, in patients with chronic alcoholism. This was first described in Korsakoff (1887). In this paper, he described chronic alcoholic patients who suffered from retrograde amnesia (failure to remember events before the onset of amnesia). Subsequently, Gudden (1896) reported that the mammillary bodies of the brain atrophied in these cases.

Over the years, studies on such patients and on patients who had undergone neurosurgery to treat intractable epilepsy have revealed how memory works. We now understand that memory is divided into short-term memory, where information is held for a few seconds, and long-term memory, where information is consolidated and stored permanently. Memory can also be divided into another three types: episodic memory (the experience related to life events of the individual), semantic memory (knowledge of facts, language and concepts) and implicit memory (procedural learning and classical conditioning) (Kopelman 2002). Neuroimaging has identified key areas of the brain involved in memory (Aggleton 2014; Moscovitch et al. 2006), and they include the hippocampus and parahippocampus, the prefrontal cortex, the basal forebrain, the anterior thalamic nuclei and the cingulate cortex. This is very much an ongoing area of research, with new discoveries and theories reported often.

Memorising information will cause changes in the related brain areas. For example, budding London taxi drivers have to memorise all the roads and major landmarks of London. They then have to pass a test called ‘The Knowledge’ before they can become qualified drivers. NMR scans show that they have a posterior hippocampus larger than the population average (Maguire et al. 1997). The volume of the posterior hippocampus correlated positively with the amount of time spent as a taxi driver, the correlation coefficient being \( r = 0.6 \) (Maguire et al. 2000). This is evidence that the human brain structure is quite plastic even at the adult stage. Indeed, scientists have shown that new nerve cells are still being produced in the hippocampus well into the eighth decade of human life (Boldrini et al. 2018).

Learning is closely related to memory, but it requires more than just memory because it implies application of what is in the memory. Often it involves enlargement of some of the memory centres, and enlargement of the sensory and motor cortices involved, as well as changes in connectivity between different parts of the brain. For example, it has been shown by NMR scans that musicians have a different auditory cortex architecture (Aydin et al. 2005), and that they have a superior temporal cortex and a dorsolateral frontal cortex thicker than the population average (Bermudez et al. 2009). Studies have also been performed on illiterate subjects of around 30 years of age; after six months of literacy training, the brains of these subjects show altered connectivity (Skeide et al. 2017). This is further evidence of the plasticity of the brain even at the adult stage.

Scientists have discovered that they could manipulate the brain to promote learning. For example, Deadwyler and his co-workers took four monkeys, and recorded the activity of the neurons from regions CA1 and CA3 of the hippocampus when the monkeys were performing certain tasks. They delivered this electrical activity to the same CA1 recording locations, and found that this stimulation improved the task performance (Hampson et al. 2013). In another study, scientists paired the activity of a given place cell (these cells inform the mice its position in space, hence the name) with rewarding stimulations of cells from the medial forebrain bundle (de Lavilléon et al. 2014). They showed that this pairing caused the mice to explore the given position denoted by the place cell more often; thus, associative learning
was promoted by the stimulation. More recently, Hampson et al. (2018) recruited 22 epileptic patients who underwent electrode implantation for observation of epileptic foci. These scientists used the same electrodes for observing activity in the CA1 and CA3 regions of the hippocampus, and delivered an appropriate stimulation pattern to the CA1 region. They were able to enhance memory in these patients by over 30%.

Currently, such experiments to manipulate the brain are invasive, as they require holes to be drilled in the cranium, so that electrodes can penetrate directly into the brain. Also, the implantation of memory is restricted to learning, not episodic or semantic memory. However, it is not inconceivable that, in the future, such stimulations can be made outside the cranium, and it might be possible to implant episodic memory.

And just as memory might be implanted, it can also be altered or erased. The most notorious example is probably that of flunitrazepam (Mattila and Larni 1980; Simmons and Cupp 1998). Flunitrazepam can cause amnesia and is thus used as premedication with anaesthesia. Recent work in humans showed the drug propranolol erased the fearful memory (Kindt et al. 2009). Experiments in animals show that once memories of a fearful event are established, they appear to last forever. Memories of the fearful event include the facts of the event and the emotional memory of feeling frightened. In the experiment of Kindt et al. (2009), a fearful memory was evoked on day 1, and it was reactivated on day 2. On repeated exposure to the fearful stimuli, there was extinction on day 3, which meant the stimuli failed to evoke a conditioned response. Oral administration of propranolol before memory reactivation led to a substantial weakening of the fear response during extinction. Further experiments showed that the facts of the events were remembered, but the emotional memories were either erased or unavailable for retrieval. Procedural memory is also amenable to manipulation: it has been shown that administering the ζ inhibitory peptide blocks the enzyme protein kinase Mζ, and this blocks procedural learning in the rat (von Kraus et al. 2010).

To have mental capacity, a patient must not only understand the information, but also be able to use the information and weigh it, and be able to make a decision (Mental Capacity Act 2005, section 3). This means that even though a patient may fully understand the issues involved, if they are in such a panic that they are unable to process the knowledge to reach a decision, then the patient will lack the capacity to make the decision. Where this impairment is due to a traumatic memory, its erasure may restore a patient’s capacity.

3.3.3 Decision Making: Dual-Process Theory

Experimental psychologists have studied how humans make decisions, and they have come to suggest that we have two decision-making systems (Evans 2003; Wason and Evans 1975), system 1 and system 2. System 1 is autonomous and does not require working memory. System 2 requires working memory and is involved with cognitive decoupling and mental simulation (Stanovich and West 2000). Cognitive decoupling means the creation of copies of our mental representations about things, so that the copies can be used in simulations without affecting the original representations. These are the defining features of the two systems. Examples of system 1 thinking include: reading text on a billboard, determining that an object is at a greater distance than another and driving a car on an empty road. Examples of system 2 thinking include: counting the number of A's in a certain text, parking into a tight parking space and determine the validity of a complex logical reasoning (Kahneman 2011).

There are other common correlates of these two systems. System 1 is thought to be activated initially to generate intuitive default responses; system 2 may or may not be activated to intervene. System 1 is evolutionarily ‘older’, and possessed by some animals. System 2 is evolutionarily ‘younger’, and is probably uniquely human (Evans and Stanovich 2013). The many attributes of these two systems have been explained in detail by Kahneman (2011).

Scientists are discovering a neuroanatomical and neurophysiological basis for these two systems. McClure et al. (2004) offered test subjects different amounts of monetary rewards
at different time delays; the longer the delay, the greater the amount of money. NMR brain scans were performed on these subjects. The scientists discovered that parts of the limbic system were preferentially activated for choices in which money was available immediately. In contrast, when there was delayed gratification, parts of the prefrontal and orbitofrontal cortices were activated. The authors conclude that this and related research show that 'human behaviour is often governed by a competition between lower level, automatic processes that may reflect evolutionary adaptations to particular environments, and the more recently evolved, uniquely human capacity for abstract, domain-general reasoning and future planning'.

De Neys et al. (2008) used functional NMR scans to examine the brains of 13 subjects when asked base rate problems (Kahneman and Tversky 1973). These were questions involving statistical probability. The statistical probability sometimes agreed with social stereotypes (congruent); e.g., the subject was told about a study involving 5 Swedish people and 995 Italians; Marco was one of the subjects who was 16, loved to play football and, after a game, would go for pizza or pasta with his teammates. Statistical probability and social stereotype would both suggest Marco was Italian. The statistical probability sometimes conflicted with social stereotypes (incongruent); e.g., the subject was told about a study involving 5 engineers and 995 lawyers; Jack was one of the subjects who showed no interest in political and social issues, was generally conservative and liked sailing and mathematical puzzles. The base rate information would suggest Jack is more likely a lawyer, but social stereotype would suggest an engineer. De Neys et al. (2008) found that, when subjects were faced with an incongruent problem, and on choosing the base rate response and refraining from stereotypical thinking, the right lateral prefrontal cortex was preferentially activated. This cortex was not activated when the question was of the congruent type.

Tsujii and Watanabe (2009) applied near-infrared spectroscopy to study the activity of different parts of the brain when the subject is performing a mental task (near-infrared spectroscopy [NIRS] is a non-invasive technique which measures the amount of oxygenated haemoglobin and deoxygenated haemoglobin in the blood; it has been shown that the concentration of oxygenated haemoglobin is generally related to regional cortical activation). They asked the subject to consider if a syllogism is true or false. Some of these syllogisms agree with scientific truths, e.g., no mammals are birds, all dogs are mammals, so no dogs are birds. These are called congruent reasoning trials. Other syllogisms do not agree with scientific truths, but are logically correct, e.g., no mammals are birds, all pigeons are mammals, so no pigeons are birds. These are called incongruent reasoning trials. In addition to these primary tasks, the subjects were asked to perform a secondary task, of either low (low load) or high difficulty (high load). During the test, the brains of these subjects underwent NIRS measurements. The scientists found that, regardless of the secondary task, the subjects always performed better in congruent reasoning trials than in incongruent ones, and that they were better at the low-load secondary task than at the high-load secondary task. The left and right inferior frontal cortices were more active in incongruent reasoning trials than in congruent ones. A high-load secondary task combined with incongruent reasoning trials preferentially activated the right inferior frontal cortex.

In our lives, both system 1 and system 2 are invaluable to us. For simple matters, system 1 usually gives the correct response, and it is good at arriving at the correct response quickly. However, for more complex matters, it is imperative to use system 2 to analyse, so that one can arrive at the correct solution. The division of these two ways of thinking is not set in stone, either. For example, in the face of danger, some people tend to freeze. In the African savannah, when we were primaeval humans, this instinctive response made sense: we stopped moving, so the wild animals would not detect us. But if one encounters a plane accident, the plane has belly-landed and the cabin is filled with smoke, one’s best option is to get out as soon as possible. This requires thinking and planning. Often disaster training converts a system 2 response to a system 1 response, so that one acquires a new set of
‘instincts’ for survival in our complex society, as we are no longer hunter-gatherers living in the African savannah.

System 1 thinking probably evolved when we *Homo sapiens* first appeared as hunter-gatherers in Africa about 200,000–300,000 years ago (Bae et al. 2017). We lived as hunter-gatherers in groups of no more than 100, and the effects of our actions were limited to a small area, and extended to short time-scales like a year or two. System 1 thinking was well suited to that kind of living environment. However, we have now built up complex cultures and civilisations. These days, our actions have far-reaching consequences, sometimes affecting the environment beyond the earth. We also carry out actions which have long-lasting effects on the earth. System 1 thinking is not able to handle such complex matters. In the modern world, problems frequently arise when we should be using system 2 thinking to deal with questions in our complex society, but instead are tempted to use system 1 thinking because it is familiar, comfortable and requires less effort.

The neuroscience developments discussed in this section might provide tools which can determine whether a decision is the product of careful thought (system 2 thinking) or is instinctive (system 1) thinking. This has implications in law. Lawyers tend to agree that it is important to respect people’s decisions about their lives, at least where doing so does not cause harm to others. This is the right of autonomy. However, difficult cases arise where a person has conflicting views over how they wish to be treated. A good example is *Re MB* [1997] EWCA Civ 1361, where a woman in the late stages of pregnancy consented to a Caesarean section (necessary to save her life and the life of her baby), but refused to consent to the necessary injection (she had needle phobia). To deal with such cases legal commentators have suggested we need to break down what we mean by autonomy. Coggon (2007) has distinguished:

1. **Best desire autonomy** —leads to an action decided upon because it reflects a person’s overall desire given their own values, even if this runs contrary to their immediate desire.
2. **Current desire autonomy** —leads to an action decided upon because it reflects a person’s immediate inclinations, *i.e.*, what they think they want in a given moment without further reflection.

We might decide that, for example, best desire autonomy decisions should carry greater weight than current desire autonomy decisions. We might take that further and argue more generally that a considered autonomous decision, based on full knowledge of the facts and reflecting a person’s underlying and enduring values, might be thought to be deserving of greater moral weight than the decision based on mistakes or the one that is inconsistent with the values by which the person lives his or her life.

If that view is accepted, then, at least in ethical terms, not all autonomous decisions deserve the same level of protection. This then opens up an approach that allows us to say that where a patient’s decision is going to cause him or her serious harm, then that decision will need to be richly autonomous, and if it is not fully autonomous, we need not comply with it. Indeed, this may be what we are witnessing in the case law on vulnerable adults, which we looked at earlier in the chapter. There, the impaired decisions of people with capacity are not followed because they represent only a severely impaired exercise of autonomy. If this kind of approach is adopted, then the law will need a much more sophisticated way of determining the extent to which decisions are thought through or represent deeper values. The neuroscience developments discussed in this section might provide tools which can determine whether a decision is the product of careful thought or is instinctive.

### 3.3.4 Other Cognitive Functions

Other functions that can be investigated by modern brain scanning techniques include lie detection. Scientists have used NMR scans to discover that lying involves increased
prefrontal and parietal lobe activity (Ganis et al. 2003; Kozel et al. 2004; Nunez et al. 2005). By examining the NMR scan signals, Langleben and his co-workers (Langleben et al. 2005) were able to distinguish truth from lie on a single-event level with an accuracy of 78%. Later work showed that this difference was preserved even in schizophrenics (Kaylor-Hughes et al. 2011).

Our sense of justice can also be studied using NMR scans. For example, Singer et al. (2006) asked 16 men and 16 women to play a game as a first player; they were paired up with a second player who could play fairly and unfairly. Previous research showed that the anterior insula/fronto-insular cortex and the anterior cingulate cortex were activated when experiencing pain or observing pain in others. When the second player was inflicted pain, NMR scans showed that these parts of the brain were activated. This activation was greater for a fair second player than for an unfair second player, and the difference between the two was greater in men than in women. Interestingly, the nucleus accumbens, part of the brain associated with processing reward, was activated in men in the case of an unfair second player being inflicted pain, but it was not activated in women.

These brain scans also help us to diagnose rare conditions. Recently, a group of Dutch scientists studied the brain of normal subjects and those with dissociative identity disorder (more often known as multiple personality disorder, where two or more personalities reside in one person). By asking the subjects to read different material and imagine different things, they were able to identify brain scan features unique to dissociative identity disorder sufferers (Reinders et al. 2012). This is particularly significant, as in criminal trials, whether the accused suffers from such a disorder can seriously affect the verdict and the sentencing.

Gradually, these machines are allowing us to determine what a person is doing. Scientists are researching to determine what a person is seeing from the NMR brain scan alone (Cowen et al. 2014; Naselaris et al. 2015; Nishimoto et al. 2011; VanRullen and Reddy 2019); their results are still at a preliminary stage. In a different experiment, scientists implanted electrodes in the brain of subjects undergoing surgery for epilepsy. The subjects were asked to listen to English sentences. By analysing the signals from the electrodes, the scientists were able to reveal the representation of the entire English phonetic inventory on the superior temporal gyrus, that part of the brain involved in the auditory processing of speech. Thus the scientists could deduce what the subjects were listening to from the activity patterns recorded from the electrodes alone (Herff and Schultz 2016; Mesgarani et al. 2014). In a later study, Chang et al. (2017) analysed NMR scans made on subjects listening to music, and they could recover the music from the brain scan with reasonable accuracy (Fig. 3.12 shows an example of what is played and what is deduced from the NMR scan). Another study has shown that it is possible to recover the real-life sounds heard by the subjects from their NMR brain scans (Santoro et al. 2017). It would be easy to assume that, at some point, we might be able to find out what a person sees, hears, smells and senses, and even read the thoughts of this person using appropriate brain scans and analysis.

**Fig. 3.12** The music sequence shown in black was played, and the sequence reconstructed from the NMR scans of the three subjects, S1, S2 and S3, are shown in different colours. For easier visualisation on a treble clef, all frequencies were rounded to the nearest semitone and lowered one octave. Taken from Chang et al. (2017)
The development of these technologies has important consequences for the law. They are already helping the law to decide if an individual has dissociative identity disorder. They can help law to decide if a witness to an event is reliable.

### 3.3.5 Personality and Behaviour

Studies on the relationship of personality and behaviour began with the case of Phineas Gage. Gage was a railway worker, and was working in Vermont in 1848, when he directed some workmen to blast away some rocks. This involved boring a hole deep into the rock, putting gunpowder into the hole and installing a fuse to set off the charge. All this had to be compacted into the hole with a tamping iron. Gage did this and caused an explosion; the tamping iron flew out and went through his skull from the lower left side to the left forehead (Fig. 3.13).

![Fig. 3.13 Diagram showing the tamping iron in the skull of Phineas Gage. Taken from figure 2 of Harlow (1868)](image)

Surprisingly Gage survived this accident, and was attended by the clinician John Harlow. Harlow wrote an initial report in the year of the accident (Harlow 1848). He followed Gage up for the next 12 years until Gage died in 1860. He then wrote a further report (Harlow 1868). Before the accident, Gage was considered a hard-working responsible worker, but after the accident he became impatient, capricious and vacillating, and he lost his job. Over time, his symptoms improved somewhat, and he later became a coach driver in Chile. Anatomical observations before and after Gage’s death showed that his left frontal lobe was partly obliterated in the accident.

Over time, as cases like these accumulate, scientists and clinicians are able to correlate brain regions with emotions and personality. To quantify these correlations, scientists make use of a widely accepted structural model of personality. This was proposed by McCrae and Costa (1989), and is generally known as the ‘Big Five’ model, where a person’s tendency on five traits are scored: openness to experience, conscientiousness, extraversion, agreeableness and neuroticism. The ‘Big Five’ personality traits were put on a firm biological basis when scientists discovered a correlation between brain structure and these personality traits (Bjørnebekk et al. 2013; DeYoung et al. 2010; Riccelli et al. 2017). The results of these studies do not always agree with each other, but a consensus view is gradually emerging. It would be important to emphasise that, although there is localisation of function in the brain, this localisation is only relative. Functions of the brain are compartmentalised, but each compartment relies on other parts of the brain to fulfil its localised function. This is what we mean when saying the compartmentalisation is ‘relative’.
And of course this is most evident in the different parts of the brain giving rise to different personality traits (Sollberger et al. 2009). This should be borne in mind when reading reports of how brain structures are correlated to personality traits.

Damage to the frontal lobes from traumatic brain injury results in major behavioural changes; the patients lack energy, cannot plan ahead and show impulsive behaviour (Stuss 2011). Cipriani et al. (2015) has reviewed the personality changes in different neurodegenerative diseases, and these changes are related to specific diseased brain regions. Personality disorders have also been linked to altered brain anatomy and physiology: Kiehl (2006) has described how psychopathy, a complex personality disorder characterised by lack of empathy, guilt or remorse, poor behavioural control and impulsivity, is linked to alterations in a part of the brain called the paralimbic system, and Campanella et al. (2014) has studied brain tumour patients and correlated the location of their tumours to the changes in emotion and personality. Thus, it appears that our personality traits are partly a manifestation of brain anatomy and physiology, and partly affected by the environment. When the anatomy and physiology change because of disease or trauma, our personalities can change.

3.3.6 Criminality

Legally, one of the most dramatic behavioural changes is when a person becomes a criminal. Clinicians have known for some time that brain dysfunction is correlated with criminal behaviour (Brower and Price 2001). The advent of functional brain scans has brought new findings on the correlation between criminal behaviour and brain structure and function. Research showed that, in subjects with conduct disorders (characterised by aggressive and antisocial behaviour), there is reduced grey matter volume on both sides of the amygdala extending into the insula (Fairchild et al. 2011). Aharoni et al. (2013) examined the brains of 96 male offenders using functional NMR scans during a behavioural test and compared them with an independent sample of 102 healthy adult non-offenders. The behavioural task presented the subject with a frequently occurring target (the letter ‘X’ with an occurrence probability of 0.84) interleaved with a less frequently occurring distracter (the letter ‘K’ with an occurrence probability of 0.16). Test subjects had to depress a button if and only if they saw the target. Since the target was much more frequent than the non-target, this test involved the test subjects exercising appropriate inhibition, which involved activating the anterior cingulate cortex. These scientists discovered that subjects with low activity in the anterior cingulate cortex were more likely to re-offend than subjects with high activity. Previous work has shown that this region belongs to the limbic system and is involved in error processing, conflict monitoring and avoidance learning. These results correlate with those of Ermer et al. (2012), who found that there was reduced grey matter volume in the paralimbic regions (orbitofrontal cortex, bilateral temporal lobes and posterior cingulate cortex) in psychopathic individuals incarcerated in maximum-security prisons.

Brain injuries to individuals are correlated with criminality. A recent review shows that the prevalence of traumatic brain injury is about 60% (95% confidence interval: 48–72%) in the offender population (Shiroma et al. 2012). This is much higher than in the general population. Since these brain injuries are of different types and in different regions of the brain, the question naturally arises as to how diverse injuries are correlated with increased criminality. The work of Darby et al. (2017) might hint at an answer: they studied 17 lesion cases where the patients committed crimes after brain injuries. They found that the lesion sites were heterogeneous, but they applied lesion network analysis and found that these lesions were all connected to the same network. This criminality-related network of brain regions was functionally connected to the inferior orbitofrontal cortex and anterior temporal lobes, and was unique when compared to lesions causing other neuropsychiatric disorders. The scientists noted that this criminality-related network included regions involved in morality, value-based decision making and theory of mind, but not regions involved in cognitive control or empathy.
To summarise, there seems to be firm evidence that changes in brain anatomy and/or physiology can predispose the individual to crime. This subject is very complex, and so it is important to realise that we are far from understanding how differences in brain anatomy and physiology lead to different behaviours; e.g., Smaragdi et al. (2017) examined the cortical structures of adolescents, and found that men with conduct disorder have thicker supramarginal gyrus cortices than control subjects, but women with conduct disorder have thinner cortices; relative to controls, men with conduct disorder also show higher gyrification and surface area in the superior frontal gyrus, but the opposite pattern was observed in women. There are thus distinct differences in male and female brains.

Moreover, many studies have emphasised the importance of both the genetics and the environment; e.g., Bohman et al. (1982) studied 862 Swedish children who were all adopted before three years of age. The scientists divided criminality into two types: petty crimes unrelated to alcoholism, and criminality related to alcoholism. Non-alcoholic petty criminals were found to have an excess of biological parents with histories of petty crimes. Cloninger et al. (1982) subsequently quantified the contribution of genetic predispositions and the postnatal environment using a multivariate model. They found that the rate of criminality in the adopted person with genetic and environmental predisposing factors was 40%, but with genetic factors alone it was 12.1%, or with environmental factors alone it was 6.7%. Since the sum total of the environmental factors and genetic factors was 18.8%, well lower than the 40% of a ‘dual-factor’ person, this suggested that genetic factors interacted with the environment in a complex way. Sigvardsson et al. (1982) extended this work to include 913 adopted women as well, and found similar genetic and environmental contributions to criminality, with 11.1% of ‘dual-factor’ women being petty criminals, but with genetic factors alone, the probability was 2.2%, and with environmental factors alone, it was 2.9%. These studies were significant because of the large samples and also because Sweden was socially less heterogeneous than many countries (so there were fewer confounding factors). Moreover, these results implicating both genetic and environmental factors have been reproduced by other scientists (Barnes and Jacobs 2013; Cadoret et al. 1995).

Note that brain anatomy and physiology are only predispositions and not deterministic. It would be wrong to think that clinicians can take a look at the functional NMR images of a person’s brain, and accurately predict that the person will or will not commit crimes in the future. We should also remember that the brain is plastic and can change; e.g., preliminary experiments on four psychopathic criminals showed that one of them could be taught to change his brain activity and his emotional reactions (Sitaram et al. 2014). And the environment also plays an important role in determining one’s behaviour. Thus the current thinking on biological crime prevention is to improve the environment to promote healthy biological development (Rocque et al. 2012); for example, regular postnatal home visits of mothers reduce the probability of their children becoming criminals when they reach 15 (Olds et al. 1998) and 19 years of age (Eckenrode et al. 2010). Social learning theory is also applied to reduce crime through giving vulnerable people appropriate role models and examples to learn from (Fox 2017). Again, one acknowledges genetic influences, but one also emphasises brain plasticity.

The challenge of neuroscience is a significant one for criminal law. It is part of a much larger debate over the extent to which it is fair to hold people to account for their actions. Not only a person’s neurobiological state but also their upbringing, socio-economic background and external pressures can all play a part in impacting the extent to which a person’s decision to commit a crime can be said to be truly ‘theirs’. Criminal law has traditionally been very reluctant to look behind an assessment of whether or not the defendant had the necessary mens rea (e.g. the intent or recklessness) required for the offence. Whether the defendant was responsible for having that mens rea was irrelevant.

This is dramatically shown in the case of R v. Kingston [1995] 2 AC 355. There, the defendant (Barry Kingston) was in dispute with two former business associates. The latter hired Kevin Penn to photograph Kingston in compromising situations with a boy so that they could blackmail him. Penn lured a 15-year-old boy to his flat and gave him a drink which
allegedly contained sedative drugs and cannabis. The boy fell asleep on a bed and remembered nothing until he woke the next morning. Penn then invited Kingston to his flat and gave him some coffee. Kingston claimed that unknown to him Penn had drugged the coffee. Penn then showed Kingston the naked boy on the bed and Kingston and Penn assaulted him. Penn photographed and taped the indecent assault. Kingston’s defence was based on the fact that he had been involuntarily intoxicated. Although he admitted he had paedophilic tendencies, he claimed to have always been able to keep these under control. Kingston explained that the drugs Penn had put in his coffee had caused him to lose his inhibitions and commit the offence. The trial judge directed the jury that if they found the defendant had intentionally assaulted the boy, then he was guilty, even if that intent had been induced by the drugs administered by Penn. On appeal to the Court of Appeal Kingston’s conviction was quashed on the basis that if drugs were surreptitiously administered to a person who was thereby caused to lose his inhibitions and form an intent which he would not otherwise have formed, this was not a criminal intent. The issue was referred to the House of Lords, which restored the conviction. Lord Mustill started from the basic point that the defendant was aware of what he was doing and so had the mens rea. He noted:

The criminal law generally assumes the existence of free will. The law recognises certain exceptions, in the case of the young, those who for any reason are not fully responsible for their actions, and the vulnerable, and it acknowledges situations of duress and necessity, as also of deception and mistake. But, generally speaking, informed adults of sound mind are treated as autonomous beings able to make their own decisions how they will act, and none of the exceptions is relied on as possibly applicable in this case (paragraph 14).

He explained that none of the current defences (self defence, duress and the like) applied. He added:

To recognise a new defence of this type would be a bold step. The common law defences of duress and necessity (if it exists) and the limited common law defence of provocation are all very old. Since counsel for the appellant was not disposed to emphasise this aspect of the appeal the subject was not explored in argument, but I suspect that the recognition of a new general defence at common law has not happened in modern times.

He clearly recognised the Pandora’s box that might be opened if one accepted the argument that a defendant might not be to blame for his own desires. Criminal law simply assumes a person is, except in the narrowly accepted range of defences such as self-defence, duress, insanity, loss of control and diminished responsibility.

There is a tension here. It is clearly a fundamental principle of criminal law: defendants are not responsible for their involuntary acts. Where the defendant is acting involuntarily the primary purposes of conviction and punishment through criminal law are not capable of being fulfilled: involuntary acts cannot be deterred; there would be no wrongdoing that requires retribution; the use of a conviction to mark censure would be seriously unjust. But a parallel principle runs through criminal law: defendants are responsible for their not-involuntary acts. In the absence of an established defence of automatism, which is defined incredibly strictly, defendants are taken to be responsible for their actions. Hence, in nearly all cases, addicts are held to be responsible for their addiction and for crimes they commit as a result of addicted intoxication.

A justification for the presumption of voluntariness is offered by Gardner (1998). He has argued that allowing a denial of responsibility is to deny self-respect. He explains:

Self-respect is an attitude which everyone ought to have if they deserve it, and which, moreover, everyone ought to deserve. The self-respecting person aspires to live up to
the proper standards for success in and fitness for the life she leads, and holds herself out to be judged by those standards. It follows that it is part of the nature of self-respect that a self-respecting person wants to be able to give an intelligible rational account of herself, to be able to show that her actions were the actions of someone who aspired to live up to the proper standards for success in her life and fitness to lead it. She wants it to be the case that her actions were not truly wrongful, of if they were wrongful, that they were at any rate justified, of if they were not justified, that they were at any rate excused. A denial of responsibility rules all of this out, and there is, accordingly, the line of defence which counts as an admission of defeat for any self-respecting person.

Under Gardner’s approach a claim of lack of responsibility is a defeat for a self-respecting person. It follows that not only should the law severely restrict its access, but defendants should be reluctant to seek to rely on it.

This is a debatable claim. Those who lack mental capacity are not necessarily suffering a defeat or are worthy of less respect. We can interact with the world in a rich set of ways. Our humanness is not limited to insisting on full capacity. A person may legitimately claim, ‘I have some responsibility for my actions’, or ‘While I could comply with the law, it is much harder for me to do so than most people.’

One theory which is often thought better suited to dealing with cases of impaired responsibility is the ‘character theory’ (Sullivan 1996). This involves considering whether the act reveals bad character from the defendant. According to Sullivan, ‘conjoining the notion of lapse from good character with circumstances of destabilization but for which the agent would not have done what she did’ yields a proposal for a defence that is morally attractive and capable of being kept within manageable bounds. This might enable us to say that where a defendant’s neurological state meant they were acting ‘out of character’ and how they would not normally have acted, then a defence would be available. As Sullivan (1996) argues, this could provide a defence in R v. Kingston 1995, but it might also in other cases where the defendant acts atypically due to a neurological condition. Sullivan’s theory could become more important as scientists discover ways to interfere with the moral judgement of the subject (see Sect. 3.2.6).

That, however, is no help for a defendant’s whose genetic/neurological state is typically predisposing them to commit crime. The one area of criminal law where defendants have had some very limited success in utilising addiction as a defence is in the area of diminished responsibility, a defence which is only available to murder and even then, if successful, reduces the conviction from murder to manslaughter (Homicide Act 1957, section 2). The defence is only available if the defendant suffered from an abnormality of mental functioning which arose from a recognised medical condition. That abnormality must substantially impair the defendant’s ability to do one of three things: understand the nature of his/her conduct, form a rational judgement or exercise self-control. Finally, the defendant needs to show that the abnormality provides an explanation for the killing.

It is to be remembered that we are discussing a very limited defence here, and in particular that it is a partial defence that still leads to the conviction of the defendant. The defendant is still responsible for the death of the victim and deserves punishment for it. However, the law acknowledges that the censure that the defendant deserves is less. The defence is compatible with the proposal of Morse (2003) that we develop a verdict of ‘guilty but partially responsible’, thereby preserving the formal denouncement of guilt, with an acknowledgement that the case is more complex than that. This may be the correct balance for those whose neurological state impairs, but does not negate responsibility.

It has the recognition of the defendant as a moral being: a person (partially) responsible for his/her actions and for being accountable for them. With responsibility comes hope: the control over the condition. And with that comes dignity and self-respect, where the person can take a full place in the moral universe that other citizens inhabit. In the view of Gardner (1998), to lack responsibility for one’s actions is a pitiable state, not one to seek out.
Perhaps this is true where responsibility is entirely destroyed by incapacity. Yet the use of diminished responsibility acknowledges another aspect: that battling the condition is hard work, very hard work. Even where responsibility is diminished, it is not negated, and it is still being asserted by the person as a moral agent. The loss of the battle is a moral failure, and one deserving of some blame, but blame tempered by a compassionate acknowledgement of the difficulty of the situation facing the defendant.

3.3.7 Brain Injuries and Brain-Machine Interface
The brain is rather unique in that injuries to it usually result in irrevocable loss of neurons and function. This is in contrast to most other tissues in our body, where injuries to them would lead to repair and at least partial recovery of function. There has thus been active research in using machines to make up for the loss of brain function (Lebedev and Nicolelis 2017). There are three kinds of brain-machine interfaces: passive, active and reactive:

1. In a passive brain-machine interface, the machine monitors the brain state of the subject, and intervenes if necessary (Aricò et al. 2017). The application of a passive brain-machine interface has been proposed in complex domains where safety is critical. For example, in air traffic control, automated collision avoidance systems can be used to prevent planes from flying into each other. However, when the alarm is activated, the air traffic controller could be overwhelmed by multiple sources of information. The passive brain-machine interface can monitor the cognitive state of the air traffic controller and provide him/her with the most appropriate information in a manner most easily accessible to the human, to reduce the possibility of error. None of this is available on a routine basis, but this kind of device is being developed.

2. In an active brain-machine interface, the subject sends signal to the machine in the form of changes in the EEG or blood flow. These signals are detected by the machine, and it uses them to carry out its function; it could be moving a robotic arm, activating the speech synthesiser to speak (Slutzky 2019) or moving a lower-limb assistive device such as a wheelchair (Tariq et al. 2018).

   This is by far the best known of brain-machine interfaces, and has become quite sophisticated. The interface could be implanted into the subject’s brain and the neural signal from the subject decoded using complex computers. Some of the brain-machine interfaces for robotic arm control contain a sensory feedback to refine the movements (Bensmaia and Miller 2014).

3. In a reactive brain-machine interface, brain activity is monitored in reaction to an external stimulus given by the brain-machine interface. For example, a list of letters is shown on the screen, and the machine monitors the brain of the subject to detect attention on the part of the subject. When this is detected, the letter is chosen. By doing this repeatedly, the machine can help the subject write, draw or even drive a wheelchair (Kaufmann et al. 2014).

Most of these brain-machine interfaces contain computers in the machine to decode the brain signal and control the effector machinery. The programs in these computers can be written by scientists or they can contain a learning algorithm whereby the computer learns from ‘experience’, i.e., when the brain-machine interface is used. Thus the brain-machine interface can adapt to the user and become better with time.

One of the legal challenges of these brain-machine interfaces is to do with legal responsibility. If a human makes a mistake, then the human has the legal responsibility. But if the mistake is committed by a human-machine hybrid, where does the legal responsibility lie? One would have to understand the mistake, dissect the role of the human and the machine in executing the action, and apportion the blame. And when we talk about the machine, we also have to divide it into at least two parts: the actual machinery and the
computer program that controls it. These two parts are made by different people, and they have different responsibilities.

The legal distinction between criminal liability and responsibility under civil law can be important here. Criminal responsibility is unlikely to arise in these cases. Unless the mechanical engineer or programmer was malicious, it is unlikely there would be the necessary intent or recklessness required for the mens rea for criminal liability. The one possible exception would be gross negligence manslaughter, which can only be used where the defendant was severely negligent and this caused death. One could imagine a case involving hospital equipment that might arise.

Liability under the civil law of tort is more plausible as it is only necessary to show the defendant was negligent. The difficulty would be that it is in the nature of programming or engineering that unexpected results can emerge which can only become apparent when the machine is operating. So liability in tort law would be restricted to an injury being caused which the programmer or engineer should have reasonably foreseen.

3.4 Improving the Mind

For a long time, people have been trying to improve their minds using various means. Recently, there have been anecdotal reports suggesting that drugs used to treat patients with attention deficit hyperactivity disorder (ADHD) can be used to enhance cognitive performance in normal subjects. However, a meta-analysis of previous studies on the effect of methylphenidate and amphetamine on healthy subjects only shows a modest effect of these drugs on cognitive enhancement (Ilieva et al. 2015). Similarly, a meta-analysis of research on the effect of modafinil shows a small though significant effect on cognitive enhancement (Kredlow et al. 2019).

Another method of cognitive enhancement, though less easily available, is transcranial direct current stimulation (tDCS), especially anode stimulation. Whether this procedure is beneficial is still unclear: Mancuso et al. (2016) show a small but significant effect of stimulating the dorsolateral prefrontal cortex coupled with working memory training, Dedoncker et al. (2016) show a modest effect with anodal tDCS and no effect with cathodal tDCS, but the meta-analysis of Medina and Cason (2017) shows that previous studies have no evidential value.

One intervention has been shown definitively to have a small to moderate effect on cognitive enhancement: physical activity. Physical activity has been shown to be effective both in youth (Vazou et al. 2019) and at an older age (Etnier et al. 2019; Northey et al. 2017). Further research shows that these effects can be passed on from one generation to the next (McGreevy et al. 2019).

The legal implications of these drugs will be limited. They would be subject to the legal regulations governing any medicines. Perhaps the most interesting legal issue is whether it could be claimed that a person who failed to take such a drug before completing a complex task was negligent. Imagine, for example, a surgeon is about to start a lengthy and delicate procedure. They realise they are feeling slightly tired, but by taking a drug they can enhance their focus and energy levels so that they can perform the operation at the height of their abilities. If they fail to take the drug and cause an injury to the patient, which would have been avoided had they taken the drug, could a case be brought for negligence (Goold et al. 2014)? It seems unlikely because it would in effect compel a health care professional to take medication they do not wish to take and that would interfere with rights of bodily integrity. More plausibly a hospital trust could require doctors to choose to either take the medication before completing certain operations or decline to undertake them. If it were shown that the taking of such enhancing medication greatly improved patient safety, then the hospital might strike an appropriate balance between the protection of the rights of medical professionals and that of patients.
Medical research has taught us a considerable amount about the brains of living organisms other than humans, often because we can do experiments on animals which we cannot do on humans. These results have helped to shape our understanding of the brain of other animals. This knowledge is now helping us to re-shape our laws regarding other animals.

For a long time humans thought that there was a qualitative difference between ourselves and animals. Darwin (1859) took humans down from their pedestal in his *On the Origins of Species*, and with the subsequent publication of *The Descent of Man* (Darwin 1871), we realised that we are one amongst the many, that our physiology is qualitatively no different from that of other animals. Our intelligence, for so long our pride, is probably but an extreme form of capabilities also seen in other animals. Scientists have also examined the pathways connecting different parts of the nervous system, from insect to humans (Farris 2015), and examined the mechanisms by which brains evolve (Chakraborty and Jarvis 2015; Karten 2015). There is strong evidence that our brains are qualitatively similar to brains of other animals, but we have more neurons and more synaptic connections.

Intelligence is a very vague concept. A recent review on human and animal intelligence (Roth 2015) concluded that ‘mental or behavioural flexibility or the ability of an organism to solve problems occurring in its natural and social environment’ is a good measure of intelligence. There is a small problem with this definition, as most living organisms display the flexibility and ability required to succeed in their environment, or they would have become extinct (Niven and Chittka 2016). Macphail (1987) suggested that intelligence be considered general abilities to solve problems based on previous experience, learning and memory.

It can be seen that the animal intelligence has evolved to solve specific problems in the life of the animal. However, this ability has given the animal ‘surplus’ abilities to tackle problems outside the natural life of the animal. Macphail (1987) goes on to suggest that ‘[p]erhaps any apparently general problem-solving ability a given species possess (including, presumably, man) is a “surplus” ability conferred by the possession of some other device whose primary function is task-specific’.

Burkart *et al.* (2017) also considered the problem of domain-specific and domain-general intelligence. These scientists broadly defined intelligence as ‘the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly and learn from experience’. Domain-specific intelligence has evolved to solve particular problems, whereas domain-general intelligence has developed to solve any problems. All animals, including humans, have varying degrees of domain-specific intelligence and domain-general intelligence. Domain-specific intelligence is ‘economical’ because only a few neurons need be involved. It is also readily available, but its application is limited. Domain-general intelligence, on the other hand, requires more neuronal circuitry and the animal has to be trained before it can apply domain-general intelligence to real-life situations, but it is much more versatile. Animals living in conditions which are relatively constant, or animals that are highly resistant, tend to use domain-specific intelligence to solve problems. Animals living in rapidly changing conditions tend to develop more domain-general intelligence. Developing domain-general intelligence is contingent upon the animal learning how to use these abilities, often from their parents. In humans, a large part of this learning is supplied by our complex society and culture.

Burkart *et al.* (2017) reviewed previous research and it shows that there is convincing evidence that general intelligence (domain-general intelligence) exists in humans and in animals. Why do some species respond to domain-specific selection pressures by increasing general intelligence? Why do other species opt for domain-specific adaptations? To develop general intelligence, the animal needs a large brain. A large brain is costly in food, as the brain requires a lot of energy to function; in humans, an actively growing brain in early childhood can consume more than 60% of the total energy requirements of the individual.
(Kuzawa et al. 2014), and in adult humans, the brain accounts for 2% of the total body mass but accounts for 20% of the oxygen use (Rolfe and Brown 1997). Natural selection favours an increase in brain size when an increase in net energy intake is possible. However, a large brain slows down the organism’s development; a species’ ability to slow down its life history is a necessary condition for evolving a large brain. Therefore, to evolve a large brain, the species must be able to increase adult survival and not be subject to extrinsic mortality. The size of the brain is thus determined by two factors, the benefits of having more general intelligence which can translate into increased survival, and the cost of ‘feeding’ a hungry organ.

The physical basis of intelligence in all animals is the nervous system. All nervous systems, regardless of their complexity, consist of specialised sensory neurons to sense the environment, neurons to process the information received from the sensory neurons and to decide on a course of action, and motor neurons to carry out that action. Whilst in humans, systematic tests, no matter how imperfect, have been developed to measure our intelligence, no such general tests are available for other animals. There are a number of reasons for this. Different animals live in different habitats, some possess hands like ours, some have only claws and beaks, some are blind and others have acute senses of hearing or smell. Moreover, they have different behavioural patterns, which could potentially skew the test results. We shall only attempt an unsystematic, non-exhaustive summary of animal intelligence. We briefly discuss three features which are indicative of intelligence: use of tools, complex communication and theory of mind. We also give a brief account of some other features indicative of a complex mind.

3.5.1 Use of Tools

One of the most interesting problem-solving techniques is the use of tools, and thus tool use could be seen as indicative of problem-solving abilities. Tool use by animals has been observed for some time. The earliest documented instance of tool use was that of chimpanzees using stones to crack nuts (Beatty 1951). Subsequently, Goodall (1964) spent three years in Gombe, East Africa, and she observed chimpanzees using sticks to feed on ants, and stalks and stems to eat termites. She also noticed that these animals use leaves for drinking and leaves for wiping their bodies.

Researchers have observed tool use by orangutans in their natural, wild habitat, too. In one instance, a male orangutan was trying to go from one tree to another. The other tree was too far, so this orangutan attempted ‘tree swaying’ to bring himself closer to the destination tree. He then broke off a branch about 1 m long, held onto the tree with his left hand and the branch with his right hand, and he tried to ‘hook’ the destination tree. This distance was too far, so after two failed attempts, he dropped the branch and broke off a longer branch (about 2.5 m long). Using the same method, he managed to hook the destination tree and drew it nearer, and grasped its branches with his foot. He was then able to transfer to the destination tree. In another instance, another male was observed collecting leaves, stacking them and fashioning them into a pad. He then put this on his hands so that he could climb a thorny tree without being hurt (Fox and bin’Muhammad 2002).

Van Schaik et al. (2006) performed a systematic observation study on 26 wild orangutans (Pongo pygmaeus wurmbii) in Tuanan, Borneo. A total of 6704 hours of observation was tallied. The scientists video-recorded behaviours that could be considered innovative and analysed them. They observed tool-using behaviour, including using a stick to poke into holes to obtain insects or seeds for food, using leaves as gloves, using leaves to wipe latex off chin and biting through vines to release a tree for swaying to reach an adjacent tree.

Breuer et al. (2005) observed Western lowland gorillas (Gorilla gorilla) in Mbeli Bai in northern Republic of Congo. In one instance, a female gorilla, Leah, was seen trying to cross a pool bipedally. After a few steps the water became waist-deep, and she returned to the pool edge. She then re-entered and grabbed a straight branch of 1 m of length in front of her with her right hand. She prodded the water in front of her with the end of the stick
before proceeding further. She advanced 8–10 m using this method, until her baby cried and she returned to the entry point. This female gorilla used a tool to test water depth before walking further.

These are only a few examples of tool use by animals. Sanz et al. (2013) has edited a comprehensive review of tool use in animals, to which the reader is referred for more observations and analysis.

### 3.5.2 Complex Communication

There have been three case studies where animals learnt to handle complex communication unequivocally. These studies involve, respectively, a parrot, two dolphins and a bonobo ape.

The first case concerns the African grey parrot Alex, who was taught human language (Pepperberg 1999). This parrot acquired a vocabulary of nearly 100 words, including object words, colour words, shape phrases, numbers and action phrases. Alex has learnt to understand sequences of words. He combines colour words and object words to say ‘rose paper’, ‘green cork’ and ‘blue peg wood’ even though his trainers have never used these combinations. He can also combine words to say ‘wanna go gym’ when he wants to go to the gym, even though he has never been taught this combination by his trainers. Kako (1999) analyses this to show that Alex has some concept of syntax.

The second case concerns communication with dolphins (Herman et al. 1993, 1984), whereby the scientists taught two bottle-nosed dolphins, Akekamai and Phoenix. Akekamai was taught a sign language with signs given by the trainer, while Phoenix was taught an acoustic language based on clicks from an underwater speaker. Each language had a vocabulary of 35–40 items, and contained nouns, verbs and modifiers. The dolphins were taught to respond to sentences; correct responses were rewarded by a three-word acoustic string and food, and incorrect responses would be met with the name of the dolphin. The commands given to the dolphins were of two forms. Unrelational sentences such as pipe tail touch meant the dolphin was asked to touch the pipe of the tank with her tail. Relational sentences such as water right basket fetch meant the dolphin had to transport the basket floating to the right in the tank to one of the nearby pipes; but right water basket fetch meant that the dolphin was to transport any basket to the water pipe on the right of the tank. The dolphins could understand the syntax of these commands and carry them out successfully. Moreover, when known items were replaced with new unknown items, the dolphins could still carry the commands, though not all the time. These animals were also able to handle structurally novel sentences. This shows that these dolphins have some concept of syntax.

The third case concerns the bonobo Kanzi (Greenfield and Savage-Rumbaugh 1990). He was taught Yerkish, a language based on lexigrams developed at the Yerkes National Primate Research Center in Atlanta, Georgia, USA. Apparently he acquired his knowledge of Yerkish through natural ‘dialogue’ with his trainers; they would activate the appropriate lexigram on Kanzi’s computer keyboard whenever they said a word that had a lexigrammatic counterpart. All such activities were logged by the computer, and this allowed a systematic evaluation of Kanzi’s linguistic abilities. Analysis showed that Kanzi comprehended the words and their relationship to one another, so was able to differentiate sentences such as ‘take the potato outdoors’ and ‘go outdoors and get the potato’.

### 3.5.3 Theory of Mind

A theory of mind means that the animal can assume that it is another animal, think what the other animal would do and alter its behaviour accordingly. Premack and Woodruff (1978), in a seminal paper that explores cognitive abilities of chimpanzees, coined the term ‘theory of mind’ to describe the ability to impute mental states to oneself and to others (in the same or different animal species). Studies have shown that a number of animals are able to deduce what other animals think, to a greater or a lesser extent. It appears that many animals are able to impute mental states to oneself and to others, and the question is to
what extent. A recent study (Krupenye and Call 2019) has reviewed previous work in this field of research, and we shall briefly summarise the findings.

Krupenye and Call (2019) explain that, by 2008, scientists had found that apes were sensitive to the goals and intentions that underlie others’ actions. They gave examples where apes were more patient with individuals who would share food with them, but less so when that was not the case, and apes could tell intentional and accidental actions apart. Experimental evidence also suggested that apes were aware of what others could see and hear, and what others knew on the basis of seeing and hearing.

The authors also described experiments with Asian jays, where the males feed females during the mating season. Jays were fed two kinds of larvae, and depending on how many of one type was fed, they would prefer the other kind. Male jays who saw females pre-fed with one type of larvae would adjust what they offer to the females according to what the latter had been pre-fed.

Note that some scientists think that these observations do not necessarily imply that these animals have a theory of mind; they suggested alternatives. This review examined those alternatives and suggested experiments to discriminate between those alternatives and theory of mind explanations.

However, one of the hallmarks of a fully developed ‘theory of mind’ is to understand that the actions of another individual is driven not by reality but by beliefs about reality, even when those beliefs are false.

In a recent experiment (Krupenye et al. 2016), 7 orangutans (Pongo abelii), 14 bonobos and 19 chimpanzees watched a short video on a monitor while these gazes were recorded non-invasively by an infrared eye-tracker. Different scenarios were played on the monitor. For example, in one scenario, there were two haystacks. A man dressed as a gorilla (‘King Kong’) came to hide an object in the right haystack; this object was sought by another human dressed in normal clothes. The second human saw King Kong hide the object. He then left and closed the door. King Kong then moved the object to the left haystack and went away. The human re-appeared. Where would he be expected to look for the object? The apes’ anticipatory looks were assessed, and the researchers found that about two third of the apes looked to the right haystack where the human thought the object was hidden. The researchers then changed the scenario so that the human saw King Kong move the object to the left haystack before the human left and closed the door. When the human re-appeared, the gaze of the apes moved to the left haystack.

Subsequent experiments by another research group (Buttelmann et al. 2017) on the same three species confirmed these findings. These experiments showed that apes accurately predicted the behaviour of an animal with a false belief. It is most probable that they have a very well-developed ‘theory of mind’. These results may well lead Justice Liberatori to rule that an orangutan in the city zoo of Buenos Aires was ‘una persona no humana’ (‘a non-human person’) in 2015, although this ruling was subsequently overturned on appeal in 2016.

3.5.4 Other Features
Studies have shown that elephants grieve for their close ones (Bradshaw 2004). Experiments also show that some animals possess a sense of fair play (Brosnan and de Waal 2003), which could be considered the beginnings of a sense of morality. Thus there does not seem to be any cognitive or behavioural attribute which is unique to humans; animals possess these attributes to varying degrees.

3.5.5 Summary
We do not (yet) know how the brain works, and how consciousness arises. However, there is an often unspoken underlying assumption in modern neuroscience that our mind is a consequence of our brain functioning and that alone, and our functioning brain gives rise to our mind. Neuroscience is an empirical science and has stringent requirements for tangible evidence; it does not admit of data which are not measurable such as the soul. Neuroscience
assumes that consciousness is a property emergent from the complexity of our brains, and that animals have greater or lesser degrees of consciousness similar to ours (Bor 2012; Dehaene 2014). This ‘materialistic’ programme of research is very successful, and we are learning a great deal about how our mind functions.

Knowing all this, we shall briefly address how laws should develop towards animals in the future. We should always bear in mind that we are not qualitatively different from our evolutionary cousins. For this reason, we believe that future laws should reflect this gradation in the development of consciousness and intelligence. Many animals such as whales, primates and elephants possess such intelligence and have developed their consciousness to such an advanced state that we should not shut them up in zoos or marine parks, to be treated like slaves for our pleasure or indeed treated as property at all. It is one thing to boil ‘live’ potatoes, which have no feelings to speak of, and another thing to slaughter whales and dolphins wholesale, or to club baby seals to death or to imprison bears permanently in cages to extract their bile. It is a measure of our humanity to see how we can legislate to treat other living organisms properly, taking into account that, to a greater or lesser extent, depending on the species and the individual, they understand, feel, enjoy and suffer like we humans do.

### 3.6 Conclusion

It would not be correct to over-generalise, but as we accumulate more and more scientific data on brain function, we are slowly coming to the conclusion that the mind is brain function, and brain function is the mind. We are also gradually realising that our mind is qualitatively no different from those of other animals; many intelligent animals probably learn, feel and suffer as we do. Even out-of-body experiences can be explained using physiological principles (Blanke et al. 2004; Blanke and Mohr 2005; Brandt et al. 2009; Cheyne and Girard 2009; Heydrich and Blanke 2013), and the sense of the body floating can sometimes be induced in healthy subjects (Ehsson 2007; Schutter et al. 2006; Smith and Messier 2014). There is probably no mind-matter dichotomy.

We end this chapter with a case study of a girl, C1, born without the left cerebral hemisphere, the left basal ganglia and a large part of the left thalamus, but with an otherwise intact diencephalon and brain stem, including both lobes of the cerebellum (Asaridou et al. 2020). In normal humans, language processing is largely carried out by the left cerebral hemisphere; Broca’s area in the left frontal lobe and Wernicke’s area in the left temporal lobe are particularly important. By the time C1 was 14, her general language abilities were comparable to age-matched controls, and she was exceptional in phonology and word reading. Functional NMR scans showed that she had much more white matter (thus connectivity between brain cells) in her remaining right cerebral hemisphere than age-matched controls. Some of these connections, together with parts of her frontal lobe and both lobes of the cerebellum were recruited for speech processing. Her general cognitive, numerical and spatial recognition abilities were all normal. Thus, ‘packing’ her language abilities into the right hemisphere did not come at a cost to her other brain functions. This remarkable case illustrates the enormous plasticity of the human brain.

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4. Defining Sex

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4.1 Introduction

Few people would deny that sex plays a major role in the ordering of society. Issues including expected forms of dress, forms of behaviour, roles in the employment market and styles of speaking have all depended on sex. Indeed, the history of human kind is replete with examples of the way men have exerted power over women, through sex-determined roles and rights. That continues very much to be true today. Feminism has done much to challenge patriarchy, but it has had greater success in describing and decrying it, than in lessening its force.

While sex plays major roles in society, its legal significance is diminishing. In social terms it is still true that often the first question asked on receiving news of a new birth is, ‘Is it a boy or a girl?’ At the very start of life the law requires parents to register the birth of the child and declare the child’s sex. For example, in the UK, section 2, Births and Deaths Registration Act 1953 requires registration of birth within 42 days. On registration parents are required to declare the sex of the child. That request is repeated throughout a person’s life: ‘tick male or female’ is still commonly found in forms, be it an application for a store card or answering a survey.

Despite its social significance, there are few circumstances in which a person’s sex is relevant for substantive law. It is, in fact, a struggle to find an area of law where a person’s sex is important. Nevertheless, sex has a legal definition and that plays a key role in the social categorisations of person and is significant in the way the law interacts with men and women.

This chapter focuses on the intersex people (in the medical literature now known as the disorders of sexual development [DSD]) and argues that it poses a radical challenge to the long-standing social and legal assumption that everyone can be classified as either male or female (Feder 2014; Hughes 2008). We shall, however, be using the terminology intersex, for reasons to be explained shortly. The leading works on intersexuality from a social science viewpoint are Fausto-Sterling (2000), Feder (2014) and Davis (2015).

4.2 Distinguishing Gender and Sex

Traditionally a clear distinction has been drawn between gender and sex.¹ Sex (male or female) was seen as a ‘fact’, a scientific question determined by biology (Davis 2015; Preves 2003), whereas gender (masculinity or femininity) was the behaviour expected of persons of that sex² and so was a social construction (Valdes 1996). It was relatively uncontroversial to
claim that gender was fluid, and its meaning varied between societies and over time. By contrast sex was seen as fixed by scientific reality.

However, the distinction between sex and gender is not so straightforward (Chanter 1999). Accepting for the moment that biological features may be regarded as facts, there is still the question of which facts are selected to determine sex. There are a whole range of biological facts that could, in theory, be used to classify people. We choose a particular set of factors as indicators, but the facts selected to indicate sex reflect social roles expected of men and women (in other words gender). As Kaiser et al. (2009) claim, ‘sex is not a pure bodily and material fact, but is deeply interwoven with social and cultural constructions of gender.’ For example, in the past, women’s bodies were perceived as naturally weaker and therefore women were though unsuitable for ‘hard manual labour’. Factors reflecting weakness were designated as feminine. This means that the definition of sex (what makes a male or female body) is intertwined with gender (what behaviour is expected of that body) (Cealey-Harrison and Hood-Williams 2002; Gatens 1996; Herd 1994; Jackson and Scott 2001).

We would go further and note that it is often society, rather than nature, which has created the expectation that there be only two sexes (Chau and Herring 2002). An exploration of evolution and nature shows us that the ‘natural world’ is far more expansive about sex than the ‘two box’ approach our society tends to impose upon it. Indeed, even sticking with humankind, it is clear some societies around the world do not restrict their understanding of sex to only two sexes, men and women (Herd 1994)—all of this to demonstrate that the division between sex and gender must be treated with caution. Sex and gender are certainly not as watertight as expressed in their simplistic forms. As Krieger (2003) puts it, there are ‘biological expressions of gender’ and ‘gendered expression of biology’.

4.3 Defining Intersex States—Terminology

In recent years there has been a lively debate over the correct terminology to use for intersex conditions. The term intersex has been rejected by medical experts in the field. They met in 2006 under the auspices of the Lawson Wilkins Paediatric Endocrinology Society (LWPES) and the European Society for Paediatric Endocrinology (ESPE) and announced that the term intersex should no longer be used. Instead the term disorders of sex development (DSD) is preferred (Lee et al. 2006). That term is defined as congenital conditions in which the development of ‘chromosomal, gonadal or anatomical sex is atypical’. Since then in the medical literature DSD has largely been the preferred terminology (Topp 2013). The argument in favour of this shift in language is that it acknowledges the range of conditions which might be covered by the label DSD and makes it clear that it is not only covering the classical hermaphrodite, with sexual organs of both male and female. The change was explained in the following way: ³

The definitions of such older terms such as ‘hermaphrodite’ and ‘intersex’ were considered problematic because of a lack of consensus on definitions and because they labeled persons (rather than conditions). Further, they implicitly labeled patients with a gender, and one that was frequently inappropriate because it was incongruent with the patient’s assigned or experienced gender.

The change in terminology was also supported by Feder and Karkazis (2008) on the basis that it clarified that a patient had a disorder rather than ‘being intersex’. Intersex was not a defining characteristic, simply a disorder they had. The terminology intersex could have practical problems in meaning the individual could not access medical help if the condition is seen as an identity, rather than a medical problem.

A second argument in favour of the DSD terminology is that the term intersex is imprecise. For example, some clinicians believe the term intersex only applies when a
person’s genitalia is ambiguous, whereas the DSD terminology makes it clear the condition is broader than that. For example, hypopsadias is not intersex, but it does impact on a male child’s genitalia and is a disorder of sexual development.

A third argument is that the terminology intersex can lead to sensationalisation and prurient interest, by referring to sex, and that the term DSD avoids that (Vilain 2006).

A fourth argument notes that the terminology intersex is not without its own difficulties (Sytsma 2006). It might be seen as reinforcing the image of the binary sex divide, with an intersex individual somewhere between male and female. However, it need not have that understanding. The prefix ‘inter’ can also indicate ‘among’, as well as ‘between’ (Oxford English Dictionary 1989). Intersex can be seen as an interlocutor speaking among the sexes (Herring 2017).

Despite these arguments in favour, it is notable that, although the new terminology of DSD has been adopted by some clinicians, it has not received wider use; for example, it has been rejected by the Intersex Society of North America and the UK Intersex Association. And so in this book we have retained the terminology intersex (Holmes 2011). There are a range of reasons why the term DSD has not been found acceptable.

First, the terminology of ‘disorder’, which implies there is something wrong with having an intersex condition. The term disorder might also imply the problem should be ‘fixed’ and is problematic. Whilst some disorders of sexual development, e.g., hypopsadias, are indeed problems to be fixed, most of the intersex conditions are not. This terminology suggests the condition causes problems, whereas being intersex per se only causes difficulties because of society’s attitudes towards sexual identity. As the Androgen Insensitivity Syndrome Support Group (AISSG) explained:

The word ‘disorder’ implies there is something wrong, pathological, stigmatising. Intersex, in most cases, is not life-threatening, and is only life-limiting [emphasis in original] because society, and medicine, treat [emphasis in original] it as a disorder. The UK Intersex Association regards the use of the term ‘Disorders’ as cruelly – and completely unnecessarily – pathologising and stigmatising what we regard as perfectly natural variations in human development.

In particular Topp (2013) remarks,

Disorder of Sex Development is essentialist at its core because it perpetuates reliance on the binary two-sex system by assuming that there are only two naturally occurring groups — men and women — and those outside are disordered. Reliance on gender essentialism necessarily erases the experiences and even bodies of those who do not easily fit into either category.

The second is that intersex activists have done much to raise the profile and understanding of intersex conditions amongst politicians and the general public, and this will be undone with the change in terminology. For example, it has become common to refer to LGBTQI, with the I referring to intersex. Although at one time the term intersex had negative, or at least somewhat exotic, connotations in the past, it has now been appropriated as a positive identity (Topp 2013). The term ‘intersex’ as become widely used around the world and developed as a visible identity category (Holmes 2011). The Intersex International Organisation, for example, has developed an international profile for intersex people and national-based organisations have largely used that terminology. The term has given a political and social identity to those publically active as intersex people.

Third, it was notable that the Conference that led to the widespread adoption of DSD was primarily attended by clinicians, with only a limited involvement of those with intersex
conditions. Only two individuals with intersex conditions were asked to participate in the Conference and they were both American. The organisation Intersex International complains that the DSD Consortium consulted almost no intersex people before making the decision to change ‘intersex’ to ‘disorders of sex development’. Given the long history of imposed medical treatments on intersex people that should not have happened (Karkazis 2008; Preves 2003), it was seen as a term imposed by the medical profession. As we shall see in the history of the medical profession imposing treatment on intersex children, this was unfortunate. Georgiann Davis, in her study of intersex people, found two-thirds rejected the terminology of DSD and identified as intersex (Davis 2015).

A fourth argument raised by Dreger (1998) is that intersex can be taken as an identity, whereas reference to DSD indicates ‘something that went funny in development’ and does not go to identity. It is not terminology that encourages parents to be open to rethink their understanding of sex and gender and the divisions between people. As Eckert (2016) argues,

DSD veils the effects that [the medicalisation of intersex] has on the embodiment of intersexualised infants and limits the space of possibility for embodiment without surgical experience. Moreover, it reinstalls the notion of development ... to pathologize that which disrupts the hetero-relational organization of the sexes/genders.

The argument over terminology is ongoing (Merrick 2017). Notably the terminology intersex has been used in recent European-level documents, including a resolution passed by the European Parliament in 2017 and a Council for Europe Paper published in 2015, titled Human Rights and Intersex People. This is, perhaps, a sign that outside technical medical literature, the term intersex is very much in use.

It should be noted that there are some intersex conditions where a pathology develops which can lead to death. Many intersex conditions indeed have no implications for the subject’s health, but not all. So the term disorders of sex development is appropriate in, for example, congenital adrenal hyperplasia. This condition can be fatal if not treated, so it is acceptable to call it a disease. Thus we suggest that ‘intersex’ be used as an identity for people who feel this best describes them, and ‘disorders of sex development’ be used by clinicians and scientists to describe the physiological and biochemical conditions.

### 4.4 Approaches to Intersexuality

In this section we will explain the way that intersex conditions are commonly explained in medical terminology.

The development of a fertilised ovum into a sexed individual is a complex process and many factors are involved. Three separate processes can be observed:

1. **Sex determination.** This refers to the genetic events that bring about male or female gonadal development (*i.e.* the development of testes or ovaries).

2. **Sex differentiation.** This refers to all subsequent morphogenetic and physiological events that establish functional sexuality, sexual dimorphism and secondary sexual characteristics. Morphogenesis refers to the embryological processes that lead to the formation of tissues, organs and other structures. Sexual dimorphism means the differences in anatomy and physiology of individuals of the two sexes.

3. **Establishment of fertility.** This refers to the survival and development of the germ cells in the ovary or testis. If germ cells fail to survive and develop, even when a testis or ovary is clearly present, eggs and spermatozoa will not form and the individual will not be able to have children.
In a typical embryo (or more properly zygote) the sex of the individual is primarily determined by the genes, which reside almost exclusively on the chromosomes.9

4.4.1 Sex Determination
Sex determination of a typical female individual depends on:
1. the absence of the Y chromosome,
2. two intact X chromosomes and
3. certain non-sex chromosomes (called autosomes).
The determination of a typical male individual depends on:
1. the presence of the Y chromosome (in particular, the SRY gene); and
2. a number of other genes residing on the X chromosome and the autosomes.

Genes on chromosomes dictate gonadal development and thereafter the expected sex differentiation. Research has been able to document the effect of specific genes on sex determination (Bashamboo and McElreavey 2015; Vaiman and Pailhoux 2000). Having established the correct gonads, the embryo proceeds to elaborate the primary sexual organs such as the penis or the vagina, depending on the sex of the individual.

In the case of intersexual individuals this complex process can be disrupted, leading to incomplete sex determination and/or differentiation. Some of the ways these processes can be disrupted will be briefly outlined below.

Four particular kinds of genetic abnormality in sex determination are as follows:

Cellular Mosaicism
This is a very rare state, where the cells of an individual are derived from two distinct fertilised ova. Some cases can give rise to ‘true hermaphroditism’, where the individual possesses male 46XY and female 46XX karyotype cells (Berger-Zaslav et al. 2009). Some individuals with the 45XO/46XY karyotype would have cells of two types: some of which have XY chromosomes and other cells only one X chromosome (Yordam et al. 2001). There have also been reports of 47XXY/46XX karyotype, where one group of cells have three sex chromosomes XXX, also commonly known as Klinefelter syndrome, and the other cells have the normal complement (Kanaka-Gantenbein et al. 2007; Nor and Jalaludin 2016; Talreja et al. 2015).

Disruptions Caused by Gene Translocations
When normal genes are translocated to the wrong chromosome, sexual determination can become abnormal. For example, if a gene for female sex determination on the X chromosome is translocated to the Y chromosome, or vice versa, this can lead to sex-reversed states (Schiebel et al. 1997) or hermaphroditism (Modan-Moses et al. 2003). Some of these XX individuals are true hermaphrodites, possessing both testicular and ovarian tissue (Kusz et al. 1999; Sarafoglou and Ostrer 2000). Some of these gene translocations are compounded by other disorders, for example, a 45XO/46X,idic(Yq) karyotype (Teraoka et al. 1998). In this case, a 45XO/46X,idic(Yq) mosaic possesses a clone of 45XO cells, and another clone of 46XY cells, where the Y chromosome is a mutant with two centromeres, the q-arm of the chromosome is repeated but the p-arm of the chromosome is missing (normal chromosomes have one centromere, flanked on two sides by the p-arm and the q-arm). This is a case of mosaicism combined with gene translocations.

Gene Mutations in Sex Determination
This describes the situation where the genes are on the correct chromosome, but the gene sequence has undergone either spontaneous or inherited mutation. Recent reviews have described testis (Rey and Grinspon 2011; Sekido and Lovell-Badge 2013) and ovary development (Biaso-Lauber and Chaboissier 2015; Tevosian 2013). A large number of genes participate in sex determination, and their interactions are essential to this process (Biaso-Lauber 2010; Eggers and Sinclair 2012). The following examples are only a small subset of cases where sex determination is abnormal:

1. A large number of XY individuals with SRY gene mutations have been documented. This can lead to individuals with complete or partial gonadal dysgenesis (abnormal development) (Bashamboo and McElreavey 2015; McElreavey and Fellous 1999).

2. In XX individuals, gene deletions on the X chromosome have been documented to cause ovarian failure (Chassot et al. 2014; Simpson and Rajkovic 1999).

3. The mutation of the DAX-1 gene, which resides on the X chromosome, can lead to atypical development of gonads (Muscatelli et al. 1994) or even sex reversal (Bardoni et al. 1994).

4. Autosomal genes are also essential in sex determination. For example, the WT1 gene is implicated in early gonadal development; mutations of this gene can also lead to complete or partial gonadal dysgenesis (Davies et al. 1999). Mutation of the SOX9 gene can lead to sex reversal in XY individuals (Wagner et al. 1994).

   Autosomal genes involved in male sex determination include the SF-1 (Achermann et al. 1999) and the DAX-1 (Goodfellow and Camerino 1999). In XX individuals, mutations in the follicle-stimulating hormone receptor gene on chromosome 2 can lead to gonadal dysgenesis (Aittomaki et al. 1996). The Wnt-4 gene, which resides on chromosome 1, can lead to sex reversal if over-expressed (Jordan et al. 2001). Another important autosomal gene lies on chromosome 15. This gene ensures the production of an enzyme (cytochrome P-450 aromatase) which causes the conversion of androgens to oestrogens. Mutation of this gene can lead to non-functional ovaries (Ito et al. 1993).

**4.4.2 Sex Differentiation**

Having established the correct gonads, the embryo proceeds to elaborate the secondary sexual organs (the penis, scrotum, prostate and other secondary sex glands, epididymus, vas deferens etc. or the vagina, uterus and oviduct). It does this in the typical male through the secretion of hormones from the testis, notably androgens (Batch et al. 1992) and a hormone called the anti-Müllerian hormone (Josso et al. 1991). In the absence of these hormones, female genitalia develop. The course of sex differentiation sometimes does not yield male and female genitalia, but leads to ‘secondary intersex states’, in which there is ambiguity about genitalia or reversed genitalia, inappropriate to the gonads and/or sex-chromosome constitution.

Many of these intersex states result from genetic mutations. In sexual development, the ‘master hormone’ is the gonadotrophin-releasing hormone (GnRH), which stimulates the sexual organs to secrete androgens or oestrogens, as appropriate. A number of genetic defects can lead to non-action of the GnRH, leading to a congenital hypogonadotrophic hypogonadism (CHH) (Boehm et al. 2015). CHH is a clinically heterogeneous condition. In boys, this condition is often characterised by maldescended testes and micropenis. When the subject grows up, there is delayed or absent puberty in both boys and girls, and they cannot have children.

In XY individuals, a genetic condition known as androgen insensitivity can result in the presence of a short vagina and the development of a female external appearance, including breast development. However, internally there is a testis, but no other male internal structures and also no uterus, cervix and Fallopian tubes. This condition arises because,
even though androgen secretion is normal, the androgen receptor through which the androgens work is abnormal (Gottlieb et al. 1999, 1998; Hughes et al. 2012; Jääskeläinen 2012). The individual’s tissues are ‘blind’ to the androgens. The condition is of varying severity. The extreme form is described above (complete androgen insensitivity), while the milder forms show varying degrees of external genital intersex states (incomplete androgen insensitivity).

Another form of sex differentiation abnormality is the persistence in XY individuals with testes of those embryonic rudiments, which would give rise to elements of the female reproductive tract such as the cervix, uterus and oviduct (Belville et al. 1999). This condition arises because of genetic defects in the anti-Müllerian hormone system (Mullen and Behringer 2014).

Secondary intersex states involving XX individuals with ovaries can also occur genetically. For example, in congenital adrenal hyperplasia, one of the enzymes for the production of the stress hormone cortisol by the adrenal is defective (Miller and Auchus 2011; Speiser and White 2003). This leads to increased levels of androgen production by the adrenal gland. The high androgen levels can lead to varying degrees to characteristics traditionally seen as male, such as increased clitoral size and, in extreme states, full penile development (Collett-Solberg 2001). This condition can be diagnosed prenatally, and treatment is available (Nimkarn and New 2007). This is an example of a condition which is intersex but is also a physical illness. The subject does not produce adequate levels of aldosterone, a hormone involved in electrolyte balance, and the stress hormone cortisol. Left untreated, the subject could die of lack of aldosterone and cortisol. New developments are at hand to diagnose this condition before nine weeks of gestation, so that dexamethasone could be administered to 46XX individuals at risk of virilisation (Kazmi et al. 2017). Prenatal dexamethasone does not eliminate the problems due to lack of cortisol and aldosterone, but it eliminates the intersex complications due to this genetic defect.

Other types of secondary intersex states have been observed in XX individuals with ovaries, such as septa in the vagina, an absent vagina, fused labia, cervical absence and abnormally shaped, septated or duplicated uteri (Dietrich et al. 2014a, b; Simpson 1999). Some of these states have been mapped to a specific genetic mutation; for example, deletion of part of chromosome 4 is correlated with an absent uterus (Wilcock et al. 1970).

4.4.3 Establishment of Fertility

Many of the above primary and secondary intersex states compromise fertility. Thus, abnormal or missing external or internal genitalia may prevent coition and/or the successful establishment of pregnancy. Wherever a gonad contains germ cells that are not genetically concordant (i.e. XX sperm precursors in a testis or XY egg precursors in a testis), the individual will not be able to have children. This is because eggs require two X chromosomes for their development, whereas two XX chromosomes are lethal for sperm development.

Such a situation also means that a subgroup of people who suffer from a discrete form of atypical sexual development involving the gain or loss of entire sex chromosomes will also not be able to have children. Thus, in the presence of only one X chromosome (XO), an ovary does develop, as do the secondary sex organs, so technically this person would not be classed medically as intersex. However, all the eggs die and so the ovary becomes secondarily abnormal (‘gonadal dysgenesis’) (Speed 1986).

4.4.4 Summary

An individual with any of the states described above may then be classed as intersex in medical terms. It is important to appreciate that the label ‘intersex’ in fact covers a wide range of medical states in which, in different ways, sex differentiation or sex determination has not taken place as expected. What links intersexual individuals is that they cannot be categorised unequivocally as either male or female, using the traditional definitions of these terms.
It should be noted that intersexual states are not unique to humanity. The phenomenon has been observed in fish (Kinnison et al. 2000) and other mammals (Cole et al. 1997; Markandeya et al. 1998; Pailhoux et al. 1997; Robinson et al. 1996; Watson et al. 1997). In fact intersexual states can be seen as playing an important role in the evolutionary process or natural selection (Darwin 1859).

In all species, there is random variation of the configuration and characteristics of the genes, (the genotype) leading to variation in observed characteristics (the phenotype) of the individual. This variation means that, if there is a change in the external environment, although some individuals in the species may not be able to survive, others may be able to survive and reproduce, thanks to a slightly different genotype and a phenotype. If there were no variation at all, then when the external environment changes, the species could become very vulnerable to extinction. The variation in the genotype and hence the phenotype is largely random, so whilst some variations may confer survival and reproductive advantages in a changed external environment, other variations may be harmful to the survival of the individual. Seen from the perspective of the species, this phenomenon of random variation in sexual structures, though sometimes deleterious to particular individuals, is essential to the survival of the species. Whether intersexual states may confer some survival advantage to humans under certain states is still unclear, though in some species, it has already been demonstrated that intersexual states are linked to the environment (Dunn et al. 1996). Thus intersexual states in humans, being a variation that may or may not have survival advantages, could be viewed in the same light as variations in hair colour or body height (Aaronson and Aaronson 2010).

From this discussion three crucial points should be emphasised. First, it is not possible to classify everyone as clearly male or female (Dreger 1998). Knowing everything there is to know about an individual, it is still not always possible to assign that person into the accepted description of male or female.

Second, that a simple solution of saying that there are three sexes (Fausto-Sterling 2000): male, female and intersex is over-simplistic. The range of intersex states is too large and diverse for them to be sensibly lumped together in one classification simply on the basis of not clearly falling into the category of male or female. It would even be a simplification to suggest that people can be placed on a scale of maleness and femaleness, because in some respects a person may be classified as male and in other aspects female. A person may, for example, be at one point in such a scale in respect of chromosomes and at another point in relation to breast development.

Third, intersexual states should not be seen as an illness, except in cases where the condition can be life-threatening; for example, congenital adrenal hyperplasia can lead to electrolyte imbalance and death. Non-life-threatening intersexual states should be regarded as a natural aspect of humanity, and indeed in other animals could be essential to survival of the species. We will be returning to these points later in this chapter.

4.4.5 Non-medical Definitions

As Dreger and Herndon (2009) point out, the fact a person is labelled intersex in fact tells us nothing specific about a person’s genes, anatomy, physiology, developmental history or psychology. Interestingly, English law has always acknowledged the existence of at least a third sex. Henry de Bracton wrote, in his De legibus et consuetudinibus Angliae, that mankind is classed as ‘male, female or hermaphrodite’, and that ‘a hermaphrodite is classed with male or female according to the predominance of the sexual organs’ (see de Bracton (c.1235) and Fig. 4.1). Edward Coke wrote on the English law of succession, ‘Every heire is either a male, a female, or an hermaphrodite, that is both male and female’ (Coke 1628). Biologists (Dufossé 1854) and the medical profession (Neumann et al. 1967) have known for a long time that the two-sex description is inadequate, but it persists partly because of the expectations of society. Most parents expect to be told that their newborn is a boy or a girl,
not ‘your newborn is not quite a boy nor a girl’. Many of them are not interested in the medical science behind their child’s condition.¹⁰

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Fig. 4.1 Henry de Bracton’s *De legibus et consuetudinibus Angliae* (On the Laws and Customs of England), ca. 1300 HLS MS 1, f. 14r., published by kind permission of Harvard Law School Library, Historical and Special Collections. The text outlined in yellow discusses men, women and hermaphrodites, and acknowledges the existence of a third sex

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### 4.5 Statistics

There is no consensus over the exact rate of intersex children. In part this is because until relatively recently, doctors kept the intersex status of a baby secret and so statistics were hard to come by (Dreger 2000). Further, the precise rate depends on the definition used. One leading study estimated ‘conservatively’ that between 1 and 2 newborn babies per 1000 receive ‘corrective genital surgery’ as a result of intersex states (Blackless *et al.* 2000). The same study suggested that 17 babies per 1000 born could be labelled intersex, even if not to such an extent to require surgery (Greenberg 2002; Herd 1994). Diamond, a leading expert clinician in the field, argues that ‘more than one in every hundred new-borns
has an intersex condition’ (Diamond and Sigmundson 1997). The highest figure we have found is Gurney’s suggestion of 1.7% of births being intersex (Gurney 2007). That is relied upon by the United Nations when they claim that ‘up to 1.7 percent of babies are born with sex characteristics that don’t fit typical definitions of male and female’. That makes being intersex almost as common as being a redhead!11

4.6 Medical Practice in Response to Intersexual States

For many years, the work of John Money dominated the medical response to intersex conditions (Money 1968, 1998). The reception to his work has been discussed in Kipnis and Diamond (1998), and more current approaches to medical practice in this area have been summarised by Diamond and Sigmundson (1997) and Beh and Diamond (2000). However, Money’s approach has been highly influential; it was based on the view that sex was not fixed by biology. Therefore, a doctor should decide the best sex for an intersexual child as early as possible (and by 24 months at the very latest). Having assigned the sex, surgery should be carried out so that the child’s outward appearance matched the assigned sex and that the child be raised in accordance with that sex. It was crucial, he argued, to ensure that doubts over the child’s sexual identity did not persist, to avoid severe psychological harm. In fact Money recommended that the individual should never be told their medical history (Money 1968, 1998). If medical professionals felt the need to give parents information, they should be told that their child’s sexual organs were ‘unfinished’ and that surgery ensured a natural completion (Money 1968). Money appreciated this was not, strictly speaking, true, but was a way of helping parents raise their children in line with the assigned sex, which he saw as essential to the child’s successful development.

Money’s views have come under increasing challenge (Creighton et al. 2001; Martin 2002), not least because his approach was substantially built on a study of one patient, widely known as the Joan/John case. John’s penis was accidentally removed during a circumcision and Money, in consultation with the parents, advised that the baby be brought up as a girl, Joan (Money 1968). Surgery was performed so that the baby appeared to be female. Money argued that as long as the child was raised as a girl and not told about her medical history she would successfully live as a woman. He reported that this indeed occurred and Joan had grown up as a normal girl. Further research, however, revealed that this claim was inaccurate (Diamond and Sigmundson 1997). Later in life Joan had rejected her sex and lived as a man, and was married with an adopted child (Colapinto 2000). Further, John was profoundly distressed by the way he had been treated during his childhood and adolescence.

Another powerful source of challenge to Money’s approach is studies of intersex people who were not given the surgery that his approach would have recommended (Bin-Abbas et al. 1999; Reilly and Woodhouse 1989). These studies found that the individuals did not suffer psychological harm from not having had the surgery and having bodies that were not designed to fit a male or female paradigm. This led to an increasing acceptance of the view that, unless there is some specific health reason, surgery should not be performed until the individual is old enough to decide for themselves what surgery, if any, they wish to have performed.

The timing of management, if any, is crucial. Around 95% of congenital adrenal hyperplasia is caused by deficiency of the 21-hydroxy-lase enzyme; it can range in severity from the salt-wasting form, where the individual’s life is endangered, to the attenuated form, where there are androgen effects on 46XX individuals. Mulaikal et al. (1987) studied 80 subjects with congenital adrenal hyperplasia, which increases the androgen level in these 46XX people. Of the 52 subjects with adequate vaginal reconstruction, 75% had heterosexual experiences, 2% were homo- or bisexual, and the other 23% were not sexually active. Of the 28 without adequate vaginal reconstruction, 25% had heterosexual experiences, 11% were homo- or bisexual and 64% were not sexually active. The authors’
conclusion was that ‘a greater emphasis on adequate surgical correction earlier in adolescence, as well as stricter medical management, will be needed to improve the sexual experience and fertility of these patients’.

Several ethics groups have called on clear national guidance to ensure that non-urgent treatment is not performed on children with intersex conditions (Australian Senate 2013). Some countries are clearly still following the Money approach (Guillot et al. 2015). Many countries have voiced their concerns about their treatment of intersex people, especially children, who are not able to consent (Greenberg 2017). Such criticisms have led many doctors to adopt a new approach towards intersex states (Lee et al. 2016). Their approach is based on a perspective which does not see intersexual people as abnormal or ‘ill’ and in need of ‘mending’ by surgery so that they can live as male or female, except for those intersexual states where a physical illness is involved such as congenital adrenal hyperplasia. Rather, intersex states with no attendant illnesses are seen as a variation from the standard (just as an unusual hair colour may be) (Dreger 1998). This shift in medical practice and attitude has led to the setting up of various working groups, to move away from the Money approach and develop a more sensitive response to intersexual babies. The report by Lee et al. (2006) recommended the following guidance:

1. Gender assignment must be avoided before expert evaluation in newborns;
2. Evaluation and long-term management must be performed at a centre with an experienced multidisciplinary team;
3. All individuals should receive a gender assignment;
4. Open communication with patients and families is essential, and participation in decision making is encouraged; and
5. Patient and family concerns should be respected and addressed in strict confidence.

There is general acceptance that some intersex states require immediate surgery to ensure the medical well-being of the baby (e.g. to repair any defects in the genito-urinary system so that physiological functions can be carried out normally). What is disputed are operations which are essentially cosmetic: performed just so that the child will appear to accord with one sex or the other. Increasingly, it is accepted that cosmetic surgery should normally be avoided at birth and delayed until later, although there is no agreement on when that should be. Greenberg (2017) notes that parents may not have the legal authority to consent to surgery of their children, and even if they have, informed consent practices may need to be improved to protect the rights of the children. It appears that a more sensible approach is to allow the children to choose later, especially when their sexual identity can change during puberty.

Despite this progress, it is clear that there is still some diversity of practice. In 2013 the Australian Senate enquiry found ‘no medical consensus around the conduct of normalising surgery’ on intersex children (Australian Senate 2013). An Australian study of 272 adults with atypical sex characteristics found 60% had received medical interventions, with a majority claiming to have had negative consequences as a result (Jones et al. 2016).

Juan Mendez, the United Nations Special Rapporteur on Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment, included genital-normalising surgeries under the guise of so-called reparative therapies. He reported that ‘certain forms of abuses in health-care settings that may cross a threshold of mistreatment that is tantamount to torture or cruel, inhuman or degrading treatment or punishment’. The report asserted that ‘[t]he Special Rapporteur calls upon all States to repeal any law allowing intrusive and irreversible treatments, including forced genital-normalizing surgery ... when enforced or administered without the free and informed consent of the person concerned’ (Hupf 2015).
European Parliament resolution of 14 February 2017 on promoting gender equality in mental health and clinical research acknowledged that ‘intersex persons subject to genital mutilation also experience effects on their physical, psychological and sexual and reproductive health’ and ‘calls on the Member States to prevent, ban and prosecute female genital mutilation and genital mutilation affecting intersex persons, and to provide mental health support, in conjunction with physical care, to victims and to those individuals likely to be targeted’.

There is now a widespread acceptance that doctors should wait until the child is sufficiently mature to decide for themselves what surgery, if any, should be performed (Greenberg 2017; Krishna et al. 2017; Lee et al. 2006). Whatever point in time the surgery is proposed, we suggest that a strong case can be made for intervention to follow two key principles:

1. The surgery should be the minimal thought necessary for the well-being of the child or the patient.
2. Where possible the surgery should be reversible. This would facilitate reversal of the decision made during their childhood, should the individual wish it later in life. Alternatively, if better surgical methods were available in the future, the old reconstruction could be undone, and the new methods applied.

4.6.1 Parents

An article in the Journal of Pediatrics and Children’s Health (Low and Hutson 2003) claims that ‘[n]ext to perinatal death, genital ambiguity is likely to be the most devastating condition to face any parent of a newborn’. That may well be an exaggeration, but one of the messages from parents of children with intersex conditions is that they do not know how to treat a child who is intersex because they cannot follow a well-known path (Murray 2009). Many parents, feeling deeply insecure in their new status and aware of the responsibilities of being a parent, rely on social traditions and expectations so they feel they are ‘doing the right thing’. Yet these traditions are often deeply engrained by conventions based on sex. There is, therefore, no well-trodden path for the parents of an intersex child. The parents cannot keep the condition secret because from the very first ‘is it a boy or a girl?’ parents are required to disclose the ‘fact’ of their child’s gender, in a way they would not with many other medical or non-medical matters relating to the child.

It should be acknowledged that the new approach might prove difficult for some parents. The first difficulty is to explain the situation to the parents. One study shows that 40% of parents did not think they had completely understood their child’s diagnosis (Bennecke et al. 2016). In addition to a proper explanation to ensure parents have understood, researchers in this field have also emphasised the need for candour and honesty when discussing the prognosis with parents (Diamond and Beh 2008; Greenberg 2017; Krishna et al. 2017).

Moreover, the social expectations and gendered divisions make it very difficult to raise a child as neither male nor female (Glassberg 1998, 1999). Perhaps many will raise the child as either a boy or a girl (while being open to the possibility of the child choosing a different sex when older) (Diamond and Sigmundson 1997). It may be the ideal that these children are raised as neither male nor female, but as intersex, thereby giving them the maximum opportunity to decide once they are older whether they wish to live as male, female or neither of these (Warne 1998). Grabham (2012) argues the surgical response to intersex reveals the unease society feels with the challenge intersex bodies provide for the assumptions society makes (Karkazis 2008). Indeed it might be this that explains why secrecy is important to some parents, who feel shame their child is not classified by the category society realises is important (Meoded-Danon and Yanay 2016).
It is interesting that the current UK guidance seems to put a lot of weight on the views of parents, while emphasising the importance of clinicians informing parents (Ahmed et al. 2016). It states:

It is very likely that families’ decisions will be shaped by their own expectations, experiences, and their understanding of sex and gender roles within the religious and cultural context of their own social networks. Some parents may consider early genital surgery as a mechanism that could possibly protect their child from the risk of future stigma ... This will require a thorough discussion with several members of the MDT team including the clinical psychologist, surgeons, gynaecologist and nurses so that the parents are fully informed of the controversies around undertaking or withholding early genital surgery.

Notably this does not seem to rule out early genital surgery where parents have strong views in favour of it (Karkazis et al. 2010). That may acknowledge that denying the surgery may cause parents such severe distress that they are unable to perform the tasks of parenting effectively.

4.7 Legal Definition of Sex

Given the huge social significance of sex at a social level, it is perhaps surprising that there are very few situations in which the law requires determination of sex. In part this is explained by the law’s formal commitment to treat men and women equally by giving them the same legal rights (Grenfell 2002). One of the most significant areas where it is necessary to distinguish male and female is the law on marriage, and it is in this area that most of the detailed discussion on the legal definition of sex has taken place. The issue is also relevant in certain sexual offences, which can only be committed by or against a man or a woman.

It is little surprise therefore that in legal culture too the binary divide is deeply entrenched. We find it even in the Universal Declaration of Human Rights, where Article 16 makes the same assumption: ‘Men and women of full age, without any limitation due to race, nationality or religion, have the right to marry and to found a family.’

The leading case on the definition of sex in English law is still Corbett v. Corbett [1971] P 83, where April Ashley’s sex fell to be determined for the purpose of marriage. The case was presented as one where the applicant had been born a man, but as an adult underwent a surgical operation removing her ‘male organs’ and creating the ‘female organs’. Nowadays Ms Ashley would be recognised as a transwoman. She was assessed as male. Key to Ormrod J’s reasoning were four points:

1. That sex is ‘fixed at birth (at the latest) and cannot be changed, either by the natural development of organs of the opposite sex, or by medical or surgical means’ (Corbett v. Corbett [1971] P 83 at 104).

2. Gonadal, chromosomal and genital tests at birth determined the sex. Ormrod J explicitly rejected an argument that psychological sex was relevant for the law’s definition of sex.

3. In determining a person’s sex for the purpose of marriage, the capacity for heterosexual intercourse with their partner was crucial (This did not require the couple to be fertile; see Baxter v. Baxter [1948] AC 274). This was because Ormrod J saw heterosexual intercourse as key to the understanding of marriage.

4. Certainty as to sex was crucial for the law. The law should not permit people to flit between one sex and the other; nor should there be people about whom the law cannot produce a clear answer whether they are male or female. By denying the relevance of psychological attachment to a sex and focussing on the biological ‘facts’ at birth he was able to ensure a legal definition of sex that was certain and fixed.
able to ensure a legal definition of sex that was certain and fixed.

_Corbett v. Corbett_ has come to be regarded as the leading case on the legal definition of sex, not only in England and Wales, but in many other countries. Its persistence is in part due to the perceived expertise brought to the case by Ormrod J himself (he was medically qualified), but also the certainty, so beloved of lawyers, that the test appeared to provide.

The legal position of intersex people was considered by Charles J in _W v. W (Nullity: Gender)_ 14, who was required to consider the validity of a marriage between a male applicant and the respondent. Charles J started by applying the Corbett test. He found that the respondent’s sex was not resolved by considering her chromosomal, gonadal and genital factors. The respondent had partial androgen-insensitivity syndrome and Charles J concluded that the respondent was chromosomally male, gonadally intersex, genitally intersex and psychologically female. Ormrod J in _Corbett_ had acknowledged that his test would not provide an assignation of sex for some intersex people and left such cases to another day, although he hinted that the genital factor should be the determining criterion in a case of doubt. Charles J did not take up this suggestion. He proposed that in cases where the Corbett factors did not all point in one direction, all of the following factors should be considered:

1. chromosomal factors,
2. gonadal factors (i.e. presence or absence of testes or ovaries),
3. genital factors (including internal sex organs),
4. psychological factors,
5. hormonal factors and
6. secondary sexual characteristics (such as distribution of hair, breast development, physique etc.).

Although Charles J does not say so explicitly, we have suggested that where these factors point in conflicting directions, the individual’s psychological attachment to one sex or the other is likely to be regarded as the crucial factor. This list was approved by Lord Nicholls in the House of Lords in _Bellinger v. Bellinger_ [2003] UKHL 21, without any indication of the weighting of the factors, although he also added the style of upbringing and living. These factors require some elaboration:

1. Chromosomal sex is the presence of the XY or XX chromosomes, or other less common chromosomal combinations, e.g., XXY.
2. By gonadal sex is meant the state of the gonads, the presence or absence of the testes or the ovaries.
3. The genital sex is defined by the state of the primary sexual organs, the presence or absence of the penis, the scrotum and the tubular system or the vagina, the cervix, the uterus and the Fallopian tubes.
4. Psychological ‘sex’ is much more difficult to define; it encompasses what the individual feels himself/herself to be. To what extent these feelings are the result of structures in the brain or the result of social/cultural factors is a matter of debate.
5. The hormonal factors, as explained earlier, are ultimately an expression of the chromosomal factors, because almost all genes for hormones are found on the chromosomes. The hormonal factors are important in sex determination and in sex differentiation; they influence how genes are expressed to give rise to gonads, primary
sexual organs and secondary sexual characteristics. In fact it could be argued that as hormonal factors are so dependent on chromosomal factors, there is little point in adding them as a separate criterion.

6. By secondary sexual characteristics are meant those characteristics that are not directly related to reproduction, but that commonly differ between males and females, for example, breast development, hair growth patterns or fat deposition patterns. The secondary sexual characteristics are ultimately effects of hormonal action.

Charles J gave no indication of how to weigh the six factors when they point in different directions. It seems it is not simply a case of seeing whether the majority of these factors lie on one side of the line or another. Rather it a matter for the judge’s discretion, considering all of these factors. Although Charles J does not say so explicitly, we suggest that where these factors point in conflicting directions, the individual’s psychological attachment to one sex or the other is likely to be regarded as the crucial factor. On the facts of W v. W Charles J found that the respondent was female.

4.8 Gender Recognition Act 2004

The Gender Recognition Act 2004 allows a person to apply for a certificate to recognise their ‘acquired sex’. The Gender Recognition Panel must issue the certificate on the receipt of medical evidence that the applicant has gender dysphoria, has lived in the acquired gender for two years, intends to continue living in the gender until death and certain other evidential requirements. There is no need for any surgery to have been performed. When the certificate is granted, apart from a few exceptions, ‘the person’s gender becomes for all purposes the acquired gender’.

While the Act is welcome in that it provides a way for some transpeople to have their sex recognised and it clearly has had a significantly beneficial impact on the lives of some people, some commentators have recognised a shift from seeing sex as fixed at birth by one’s genital towards recognising the need to respect the decision of an individual in regards to their sex. That view may be reinforced by the fact the legislation does not require surgery to have been performed. This means a person with a penis could be a woman under the Act, hence removing the tie between genitalia and sex which has underpinned the law’s general approach to the issue. Cowan (2005) claims that, ‘in contradistinction to the development of case law, new legislation in the U.K. has moved away from sex as the defining characteristic of sexual identity and embraced gender as its champion’.

The legislation certainly has a number of problems with it.

First, the Act reinforces the idea that a person’s sex is important as a matter of law. For those, like us, who believe the law should abandon the male/female divide, the better response to the issue would be to pass legislation making it unlawful to rely on sex-based distinction and to make it clear the distinction was one that was not recognised by the law.

Second, the Act does nothing for those who wish to be recognised as neither male nor female. This is particularly egregious in the case of an intersex person, who is, by the current law, required to have a fictitious sex.

Third, the Act requires the applicant to prove they have or have had gender dysphoria. This must be shown by two medical reports. The neural basis behind gender dysphoria has been comprehensively and critically reviewed recently (Smith et al. 2015). Some scientist would view it as a form of body dysphoria (Fisher et al. 2016), which can take extreme manifestations (Dyer 2000). At the moment, we really are very far from understanding gender identity, so it would seem that some degree of caution is wise.

4.8.1 Other Jurisdictions and the Definition of Sex
South Africa added intersex to the attribute of sex in discrimination law in 2005 and Australia in 2013.

In Colombia, in the Gonzalez No. T-477/95 case, the court found that the applicant’s ‘fundamental right to human dignity and gender identity’ had been violated by the surgery. The court added that ‘doctors could not alter the gender of a patient, regardless of the patient’s age, without the patient’s own informed consent’. Subsequent decisions reinforced that in Ramos No. SU-337/99 (Colombia), with the court saying ‘that it would be wrong for anyone to consent to a sex change operation other than the child herself’.

In Nepal the Supreme Court in Pant v. Nepal [2007] Writ No. 917 recognised the category of ‘other’ for sex identify documentation. The court accepted this was a self-identification term. This is one of the more progressive states’ approach to intersex people.

Puerto Rico allows the category of ‘ambiguous genitalia’ to be used on identity documents. However, this is envisaged as a temporary measure at birth, the assumption being it will be a matter resolved soon (Hupf 2015). The phrase ambiguous may also imply that the truth is not readily apparent, rather than being clear. Also, it does not cover all intersex conditions, only those where genitals are ambiguous.

In 2013 Germany recognised a ‘third sex’ category on birth certificates, allowing X, rather than M or F on passports. The law justified in part to take pressure off parents from making hasty decisions about sex-assigning surgery. There are concerns that parents may, however, find the X category stigmatising and feel pressured into surgery, especially as the X category has broader significance in terms of marriage or health law. Further the decision does not prohibit cosmetic genital surgery.

Malta become the first country in the world to ban cosmetic genital ‘normalising surgery’ without consent with the Gender Identity, Gender Expression and Sex Characteristics Act 2015. The legislation also bans discrimination on the basis of having atypical sex characteristics and allows for X to be used as a sex category on passports and other identity documents.

### 4.9 Criticisms of the Legal Definition

We will now focus on the difficulties with the current law’s approach (Fishbayn 2007).

#### 4.9.1 Two-Box Approach

First, the current law only offers the option of male or female. The Gender Recognition Act does not permit an application to be recognised as being intersex. W v. W, while acknowledging that at birth an individual’s sex may be ambiguous, requires a resolution of that ambiguity by a consideration of a range of factors, with the only options being either male or female.

This is a remarkable position for the law to take. English law which requires an intersex person to take a legal description of sex which is false is bizarre and reflects the strength of the grip of binary sex paradigm. It requires people to register a lie.

#### 4.9.2 Performance of Sex

Second, a person’s genitalia, and particularly their capacity to engage in one specific kind of sexual act, namely heterosexual vaginal intercourse, have been elevated to a central role in the definition of sex. In Corbett the crucial question for determining sex was whether April Ashley was capable of naturally ‘performing the essential role of a women in marriage’. That essential role is engaging in heterosexual intercourse. Hence our sex becomes restricted to the ability or willingness to engage in one particular act. Those unable, unwilling, or uninterested in performing that act are, by implication, not fully being female or male.

In the Bellinger decision Lord Hope states:

[Medical science] cannot turn a woman into a man or a man into a woman ... At best, what is provided is no more than an imitation of the more obvious parts of that
In this imagination, parts of the body are mere equipment. But, equipment to perform what task? For Lord Hope it is clear the task at hand is heterosexual intercourse, and it is possession of the 'equipment' needed to perform the privileged sex act which renders a person male or female.

The elevation of sexual performance as the definition of sex is remarkable. First, surely sexual intercourse is not key to marriage. Companionship, emotional comfort, intimacy and mutual support are, in our view, of far more importance. This point is, in fact, recognised in section 11 of the Matrimonial Causes Act 1973, which states that non-consummation of marriage renders a marriage voidable, rather than void. Therefore, the lack of consummation of a marriage will only invalidate a marriage if either party to the marriage complains about it to the court. If both parties are happy with the absence of sexual intercourse, the marriage is valid at law. The Marriage (Same-Sex Couples) Act 2013, at last, permits same-sex couples to marry; paragraph 4 of Schedule 4 states that same-sex couples will not be able to rely on the consummation grounds for having a marriage annulled. This, in our view, is the better way forward, and opposite-sex marriage rules need to catch up with same-sex marriage rules.

4.9.3 Over-emphasis on Bodily Factors
Thorpe LJ in Bellinger criticised the Corbett test in the following terms:

> In my opinion the test that is confined to physiological factors, whilst attractive for its simplicity and apparent certainty of outcome, is manifestly incomplete. There is no logic or principle in excluding one vital component of the personality, the psyche.

In other words the Corbett approach to defining sex focuses wrongly on physical factors and downplays the person’s psychological factors. Indeed it is interesting that in other areas of the law, the House of Lords has been unwilling to accept that a clear demarcation between the body and the mind can be drawn. For example, in R v. Ireland and R v. Burstow [1997] UKHL 34, the House of Lords defined the statutory terms actual bodily harm and grievous bodily harm as including psychological harms. Yet this demarcation is precisely what the Corbett test draws. Whittle (2002) makes the point eloquently, ‘[W]hat makes a person is what takes place between the ears and not between the legs.’

4.10 Moving Beyond the Two-Box Approach
How is the law to respond to the clear evidence that people who are intersex exist and they do not all want to be classified as male or female? One possibility would be for the law and society to recognise that that there are three sexes: male, female and intersex. The only legal reform that would then be required would be to state how the law on marriage, sexual offences and other areas apply to intersex people. In our view, it would not be satisfactory simply to recognise three sexes. As noted above, the term ‘intersex’ in fact covers a wide range of states, and it would be quite misleading to group all of these into one heading. Indeed support groups have been set up by individuals showing particular intersex states, e.g., Androgen Insensitivity Syndrome Support Group; Congenital Adrenal Hyperplasia Group.

It seems better, therefore, to simply do away with sex as having any legal significance. People should be entitled to see whatever sexual identity they wish for themselves. Rothblatt has promoted ‘sexual continuism’ (Rothblatt 1995):

> [L]abeling people as male or female, upon birth, exalts biology over sociology. Instead, the new feminist principles inspire us to permit all people to self-identify their sexual
status along a broad continuum of possibilities and to create such cultures of gender as human ingenuity may develop.

4.10.1 Abolishing Sex as a Category

The best approach is to do away with all sex categories (Murray 2009). Although most people fall neatly into male or female categories, and there is congruence in their sex and gender identities, there are a small minority who do not. The law and society must take them into account.

Around the world most governments and legal systems claim to seek to promote equality between the sexes. Debates within the feminist movement have revealed that the promotion of equality does not necessarily require the law to ignore or diminish the differences between men and women (Fredman 2001). But rather the law should seek to ensure that inequality should not result from the differences. If maleness and femaleness were abolished as legal categories, this might be thought to inhibit such policies (Colker 1996). We suggest not. Moves to ensure that the care for children is afforded proper social, economic and political recognition; that pregnant workers are protected; that those doing the same jobs are granted equal pay can, of course, be taken without the need to refer explicitly to definitions of sex. Policies could be directed to prevent discrimination against groups of people engaging in activities traditionally understood to be performed by women (e.g., child care), without the need for a reference to sex.

The most likely opposition to a gender-neutral law would come from feminists of difference (Jaggar 1998). They argue that we should take into account sexual differences, but ensure that they do not produce inequality (Rhode 1989). We need a law to recognise there are differences that exist between men and women, but make certain that women or men are not disadvantaged as a result of them. These feminists make the powerful argument that a law and society which takes no account of sex will end up disadvantaging women. Promoting ‘gender-blind’ law will not promote equality because men and women are not starting on an equal footing. The danger with a straightforward liberal approach is that women can only achieve equality by succeeding under the male norm (Cornell 1991; Rhode 1998).

These arguments are well known and have been made extensively elsewhere and we will not repeat them here (Lacey 2004). We are convinced by them, but do not believe they require gender-specific laws. The way to tackle the disadvantages that women in general face is not through laws which distinguish between men and women on their face, but on laws which tackle the particular cause of inequality. For example, the inequality that is caused to women by the fact that women undertake the majority of child care can be tackled by laws which protect the interests of child carers, and can do so without reference to sex. Indeed, following the UK’s Gender Recognition Act 2004, a person can be the mother of one child and the father of another: that would be where a woman gave birth to a child; subsequently, the person was granted a gender recognition certificate and attended a licence clinic offering fertility services with a female partner, who gave birth as a result of such services.

The benefit of using, say, child care, as the basis of protecting groups, rather than sex, is (at least) twofold. First, it means that there is no assumption that women and not men undertake child care. One of the difficulties in sex-specific legislation which is designed to promote gender equality is that it can simply reinforce gender stereotypes. Second, the non-sex-specific approach identifies clearly the source of the disadvantage (child care). This may make it less controversial in political terms and assist in clear thinking about how to target policies designed to remedy the disadvantage.

There are, we accept, disadvantages of a gender-neutral approach to legal provisions. In particular, it might be said to mask social reality (Becker 1999; West 2000). For example, the reality is that the majority of child care is undertaken by women and this should not be disguised by gender-neutral terminology. Further, treating each aspect of disadvantage that
typically affects women separately ignores the way that disadvantages interact to affect women (Crenshaw 1988). To combat these legitimate concerns, we should clarify our claim about what the appropriate legal response to disadvantage is, and indeed to determine what is a disadvantage. We are not advocating a gender-free policy, politics or debate. It is crucial that we are alert to the disadvantages that those identified as women suffer and seek to combat them (Smart 1989). We must recognise and expose the ways that those regarded as women in general suffer through violence and economic pressures.

This approach is not without problems. For example, in prisons, there is sex segregation, the segregation being seen as necessary, as denial of sex relations is seen as part of the punishment and that assaults against women may increase if there is not segregation. However, several points can be made about this traditional explanation. It seems to assume that all prisoners are heterosexual. Further, it seems to downplay the current rates of sexual violence in prison. The proper response to these concerns is to ensure that there is effective protection of prisoners from violence.

Another tricky issue is sport, where in many sports a distinction is made between male and female athletes. We think there is a good case for saying there should be categories of athletes to ensure competition between people of roughly equal physical ability. For example, we could measure the levels of hormones responsible for developing muscle bulk to categorise intersex athletes.

4.11 Conclusion

Although the large majority of humans fall neatly into male and female, both in terms of sex and in terms of gender, we must also accommodate the minority who fall into neither group. Around 1% of children born can be classified as intersex. The traditional medical response to intersexual babies is that they must be assigned as male or female as quickly as possible and then surgery be used to design their bodies to confirm to the outward appearance expected of that sex. This is nowadays accepted by only a few doctors. Until recently the law has followed the traditional medical approach in assuming that a person’s sex must be either male or female. However, both these legal and medical assumptions have been challenged.

This chapter has outlined the research and pressures which led to a change in medical practice amongst many of the experts in the field. It is no longer assumed that an intersexual person can be correctly assigned to one sex or the other. Indeed many advocate not performing surgery until the child is old enough to decide their sexual identity for themselves. Further, it is becoming increasingly acceptable and common for an individual to choose to live as an intersex individual. It is no longer possible to define all people as male or female and the law must cease to use sex as a legal category. The law can lead the way by accepting that people should not be restricted to being either male or female.

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Footnotes

1 For a stimulating discussion on whether it is possible to define what is a woman without reference to gender or sex, see Moi (2001).

2 There is much debate over the extent to which sexual identity, the sex which a person regards themselves as having, is an aspect of gender; see Cealey-Harrison and Hood-Williams (2002).

3 Accord Alliance; at the time of writing, the website address is [https://www.accordalliance.org/glossary/disorders-of-sex-development/](https://www.accordalliance.org/glossary/disorders-of-sex-development/)

4 At the time of writing, the website address is [http://www.ukia.co.uk/ukia/dsd.html](http://www.ukia.co.uk/ukia/dsd.html)

5 Androgen Insensitivity Syndrome Support Group 2011; at the time of writing, the website address is [http://www.aissg.org](http://www.aissg.org).

6 At the time of writing, the website address is [http://www.ukia.co.uk/ukia/dsd.html](http://www.ukia.co.uk/ukia/dsd.html)

7 Androgen Insensitivity Syndrome Support Group 2011; at the time of writing, the website address is [http://www.aissg.org](http://www.aissg.org)

8 At the time of writing, the website address is [https://olieurope.org/](https://olieurope.org/)

9 See Sect. 2.3.1 for further discussion of mitochondrial genes.

10 One of the authors is a qualified doctor, and has met with situations where the author would try to explain the details of a disease to a patient, when the patient interrupts and says, ‘I am not interested in all that. Just tell me what I should do.’ In extreme cases, the patient has a mental block and refuses to take in anything that is said, and has to rely on a relative or friend to write down the clinical suggestions for the patient.

11 At the time of writing, the website address is [https://www.unfe.org/intersex-awareness-new/](https://www.unfe.org/intersex-awareness-new/)

12 There is an interesting analogy here with children’s rights to know their genetic origins.

5. Body Ownership

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Is your body yours? This may seem a strange question to ask, eliciting the immediate response: ‘Of course it is; whose else could it be?’ Indeed, although there has been much debate among lawyers and philosophers over whether bodies are property and whether people can be said to own their bodies, there is a widespread assumption that your body is yours in some sense. It is that assumption which we wish to challenge in this chapter.

Related to this assumption is the problem of body ownership. Who owns our bodies? For centuries the common law took the view that the body and body parts were res nullius (Wall 2015). They could not be owned or subject to property rights. That fitted in with Christian theology, which taught that people were created by God and it was presumptuous of anyone to claim they owned what belonged to God. It also was compatible with the predominant philosophical approaches to property which claimed that property claims emanated from labour. As a person could not claim to have produced their body as a result of their labour, they could not claim to own it. But, perhaps most significantly, there was simply no need for the body to be regarded as property. The power to buy and sell bodies might appeal to slave masters or grave robbers, but no decent person would have need for property rights. The law’s response to the body was, therefore, limited to criminal offences prohibiting assaults, batteries and the like, and a limited number of offences dealing with the interference in proper burial.

Times change. Now the theological concerns play little role in legal thought. The philosophical argument that bodies are not produced by labour seem outdated in this age of gym membership, cosmetic surgery, steroid use, body adornment, etc. But most significantly there are perfectly good reasons why a person might want a property interest, or something like it, in their body. They may wish a hospital to store their gametes for use in assisted reproduction or to retain an organ or other human material for transplant or treatment, and researchers may wish to store human material for research. The idea that people should be permitted to buy and sell parts of their bodies has some highly respectable advocates (Hardcastle 2007). The res nullius approach no longer seems fit for the purpose.

That is all relatively uncontroversial. But if we abandon res nullius, what is to replace it? That is where the consensus breaks down and there has been lively debate over the correct alternative (Goold et al. 2014). To over-simplify, the debate is between those who advocate an approach based on a claim that bodies should be regarded as property and those who argue that bodies should not be treated as property but protected by other kinds of non-property rights, such as rights to privacy or bodily integrity, and that communal interests in bodies need to be protected. Those who reject the property approach tend to support the
creation of a statute to govern the issues. It seems, however, that the property-based approach is the most popular among legal academics (Goold et al. 2014).

5.1 How the Law Views the Human Body

For lawyers the exact relationship with our bodies has raised a host of complex questions. Generally commentators have divided into one of three camps.

There are those who argue that bodies should be regarded as property, capable of being owned and transferred (Björkman and Hansen 2006); those who reject the property approach and instead argue that rights such as ‘rights to bodily integrity’, ‘rights to privacy’ or ‘rights to autonomy’ should be used to protect the body’s special status; and a third group who believe that there is something to be said for both views and the ideal solution lies in finding the appropriate mix of both the property and integrity/privacy approaches. The significance of this dispute can be seen in the context of various legal issues: if a fan cuts off a piece of his favourite actor’s hair should this be regarded as theft or an offence against the person, or both? When considering the issue of live organ donation, are organs to be treated as property which can be bought or sold like any other thing or does the unique status of the body mean that it should not be commercialised by treating it as property? Who should have control over organs and parts of bodies when they have been removed from a person or cadaver? If an individual’s DNA structure is used by scientists to create a valuable commodity, in what sense, if any, should the individual be able to claim ownership in it? Should confidential medical information about someone be regarded as property or should it be protected through a right of privacy (Laurie 2002a)?

Philosophers too have long debated whether our bodies should be seen as us or part of us (Proudfoot 2003). In other words, whether our essential being is our minds which inhabit a body, or whether our bodies are central to our identity. Are our bodies tools to be used by us for our own ends or are our bodies in fact part of the essence of who we are?

What lies at the centre of these debates is an assumption that our bodies are ours. The debate is over the way it is appropriate to describe that sense of ‘oursness’ in legal or philosophical terms. At the heart of our challenge to this assumption are three claims. The first is that our bodies are interconnected with and interdependent on other bodies. Second, our bodies are constantly interacting with the world around us. Their survival, meaning and sustenance depend on other bodies and the wider environment. Thirdly, our bodies are not static organisms; they are changing and interacting with material around them. These points lead us to conclude that to say ‘my body is mine’ is only a part of a picture. Before developing these points it would be useful to summarise the way in which the dispute over the nature of the body has been conducted in most of the legal material.

The issue about ownership of human material can arise in the different context of intellectual property law. To clarify, if there is a piece of human material there are two legal issues around ownership. The first is who owns the sample itself. This is governed by standard property law. The second is who owns the information contained within that sample. The issue is around in the US Supreme Court case of Association for Molecular Pathology v. Myriad Genetics [2013] 133 S. Ct 2107. There a patent was obtained for patents for DNA sequences in connection with BRCA1 and BRCA2 genes, which are connected with breast and ovarian cancer. The Supreme Court drew a distinction between naturally occurring DNA sequences which were a product of nature and so could not be owned by one company and complementary DNA (cDNA) which was synthetically created strands of nucleotides, created in a laboratory, which could be patented. Clearly here the courts are seeking to prevent companies seeking a patent for something that is not truly an invention, but occurs naturally, while encouraging scientific research on developing new products by manipulating naturally occurring DNA and other biological material.

5.2 The Law: Bodies as Property
There has been much academic discussion over whether it can be said that the law recognises our bodies as property which we own (Dworkin and Kennedy 1993; Matthews 1995). Justice Gage recently accepted the law was uncertain and unclear.\(^3\) The safest thing that can be said is that there are some respects in which the body can be treated as property and other respects in which it cannot be. The traditional rule has been that there is no property in the human body. This has been understood to represent the common law,\(^4\) although explicit authority for the proposition is, in fact, limited (Magnusson 1998).

The law appears rather less reluctant to find that separated body parts or products are property. Hair,\(^5\) blood,\(^6\) and urine\(^7\) have all been found to be property for the purposes of the Theft Act 1968. By contrast, damage to hair has also been treated as an assault occasioning actual bodily harm, that is, an offence against the person rather than a property offence.\(^8\) In \(R v. Kelly\)\(^9\) the Court of Appeal held that

parts of a corpse are capable of being property ... if they have acquired different attributes by virtue of the application of skill, such as dissection or preservation techniques, for exhibition or teaching purposes.

Although the court did not say so explicitly, presumably the person who applied the skill was the person who became owner. The Court of Appeal went further and suggested that if body parts attracted a ‘use or significance beyond their mere existence’, they could become property. Examples given by Rose LJ included an organ intended for use in a transplant operation or bodily material removed as an exhibit for a trial (Grubb 1998). In \(Kelly\) itself, the body parts had been preserved and used as anatomical specimens and hence were held to amount to property. It might also explain why drivers who removed their blood or urine samples taken by the police to test alcohol levels could be convicted of theft.\(^10\) The courts are yet to explain why it is that when an item acquires significance, it becomes property, and who the owner is at that point.

In \(Dobson v. Northern Tyneside Health Authority\)\(^11\) reliance was placed on the view in \(Doodeward v. Spence\)\(^12\), where Griffith CJ stated:

When a person has by lawful exercise of work or skill so dealt with a human body or part of a human body in his lawful possession that it has acquired some attributes differentiating it from a mere corpse awaiting burial, he acquires a right to retain possession of it, at least as against any person not entitled to have it delivered to him for the purposes of burial.

These cases leave undecided what kind of skill must be exercised on a part of a body in order for it to acquire the nature of property. The exercise of skill in dissection or preservation may well be sufficient.\(^13\) However, in \(Dobson v. Northern Tyneside Health Authority\) n. 20 at 479, Peter Gibson LJ stated that ‘mere preservation’ would not be sufficient to render the brain property.

Similarly there is a rather uneasy legal situation in respect of corpses. The executors or a hospital can claim lawful possession of a corpse, even though it cannot be owned\(^14\) (Skene 2002b). In \(AB v. Leeds Teaching Hospital NHS Trust\)\(^15\) the parents could not claim any kind of property rights to material removed from their children in the course of a post-mortem, although Gage J made it clear that it might have been different if the parents had requested the return of an organ when consenting to a post-mortem.\(^16\) Brazier (2002) expresses her views on the current law following \(AB v. Leeds Teaching Hospital NHS Trust\)\(^17\) thus:

The deceased did not own their body and could not bequeath it to their estate. The estate can claim the body for decent disposal, although not necessarily disposal as the deceased would have wished. Parts are taken from the body without either the deceased’s or their family’s approval. Put to the uses of medicine, these body parts...
become, as if by magic, property, but property owned by persons unknown, for purposes unforeseen by the deceased. If that represents the law, the law is an ass.

There are further uncertainties over who has control over or ownership of corpses, arising from *Lewisham Hospital NHS Trust v. Hamuth & Ors* [2006] EWHC 1609 (Ch). This case involved a dispute over a corpse which sat in a hospital mortuary. There was a dispute between family members over whether the body should be cremated or buried in a family plot in a cemetery. This reflected a dispute over a will which made one family member the executor. The court determined there was ‘no direct authority on the issue’ over how to deal with such a dispute. In the end, the fact that the hospital was in ‘lawful possession’ of the body, it was for them to decide which family member to allow to deal with the corpse. That hardly seems a satisfactory way to proceed. The judgement noted that the hospital intended to give it to family members who were going to bury the body and ‘there is no reason to suppose that that is not an entirely appropriate way for the deceased’s body to be given its resting place’. This seems to indicate the case was not treating the issue in the same way as a dispute over a piece of the deceased’s estate.

It also remains to be seen whether or not the case-law indicating that a part of the body can become property if it is subject to the exercise of work or skill applies to whole bodies. Presumably it does. It would be difficult to explain why skilful preservation of a part of a body turns it into property, while that is not so if the same thing is done to a whole corpse. After all, it would be surprising if Gunther von Hagens’ plastinated corpses could not be property.

Few would claim that the current law on whether and when the body or its parts can be owned is satisfactory. It is clear that parts of the body and indeed corpses can be property in some circumstances and for some purposes. Complete bodies of alive people, it appears, cannot be. But it is difficult to make a more authoritative statement than that about the law.

5.3 The Law on Integrity Rights and the Body
The law certainly protects individuals’ rights to their bodies. The criminal law, through the Offences Against the Person Act 1861 and the Sexual Offences Act 2003, protects an individual’s right to bodily integrity: the principle that a person may not be touched without their consent. For example, a doctor is not permitted to operate on a competent pregnant woman without her consent in order to save her life or that of her fetus.

However, the position in relation to removed parts of the body is far less straightforward. The law has traditionally regarded an interference with a removed part of the body as a theft, if anything at all, rather than an offence against the person. In other words the rights claimed are ones connected to a property model, rather than one based on a right to bodily or autonomy.

The uncertain position of the body in the law is reflected in the Human Tissue Act 2004 (Liddell and Hall 2005). The Act does not directly address the question of whether a person owns bodily material once it has been removed. The Act’s regulation of use of bodily material focuses on the requirement for consent, rather than the granting (or affirming) of property rights in removed material. Section 32(9) refers to human material which has become property by the application of human skill. Unfortunately it fails to give guidance as to whether human material can become property by other means and, if so, who owns it. This is particularly disappointing given that the Act is intended to provide a comprehensive framework for issues relating to the use and storage of bodily material. Pattinson (2006) has argued that section 32(9)

... clearly provides statutory support for the claim that human material can be property where human skill has been applied to it (e.g., the Dobson-Kelly position). Material that is property by virtue of the application of human skill is excluded from
the offence relating to commercial dealings. Expressed in this way, it should be clear that the Act need not be taken to prevent human material being property by virtue of some other reasons; it merely does not exclude human material that is property for other reasons from the prohibition on commercial dealings.

While this is true as a matter of literal interpretation, it is hard to conceive of a reason why human material which was property by virtue of the application of skill could be dealt with commercially, but human material which was property for some other reason could not be. Normally, the law draws no distinction between the precise way in which an item acquired property status. The more natural reading is that Parliament was indicating that the application of human skill is the only way a body can become property.

The failure of the Act to identify precisely if and when bodily material can be property causes a difficulty which goes to the heart of the legislation. Although Parliament, through the Human Tissue Act 2004, intended to reinforce the notion that we have a right to control the use of our bodily materials, it is far from clear what the source of that right is. In particular, whether it comes from a property approach or an integrity/privacy-based approach. Price (2005) concludes:

It would appear that the legislature ultimately moored the statutory framework in the 2004 Act to a rationale principally based upon the infringement of personal integrity \textit{i.e.}, to the validity of the consent governing \textit{removal} of the tissue (further uses are \textit{implicitly} consented to, \textit{i.e.}, they are ‘part of the deal’ in receiving medical treatment). Arguably, however, it is philosophically grounded in property rights and interests even despite the modifications to the Bill obviating the need for consent, but which in any event only apply to non-identifiable tissue as regards research.

5.4 Disputes over the Approaches
It is not possible here to do justice to the rich material advocating either a property approach or an integrity/privacy-based approach. But some of the key issues will be briefly mentioned. The interested reader is referred to more detailed discussions published previously (Boulier 1995; Laurie 2002a; Munzer 1990; Rao 2000; Shildrick 1997).

The word ‘property’ is used to describe not only a thing, but also a relationship between a person and a thing. So a book is a piece of property, but to say the book is ‘my property’ is to describe a structure of legal rights and obligations between me and my book. When a person owns a piece of property that usually donates a number of rights or entitlements, \textit{e.g.}, the right to use or enjoy the property, the right to exclude others from using the property and the right to sell or transfer the property to someone else (Harris 1996b). ‘Full-blooded ownership’ involves possession of all of these rights. But a lesser form of ownership may involve only some of them.

Seeing a body as a piece of property enables not only control over what is done with the body while it is part of the individual, but, more significantly, rights over the piece of property once it is removed from the person (Mason and Laurie 2001). The notion of property also carries with it the right to deal with one’s property as one wishes and this may be regarded as attractive to those keen to promote a liberal view of what one is entitled to do with one’s own body.

An integrity/privacy-based approach focuses on the right to dignity, which is closely connected to the right to autonomy and rights to bodily integrity. At their heart is the notion that we have a fundamental right to control what happens to our bodies, who touches them, when and how. Central then is the notion of consent, that there should be no touching or interference with our bodies without our consent. Control over our bodies is crucial for autonomy and our coherence as people (Andrews and Nelkin 2001). There is, however, a dispute over the role that dignity plays here (Beyleveld and Brownsword 2001). There are some who regard dignity as a restraint on how individuals deal with their bodies: even
though a person may have consented to take part in an activity, it may be outlawed because the activity violates the proper respect and dignity owed to the body. Such an argument is sometimes used to oppose the legality of selling one’s organs. To others, however, dignity is about respecting the wishes of an individual over what he/she wishes to do with his/her body (Savulescu 2003b). The Medical Research Council (2000) found no repulsion at the notion of payment for bodily samples amongst younger people in the general public, for example. To respect a person’s dignity is to respect that person’s decisions for his or her body.

Why does it matter which of these approaches is adopted? As the following points make clear, this is not just a dispute over labels.

5.4.1 Control over Removed Body Parts
The main benefit claimed by the property model is that it enables individuals to retain control over parts of their bodies when they are removed. An integrity/privacy-based model may provide protection against a person’s bodily part being removed against his/her wishes through its emphasis on the right to bodily integrity, but it provides no obvious rights over removed bodily material and no claim to any profits created through the use of such material.

Laurie (2002a) puts the argument in the following way:

A personal property paradigm could, in fact, serve an all-important role in completing the picture of adequate protection for the personality in tandem with other protections such as autonomy, confidentiality and privacy. However, the added value of a property model lies in its ability to empower individuals and communities and to provide the crucial continuing control over samples or information through which ongoing moral and legal influence may be exerted.

It may be that this criticism of an integrity/privacy-based model could be overcome by developing some kind of privacy right to control separated body parts, but such a right would not be directly analogous to privacy rights as recognised in the law to date.

5.4.2 Dignity
To some supporters of an integrity/privacy-based model, it is disrespectful to treat the body akin to property which can be traded (Skene 2002a). Can it be right to suggest that the legal relationship we have with our televisions should be the same in the eyes of the law as that we have with our bodies? To regard the body as property is demeaning and degrading to the body (Munzer 1994; Ryan 1994). It is too close to slavery (Laurie 2002b). There are some things that are too precious to be owned.

Gage J, in a case about whether pathologists legally wronged parents by retaining parts of their children’s bodies after post-mortems, noted that it appeared ‘inappropriate’ that the case had to be discussed in terms of who owned the dead children’s bodies. The principles that should govern bodies are consent, dignity and respect (Brazier 2003a). These values are not captured by the property model, integrity/privacy-based approach supporters argue (Brownword 2003).

Rao (2000), preferring an autonomy-based approach as the way of protecting the body, argues that property rights are useful for protecting market values, but that privacy rights are appropriate for spiritual ones. Our bodies are not just property; they are the medium through which we interact with the world. Our relationship with our bodies is not one of ‘having’ but rather of ‘existing’ (Toombs 1999). Such values are better protected by privacy rights than by property rights.

One response to these powerful arguments is that, however high minded, they are out of touch with reality. Bodies are commercialised whether we like it or not. In the Western world biotech scientists and their employers make large sums of money though research on bits of bodies. Why should they make all the gains from the body parts and not the people from whom the samples originated (Gold 1996)? Indeed the sale of bodily material such as
hair and sperm is socially acceptable. Also, many items of property carry value beyond the material wealth they represent: consider wedding rings for example. As long as we do not regard property as the only way a body is valued, we should have few objections. Indeed it is possible to regard something as property even if there are restrictions on access to it or restrictions on sale or use (Brownsword 2003). For example, pets are owned but there are criminal restrictions on how they can be treated and their interests are protected while still being regarded as property (but see Sect. 3.5 for a discussion about whether some animals should indeed be treated as property).

5.4.3 Technical Problems with Ownership of Bodies
To some there are technical difficulties in regarding the body as property (Davies and Naffine 2001; Harris 1996a). To constitute property an item has to possess certain characteristics and be subject to certain kinds of treatment. As bodies are neither transferable nor divisible, we cannot treat them as property. Further, rights of property in law come about in a variety of accepted ways (e.g. the fruits of labour). None of these apply in relation to whole bodies: they are not something that we created ourselves or were transferred to us from another. So even though we may feel as if our bodies are our own, they cannot be regarded as property in the way that that term has been understood by property law (Harris 1996a).

There may also be a logical problem in saying that we own ourselves, as there needs to be a clear separation between ‘the owner’ and ‘the owned’. We can only say we own our bodies if we see a clear distinction between ‘us’ and ‘our bodies’ (Morgan 2001; Naffine 1998). This kind of reasoning leads some to prefer seeing rights in respect of the body flowing from the right of privacy where an interference with the body is an interference with the self. Rao (2000) argues:

Property produces a fragmented relationship between the body and its owner, the person ‘inside’ the body, in contrast with privacy, which creates an indivisible corporeal identity. By uncoupling the body from the person and undermining the unity of the physical being, the property paradigm facilitates fragmentation of the body itself, both literally and figuratively.

... Privacy theory, on the other hand, forecloses such bodily fragmentation by identifying the person with his or her physical presence. Hence, privacy shields the individual against corporeal invasion and alteration and preserves the unity and integrity of the embodied being.

It is sometimes said that property rights are preferable to privacy rights because they provide a positive set of claims for an individual over their body, though privacy rights are negative and focus on preventing people doing things to your body (Laurie 2002a). While, therefore, they may be useful to prevent the nonconsensual removal of bodily material, they would not provide a means to claim back the material. The problems particularly arise where the material has been passed on to a third party. While a property claim may succeed against a third party, the interference with a right of privacy or bodily integrity may only be effective against the remover. This claim, however, may depend on a particular notion of rights of autonomy or privacy.

We will now seek to argue that both of these models, based on privacy or property, overlook a crucial fact about our bodies. Our bodies are not, in a straightforward sense, ‘ours’. They are interdependent, interconnected and intermingling with other bodies. This argument will now be developed.

5.5 Interconnection of Bodies
In what way are our bodies interconnected? It is not possible, of course, to provide here a complete list, but here are some examples:

5.5.1 Placenta

Our bodies start in a relationship of connection in pregnancy. The state of interconnection between the fetus and the mother is revealed in a number of ways. The mother and fetus share fluids and space. The health and well-being of the fetus can impact on the mother’s well-being in both physical and psychological terms and the reverse is also true.

Consider, for example, the placenta. It demonstrates vividly the impossibility of treating bodies as entirely separate entities. At term, the human placenta weighs about half a kilogram, and has an area of about 8 m$^2$–14 m$^2$ for exchange between mother and fetus (Beck 1991). It is a complex and dynamic interface between embryonic and maternal tissue. Implantation of the embryo involves the trophoblastic tissue of the embryo entering maternal uterine tissue to reach the blood supply, in a manner not unlike the invasion of malignant tumours (Holtan et al. 2009; Mor et al. 2017; Voss et al. 2000). The success of this process is important to both fetus and woman: it is thought that pre-eclampsia and intra-uterine growth retardation result from inadequate invasion of the embryo trophoblast (Nandi et al. 2016; Pijnenborg 1996).

Remarkably the placenta keeps the blood of mother and fetus separate, but enables the exchange of various materials. This is achieved in this manner: by the beginning of the second month of fetal life, the trophoblast has already formed a large number of secondary and tertiary villi, or tiny finger-like protuberances, in which runs fetal blood (see Sect. 2.1.4). During the following months, the barrier between fetal and maternal blood in these villi is thinned to form the basis of exchange in the placenta. Gases such as O$_2$ and nutrients can diffuse from maternal to fetal blood, while waste such as CO$_2$ and urea can diffuse from fetal to maternal blood (Bauer et al. 1998).

The placenta, then, is a complex mix of maternal and embryonic tissue which it is not possible to describe as ‘belonging’ to either. Through it there is a constant exchange of maternal and fetal material. It is a prime example of bodily interchange which is the lot of every single person.

5.5.2 Sharing of Bloods During Birth

There is no direct exchange of blood between the mother and the fetus during pregnancy. But, during delivery, this can sometimes occur, and is the cause of haemolytic anaemia of the newborn. This condition was probably first described by Bourgeois (1609). A red blood cell antigen (Levine and Stetson 1939) was suggested to be the cause (Levine et al. 1941b). The disease happens when there is antigenic incompatibility between mother and fetus. If an individual does not possess the rhesus antigen on the red blood cells, then that individual can make anti-rhesus antibodies. If an individual possesses the rhesus antigen on the red blood cells, then the individual almost never produces anti-rhesus antibodies. If a fetus has a rhesus-positive father and a rhesus-negative mother, it produces red blood cells with rhesus antigens. If, during delivery, some of the fetal blood goes into the maternal circulation, the maternal immune system will produce anti-rhesus antibodies. When the mother is pregnant again with a rhesus-positive fetus, the anti-rhesus antibodies from the mother will cross the placenta and destroy the red blood cells of the fetus, thus causing anaemia (Levine et al. 1941a,c). Here we can see the potential impact of the interaction between two bodies (the mother and newborn) producing a potentially harmful effect for a third (in the interaction between the mother and a subsequent child).

5.5.3 Breastfeeding

Breastfeeding is another example of bodily interchange. It is widely regarded as beneficial to both mother and baby. Human milk contains a large number of constituents which are beneficial to the growth and development of the child (Andreas et al. 2015). These include
fat, proteins, hormones, nucleotides, vitamins and minerals. The proteins consist of amino acids for growth and protective proteins such as immunoglobins; studies have shown that breastfeeding protects against autoimmune diseases (Borba et al. 2018). The milk is optimised for the growth and development of the baby, in that its constituents are changing constantly over time to match the needs of the growing infant at different stages of his/her development (Ballard and Morrow 2013). In addition, the act of sucking during breastfeeding is not harmful to the dental development of the baby, as compared with bottle feeding (Boronat-Catala et al. 2017).

This interchange of fluid from the mother to the baby provides benefits both to the health of the mother and to the health of the baby. In the case of the mother, studies have shown that breastfeeding significantly reduces the risk of breast cancer (Kelsey and John 1994; Lee et al. 2003; Zheng et al. 2001, 2000), endometrial cancer (Jordan et al. 2017) and ovarian cancer (Gaitskell et al. 2018). The benefits of breastfeeding (as compared to formula-feeding) for the baby include higher levels of cognitive development (Anderson et al. 1999; Huang et al. 2014; Koh 2017) and intelligence (Brion et al. 2011; Der et al. 2006; Horta et al. 2015; Victora et al. 2015). In the case of intelligence, the cause of the benefits of breastfeeding appears not to be nutritional (Kosse 2016), and this positive association with a child’s intelligence is the net of parental intelligence (Kanazawa 2015). Unfortunately breastfeeding does, however, carry some health (Borba et al. 2018), social and economic disadvantages for the mother.

5.5.4 Personal Care
The bodies of the carer and the cared-for are interdependent. For example, not only is a child dependant on the carer, but the carer becomes dependant on the child. If the child suffers an infectious childhood illness and is required to remain indoors, in effect this quarantine is imposed on the body of the carer too. If the child will not sleep, nor, in reality, will the parent. This is true not just in child-parent relationships but in any close relationship involving caring. If, for example, a carer breaks arm, this has an impact on the person cared for and, of course, vice versa. In a relationship involving dependence, an injury to the body of either the carer or the person cared for impacts significantly on the other’s body.

And this is not limited to physical issues. It is well known that attachment relationships in childhood have wide-ranging health implications (Feeney 2000). Recent work has shown that parents’ psychiatric problems can adversely affect the physical and psychological well-being of the child (Mantymaa et al. 2003, 2004; Pearson et al. 2011). The mental ill health of one person can affect the mental health of those they care for or those who are their carers.

5.5.5 Bodies and the Meaning of Life
There is a wider sense too in which our bodies interconnect. Many of the things we most greatly value in life involve the sharing and interconnection of bodies: sex, sports, massage, shaking hands, to name but a few. It is in the meeting, intermingling and interaction of our bodies that many of life’s most meaningful events occur.

5.5.6 Genetics
The more we know about the human genome, the more we realise how similar our bodies are. Even the difference between the human genome and the orangutan genome is only about 3% (Chen and Li 2001), and the genetic differences between individual humans are even smaller (Jorde et al. 2000). Jorde and Wooding (2004) shows that the average proportion of nucleotide differences between a randomly chosen pair of humans is consistently estimated to lie between 1 in 1000 and 1 in 1500. This paper further demonstrates that 85–90% of genetic variation is found within continental groups, and only an additional 10–15% of variation is found between them. Our shared participation in the common genetic pool emphasises our shared identity. As Karpin (2005) puts it, ‘The
individual in the age of the gene is fundamentally connected and vulnerable. The individual in the age of the gene always contains a trace of the other; not-one but not-two.’

5.6 Interaction with the Environment

Our bodies are also interconnected with the wider world. Food coming often ultimately from the earth is eaten, digested and removed as excreta or urine to be returned to the earth. The body inhales and exhales air. Bacteria in our bodies play crucial roles within the body and are constantly being replenished with new bacteria from outside. Most of our body surface is a micro-environment on which thrive many microbes, including bacteria, fungi and protozoa. Indeed it has been estimated that an average human is composed of about $3 \times 10^{13}$ cells, but there are about $4 \times 10^{13}$ microbial cells living on our surfaces (Sender et al. 2016). The great Oxford physiologist J.B.S. Haldane once remarked that the Archbishop of Canterbury is 65% water. One could add that he probably has more bacterial cells on his body than human cells (Sender et al. 2016).

Indeed the study of the micro-organisms closely associated with our body has led us to think that we, together with them, form a close-knit entity called a ‘superorganism’ (Lederberg 2000). These micro-organisms not only protect us from invasions from more virulent species, but participate in maintaining a constant environment (homeostasis) for the human body. They influence host development and participate in pregnancy.

For example, the physiology of our skin is greatly influenced by the associated micro-organisms (Grice and Segre 2012). The average area of human skin is about 2 m$^2$. The density of bacteria on the skin varies from about 100 per cm$^2$ to $10^7$ per cm$^2$ (Leyden et al. 1987). There are at least hundreds of known species of such commensal bacteria, and they differ from person to person and also in different skin sites on the same person (Huttenhower et al. 2012). To protect the human from invasion by virulent bacteria (Chiller et al. 2001), the skin surface is protected mechanically by several epithelia layers and by its secretions. The commensal bacteria also protect the human by a variety of mechanisms, from competing for nutrients, niches and receptors with pathogenic bacteria to directly killing the latter (Christensen and Brueggmann 2014). For example, the cells on the top layer of the human skin are the keratinocytes, and the commensal bacterium Staphylococcus epidermidis binds to keratinocyte receptors and reduces the adherence of virulent Staphylococcus aureus (Bibel et al. 1983). Commensals also release species-specific antibiotic substances called bacteriocins, which kill pathogenic bacteria, e.g., Staphylococcus epidermidis releases at least five bacteriocins which reduce the presence of virulent strains of S. aureus (Christensen and Brueggmann 2014). The effect of commensal bacteria can also be indirect; bacteria can induce the host to increase antibody production, phagocytosis and cytokine production. For example, Staphylococcus epidermidis stimulates human keratinocytes to secrete anti-microbial peptides (Lai et al. 2010). A recent case report shows that certain strains of Staphylococcus epidermidis even protect the human from skin cancer (Nakatsuji et al. 2018).

The other major surface of the body is the human gastrointestinal tract, which is colonised by mainly bacteria, but also protozoa and fungi. The density of bacteria in the lower intestine is of the order of $10^{12}$ organisms per gram of intestine contents, with about 1000 species present (Sommer and Bäckhed 2013). This is an example of mutualism: the bacteria benefit from a stable environment rich in energy source, some bacterial compounds such as short-chain fatty acids and vitamin K1 are used by the host metabolic machinery, and the commensal flora competes with invasive micro-organisms, thereby making it difficult for pathogenic bacteria to cause disease. To allow such commensal bacteria to survive, the gastrointestinal immune system has evolved to allow bacteria to grow inside the lumen of the intestine, but any bacteria crossing the boundary of the intestine will be intercepted. This delicate balance, however, is sometimes upset in disease.
For example, the bacterium *Clostridium difficile* sometimes causes infections in hospital patients. This bacterium is not usually found in the gastrointestinal tract of most people. When toxigenic strains of this bacterium infect a patient, they produce toxins that can cause severely disturbed bowel function such as frequent diarrhoea and enlarged colon in the patient (Crobach *et al.* 2018). The causes of these infections are not clearly understood, but both the bacteria and the immune system play a role (Rees and Steiner 2018). Most worrying of all, *Clostridium difficile* causes recurrent infections in about 25% of patients, and these infections can be resistant to antibiotic treatment. A new treatment has proved to be very successful in managing recurrent *Clostridium difficile* infections: faecal transplantation. Faeces from healthy donors is introduced into the intestine of patients suffering from such recurrent infections, and this method is over 90% effective (Quraishi *et al.* 2017). However, observations are emerging that faecal transplantation can severely affect the metabolism of faeces recipients. A clinical case has been reported where a woman of normal weight received a faecal transplant from her obese daughter, and the mother became obese post-transplantation (Alang and Kelly 2015). Researchers are still unsure if the newly introduced micro-organisms are the cause for the change in the metabolism of the mother, but this observation underlines how important these micro-organisms are to our physiology. Previous work has shown the importance of gut micro-organisms in obesity (Mulders *et al.* 2018) and in host health (Zeevi *et al.* 2019). Most importantly, evidence is mounting that gut micro-organisms have significant effects on the development of the nervous system and its maintenance, and that some of the neurodegenerative diseases of old age could be linked to the gut micro-organisms of the patient (Sharon *et al.* 2016).

Even the female reproductive tract during pregnancy is not sterile. Aagaard *et al.* (2014) have found microbes associated with the placenta, and curiously they are more similar to bacteria from the oral cavity than from the reproductive tract. The communication between the trophoblast cells of the placenta and these commensal bacteria probably contributes to maintaining a normal pregnancy (Mor *et al.* 2017; Mor and Kwon 2015), although the details have not yet been fully understood.

As can be seen, these commensals are essential to our bodies’ survival; indeed to distinguish between ‘them’ and ‘us’ is complex, if not impossible. It is, therefore, quite understandable that some scientists call the genome of these micro-organisms our ‘second genome’ (Grice and Segre 2012).

### 5.7 Mutability of Our Bodies

Our bodies are constantly changing. It is insufficiently appreciated that our bodies are not static organisms, far from it. They are giving to the world and receiving from it. Our bodies constantly change with cells dying and falling off and new cells being created. By the time we die there is little of us that is biologically the same as when we were born. We have, of course, limited control over our bodies, however, much we wish. Illness, obesity, pain may befall our bodies, leaving some people with a sense of a loss of control over them.

There is a constant turnover of proteins and cells in our body. Some components have a high turnover: our intestinal lining is completely replaced about once every two days (Macallan *et al.* 1998), while the average life span of the red blood cell is about 150 days, and that of the lymphocyte, about 17 days (Young and Hay 1995). In contrast, some components are not changed at all during our lifetime: the crystallin proteins which make up our lens are not metabolised at all (Derham and Harding 2002).

There is an additional consideration: parts of our bodies can now be replaced either by natural transplants (Barnard 1968; Calne and Williams 1968; Merrill *et al.* 1956; Starzl *et al.* 1968) or by artificial organs. The artificial heart (Cook *et al.* 2015) already exists, and so does the artificial pancreas secreting insulin (Weisman *et al.* 2017) or secreting insulin and glucagon (Peters and Haidar 2018). Cochlear implants already exist to replace the natural hearing apparatus, although the sound quality needs improvement (Caldwell *et al.* 2017).
Bio-electronic implants have been developed to restore vision in some blind people (Lewis et al. 2015). Neuroprostheses are being developed to help with rehabilitation from neurodegenerative diseases or injury (Lebedev and Nicolelis 2017).

5.8 Summary
The argument we have made seeks to emphasise three points. First, our bodies are often in a state of dependency on other bodies, at least that is far from an unusual state for them to be in. Secondly, our bodies are constantly interacting and reacting with the world around us. Thirdly, our bodies are not immutable entities, but are constantly changing and recreating themselves. We need to move away from a vision of a society of bodies which are of concern only to ourselves and recognise that, to a significant degree, our bodies depend on other bodies and the world around us for their meaning and survival.

It is important that we emphasise that we are not claiming that interconnection is the only way of appreciating bodies. Indeed we accept that an argument can be made for saying that the statement ‘my body is mine’ is too weak in not emphasising enough how our bodies are part of our identity and part of us. Our bodies are not just machines that we use to achieve our ends. For many people their bodies are integral to the goals they are seeking to reach. Without our bodies the plans for our life would be unattainable. Further, our bodies represent to other people what we are: they identify us and can determine how we are treated. So, for example, the perception that a body is male or female will determine the way in which a person is treated in society and the roles expected of that person. In a real sense, then our bodies are not just ours, but us.

It can, with some justification, be pointed out that it is not just bodies which have these characteristics of mutability and interdependency of the kind we have been discussing; animals, plants and land exhibit them. Yet the law is content to describe these as property. However, we argue that the extent to which human bodies gain their meaning, use and existence depends on relations with other bodies and other organisms to a greater extent than certainly plants and land. It may well be that our argument would also justify questioning whether animals should be regarded as property, but we do not intend to pursue that question here (but see Sect. 3.5).

5.9 Practical Implications of Bodily Interconnections
What we have been arguing, however, is that an important part of the picture of our bodies is that they are giving and taking not only from the world around, but also from other bodies. This, we suggest, is part of the difficulty of finding an appropriate legal response to the classification of bodies. No one model can capture the nuances of the bodily life: that our bodies are ours, are in relationship with others, are in constant flux; yet central to our identity of ourselves.

We now consider some of the issues which have troubled those who have studied the issue of the legal categorisation of the body and suggest how considering the interconnection of bodies might assist in analysis. What follows does not purport to be the only way that the understanding of bodies we promote could be applied in a practical sense. No doubt people sharing our view could still disagree on some of these issues.

5.9.1 Moore Decision and Control of Removed Bodily Products
The decision in Moore has generated much comment in this debate. John Moore, suffering from hairy cell leukaemia, had his spleen removed. Dr Golde discovered that cells from his spleen contained potentially beneficial properties. He developed a cell line from the spleen which he eventually sold for US$15 million. The products produced as a result were said to be worth several billion dollars. Dr. Golde’s research on the spleen was carried out without Moore’s consent or knowledge.
Moore brought an action based on conversion, breach of fiduciary duty and informed consent. The Californian Supreme Court rejected the conversion claim declaring that there was no precedent on which to base a claim that people had property rights in their bodies and that it would be inappropriate for the law now to recognise one. Indeed to recognise one would cause difficulties: it would hinder medical research by restricting access to raw materials and lead to a ‘litigation lottery’. The prospect of patients ‘shopping around’ to find who would offer them the best price for their bodily parts or products was not an attractive one, but the court accepted that Moore might have a claim for breach of fiduciary duty.

Dissenting from the majority opinion in the Moore case, California Supreme Court Justice Mosk argued that the law should at least recognise Moore’s ‘right to do with his own tissue whatever the defendants [including his doctor and the University] did with it: i.e., he could have contracted with researchers and pharmaceutical companies to develop and exploit the vast commercial potential of his tissue and its products.’

To some the case shows the problem with not adopting the property approach. Vast sums of money were made by the scientists involved, but the person who made ‘everything possible’ is left with nothing. A property approach would ensure he was adequately rewarded. The difficulty is that the property approach might ensure he was over-rewarded. On the facts of that case, if we regarded the DNA sequence as his and therefore him having a claim to the money produced from his property, then in theory, he should be entitled to all the proceeds. Indeed there is a danger that valuable research into stem cell lines and DNA will be hindered if patients start claiming an interest in the products (Department of Health 2002). The door might be opened to a lawyer’s goldmine as weeks are spent in the court room attempting to ascertain whose bodily material was used in the creation of a particular product. It may be that the Moore decision is complicated by the fact that the research on Moore’s body parts was carried out without his consent and permission. The decision left the deception without any form of sanction. But to penalise the use of a person’s body parts without permission does not require us to recognise the body as property. The Human Tissue Act 2004, for example, creates a scheme which to some extent protects people’s rights to control what happens to their bodily material without explicitly giving them property rights over them.

The real issue is, of course, the money. To some to give an individual whose body by chance carries a useful DNA sequence a share in millions of dollars is iniquitous. On the other hand, is it any more or less iniquitous that the money should end up in the hands of the scientists who may have put little effort into the discovery? And, of course, people are able to make large sums of money from their outward appearance which may simply be an accident of DNA. Indeed some have suggested that genetic information that creates a useful product should be seen as owned by the community and the money put to projects that benefit the community (Harris 1996b). Skene (2002b) has summarised the issues that need to be balanced here in the following way:

We need legal principles that promote healthcare, teaching, medical research and the development of new drugs, but at the same time to take account of people’s sensitivity concerning the removal, retention and use of human bodies, excised body parts and tissue.

She believes the best balance is achieved by relying on autonomy rights rather than on property rights in respect of bodily material.

Seeing the Moore decision with the points made above concerning interconnection and mutability provides some further perspectives. First, as our bodies partake of the great giving and taking between all bodies, there is an argument that it is only just that if a body holds a key to assisting others this be made available. In other words, a moral obligation to allow one’s material to be used for the benefit of others could be said to arise. This might even lead to a presumption that an individual consents for his/her material to be used for medical research (Harris 2002). Harris (2005) has further argued:
We all benefit from the existence of the social practice of medical research. Many of us would not be here if infant mortality had not been brought under control, or antibiotics had not been invented. Most of us will continue to benefit from these and other medical advances (and indeed other advances such as clean drinking water and sanitation). Since we accept these benefits, we have an obligation in justice to contribute to the social practice which produces them.

This, however, is not an argument about who should receive the money created by the use of the material. It is, however, an argument that the provision and use of such material should be regarded as a natural reflection of the interchanges between bodies and should be encouraged and enabled by the law. If money is required to change hands and to encourage the natural use of such material, then that should be permitted.

Second, any argument that this material was just Mr Moore’s should be resisted. His body and spleen were the product of the interaction between his body, other bodies and the wider environment. The removal of the spleen and its use in another’s body could be regarded as no more than the continuation of the interchange between his body, other bodies and the wider world from which he had benefited before. Our argument that it is permissible to use people’s biological material without consent for research is not based on the utilitarian argument that to do so benefits humankind (Bovenberg 2004), but rather is based on an obligation flowing from the interconnections between bodies and the world from which the individual has benefited in the past and will benefit in the future.

5.9.2 Conceptions of Genetic Privacy
It is generally thought that medical information about oneself should be kept confidential unless you choose to make it public. However, with increasing understanding of genetics, this is no longer possible. Genetic information is not data that can be regarded as belonging to one person, but rather to their family and even wider community. An analogy might even be drawn with the way that the deep seabed can be regarded as part of the ‘common heritage of mankind’ (Strati 1991). The ethical and legal regulation of confidential information has been based on the assumption that the information is of significance only for the relevant patient. However, in the case of genetic conditions this is no longer true. In 2001, the Court of Appeal approved the use of anonymised data for research purposes, without the consent of the individuals.23

Genetic medical information is not just ‘my information’ but ‘our information’ (Gertz 2004) and it is difficult to fit within the traditional model protecting medical confidentiality (Laurie 2002a; Sommerville and English 1999). This then leads to complex issues arising when one person has tests which reveal significant genetic information about their family which he or she does not wish revealed. The Human Genetics Commission (2002) has argued:

Bearing in mind the principle of genetic solidarity and altruism, we take the view that disclosure of sensitive personal genetic information for the benefit of family members in certain circumstances may occasionally be justified. This would arise where the patient refuses to consent to such disclosure and the benefit of disclosure substantially outweighs the patient’s claim to confidentiality.

A good example of how these disputes can play out in practice is ABC v. St George’s [2015] EWHC 1394 (QB), [2017] EWCA Civ 336, [2020] EWHC 455 (QB). In this case, a man had been diagnosed with Huntington’s disease. This is an inherited neurological condition that usually manifests itself after 40 years of age and currently has no cure. The patient asked his doctors not to tell his children of the diagnosis. They complied with his wishes and that meant his children (who had a 50% chance of inheriting the disease) did not realise they could be tested, although they later accidentally found out the information. The children claimed that the doctors owed them a duty of care to inform them of the risk,
particularly as one of the children was thinking of beginning a pregnancy. The defendants were, respectively, St George’s Healthcare NHS Trust, South West London and St George’s Mental Health NHS Trust and Sussex Partnership NHS Foundation Trust.

At first instance Nicol J held that the doctors were not under a duty under the law of tort to tell the children, although it would not be a breach of confidentiality if they were told. However, the Court of Appeal held it was arguable that the doctors did owe them a duty to disclose the information. Irwin LJ, referring to the case law which requires doctors to inform patients of information about their treatment decisions, said: ‘[I]t is at least arguable that it is irrational to emphasise the need to inform patients so that they may take their own decisions about treatment, whilst at the same time depriving of any legal remedy identified individuals in respect of whom a relevant doctor has specific information which should cause them to become patients.’

However, on the rehearing, Mrs Justice Yip held that ‘[the NHS Trust] owed the claimant a duty of care to balance her interest in being informed of her genetic risk against her father’s interest and the public interest in maintaining confidentiality. The scope of that duty extended to conducting a balancing exercise and to acting in accordance with its outcome.’ However, the doctors had conducted the balancing exercise as required, and had not breached their duty of care to ABC, ‘The decision not to disclose was supported by a responsible body of medical opinion and was a matter of judgment open to the second defendant after balancing the competing interests.’

The arguments in this chapter would support an approach based on ‘genetic solidarity and altruism’. However, we would place little weight on the patient’s claim to confidentiality in the case of genetic information which is relevant to the patient’s family, as the information is not in truth the patient’s. Rather the issue is the balancing of the relatives’ right to know and right not to know, as developed in Graeme Laurie’s analysis of the issue (Laurie 2002a). He explains that privacy can be understood in two senses: spatial privacy, which is ‘a state of non-access to the individual’s physical or psychological self’, and informational privacy, which is ‘a state in which information about an individual is in a state of non-access from others’. So understood, privacy can be used to support both a right to know some information and a right not to know other information.

It is important to note that, practically, genomic anonymity can be broken relatively easily. Gymrek et al. (2013) started with the observation that surnames and Y chromosomes go together. They used ten entire genomes publicly available from the 1000 Genomes Project and developed a computer program to examine the Y chromosome and identified characteristic variations in the Y chromosome. They searched commercial genealogy databases and scoured the World Wide Web for pertinent information (age, place of residence, etc.). They were able to identify five people and their family trees with very high probabilities. This discovery prompted the US National Institutes of Health to remove age information from the database.

5.9.3 Human Tissue Act 2004
The Human Tissue Act 2004 of England and Wales (and the Human Tissue [Scotland] Act 2006) attempts to strike a delicate balance. On the one hand, it recognises the importance of ensuring that there is effective consent to the removal and use of human tissue. On the other hand, there is a recognition that the use of human tissue is enormously important for research into medical illnesses and for training (Genetics Interest Group 2004). The Act attempts to restore public trust into genetic research and the collection of human biological samples (Medical Research Council 2000), but not at the cost of severely hampering research into fatal diseases.

It might have been thought from the furore that followed the various scandals preceding the Act and some of the rhetoric from the government in connection with the Act that we would have a clear principle that body organs and materials can only be retained with consent. Although this appears as a cardinal principle, the number of exceptions to it means
that its paramountcy is greatly weakened. We cannot say to patients that ‘when the Human Tissue Act is in force no human material can be taken from your body without your consent’; we can only say that ‘no human material can be taken from your body without your consent, unless it is permitted under the Act’. Notably a person’s material can be used without their consent for training, audit or teaching. The justification of the exception that it is ‘considered intrinsic to the proper conduct of a patient’s treatment or are necessary for the public health of the nation’ will not convince everyone (Department of Health 2004).

To many the Act represents an uneasy compromise between an individual’s rights on their own bodies and the interests of society in general, or between models based on using rights or property models to protect bodily material. However, the approach adopted in this chapter sees bodies in part ours and in part in constant interchange with others and the world around us. The Act simply reflects the uneasy tension which is the truth about bodies. It is not the Act’s fault that a clear conceptual basis cannot be found; it is a reflection of the tensions that should be seen in the body.

We now proceed to discuss some provisions of the Human Tissue Act 2004.

**Organ Donation**

The law on organ donation as set out in the Human Tissue Act 2004 starts with no presumption of consent and only permits the removal of an organ from a live person or a cadaver where there is appropriate consent (Liddell and Hall 2005). In cases where organs are removed from a dead person, consent must come from the individual himself or herself; or failing that, from a person nominated by the deceased to make the decision; or failing that, from the person who is in the closest ‘qualifying relationship’ to the deceased. In the absence of consent from one of these sources, organ transplantation is not possible. Live organ transplants require not just the consent of the individual, but also the approval of the Human Tissue Authority. Before giving approval for a living organ transplant, interviews must be conducted with the donor and a report prepared for the Authority by an independent assessor (Human Tissue Authority 2006a). The law, therefore, is not willing to presume consent. Indeed in the case of live organ donations to unrelated recipients, even where there is consent, the donation is treated with suspicion: in the case of an altruistic donation, a psychiatric assessment of the donor should be carried out.

In light of the arguments above, we suggest that organ donation should not be regarded as an unnatural activity requiring an unusual degree of consent from all interested parties before it is permitted, but rather as a natural part of the interaction between bodies. The law should therefore facilitate organ donation to a much greater extent than it currently does. For example, it could presume consent in the case of the deceased, and welcome and encourage donation in cases of live organ donation. The practical issues surrounding organ donations are complex, and it is not possible to discuss how our approach can be developed in relation to organ donation in depth. We, however, argue that the law’s approach to organ donation should start by seeing it as a reflection of the natural interaction between bodies and the interdependence of bodies. As all of us have enjoyed and participated in such interactions during our lives and we can presume that it is something we would wish to continue to be involved in after death. As Leder (1999) has argued,

If the presumption [that a person consents to removal of organs for transplantation after death] is in the unlimited power of a coercive state, then this manner of organ collection will tend to be felt as intrusive, and enacted in pernicious ways. However, in a society embracing interconnection what is presumed is something quite different: that we are so intimately interwoven in nature and society that the body is never simply one’s own but part of a wider circulation. The taking of organs need not then be schematized as the Cartesian extraction of a useable resource, so much as a ceremonial offering with resonances of humility, compassion, and affirmation of life.
A presumed consent model is not, however, the only direction our approach could take. Consider the following passage from the discussion of Brazier (2003b) of claims that relatives can claim a right to have a say over what happens to a family member’s body after death:

If my relative’s body is mine, be she child, mother, or sister, I may do with my property as I wish. I may elect to sell her component parts in public auction. I may donate her for display as a plastinated exhibit.

The ‘property’ debate cannot be shirked. I use it here simply to demonstrate that consent based on ownership — this body is mine — authorises not just a right to say NO but grants untrammelled rights of disposal to the ‘owner’. Despite the language of ours and mine, it is an option most of the families I have met abhor. The sense of continuing relationship, of still being parents, sharply distinguishes their child, or their husband, from their house or their car. The interests which families perceive centre on the integrity and welfare of the family of whom the deceased is still a part, and will remain so for decades, if not generations. How the mortal remains of that person are laid to rest (or otherwise disposed of) is of overwhelming importance for the health and future of that family. The injury done to a family whose religion requires burial of the body intact, or cremation of every speck of bodily material, when organs are taken without their permission is a violation of religious freedom.

This passage emphasises the significance that a body can take in a communal life. In our terminology, such an approach could be supported on the basis that for that body within its community, full disposal is part of the proper ‘give and take’ between bodies. In that community of bodies, a burial of the full body is a reflection of the recognition of the significance of bodies.

**Not Just Cells**

Section 53(1) of the Human Tissue Act 2004 states that the Act is concerned with ‘material, other than gametes, which consists of or includes human cells’. While the drafters of the Act assumed that the phrase ‘human cells’ covered everything in our bodies, in fact, much of the ‘stuff’ of what would generally be regarded as part of the human body is not made of live cells. Here are some examples:

1. Bile consists mainly of electrolytes such as sodium and chloride ions, and organic substances such as proteins, bilirubin and fatty acids, and a very small number of cells (Dittmer 1961).
2. Pancreatic juice is a clear solution with digestive proteins. A very small number of cells are sometimes found in it (Bro-Rasmussen et al. 1956).
3. Urine contains only a very small number of cells.
4. Ear wax contains only dead cells.
5. Faeces is composed of digested and a small amount of undigested food, with a small number of cells from the digestive tract mixed with it (Berk et al. 1985).
6. Nails are explicitly excluded from the Human Tissue Act 2004 definition, but much of the nail is in fact dead cells (Stenn and Fleckman 2000). The nail unit consists of the nail plate itself, nail bed on which most of the nail rests, the nail matrix from which the nail plate grows, and the hyponychium and eponychium, which are epithelia, respectively, at the finger-tip and the dorsal proximal end of the nail plate (Fig. 5.1).
7. The human hair consists of three layers. The outermost layer is the cuticle, the middle layer is the cortex and the innermost layer is the medulla. The cortex is mechanically
the most important part of the hair shaft, and consists of cortical cells. Cortical cells are dead cells, and are composed largely (about 90%) of $\alpha$-keratin.

Hair growth takes place in the hair follicle, which is a downgrowth of the epithelium of the skin into the dermis. The follicle also contains some dermal components called the connective tissue sheath. Hair fibre is formed by the epithelium-derived cells of the hair follicle. Cells from the lowest part of the follicle divide and move towards the skin surface. As the cells move, they change shape and lose their ability for further division, and synthesise keratin. Finally the cells die and what remains is the hair shaft (Marshall et al. 1991).

It is not our claim that these examples are not covered by the Human Tissue Act 2004 (some of them do include cells), but that they demonstrate the complexity of the biological material making up our bodies, and that this cannot be readily reduced to ‘human cells’. As we have already seen in Sect. 5.6, there are equal numbers of human cells and cells from microbes on ‘our’ body.

Fig. 5.1 Diagrams showing the detailed anatomy of the finger nail. Taken from Wortsman (2018)

5.10 Body as Property?
From what has been said so far, it should be clear that the assumptions behind the debates over the legal nature of the body are questionable. Our bodies are not made of just human material; they are unstable, unbounded and interdependent. Does this mean that they cannot be property? No. But they provide good reasons why it is better not to see them in that way. Our observations challenge some of the arguments that form the basis of some claims of property ownership. A popular argument is that a body is owned by a person because it can be seen as the product of their labour. Such an argument, of course, most famously relies on John Locke’s theory of property. There are a number of difficulties with this argument, but the one that is relevant to this chapter is that some parts of the body are not generated by us. They come from outside or are generated by micro-organisms in or on our body. If labour is the source of ownership, then at the best we might claim a joint ownership with the many micro-organisms which play a crucial role in our body’s maintenance.

Another argument that is sometimes used is that recognising property rights in body parts is the most effective way of protecting the interests we have in our bodies, because they are ‘us’. This forms the basis of some of the arguments used by those promoting autonomy or privacy. Again this argument suffers various weaknesses, but for now our focus is on the point that our bodies are not just us. Our bodies contain materials which in biological terms are best understood as separate creatures. Further, material on our bodies has come from other bodies and will soon pass on to other bodies.

In the light of these observations, the debates that have pre-occupied legal philosophers and medical ethicists as to whether our bodies are our property or whether bodies are better protected by rights of bodily integrity or privacy have rather missed the point. Neither model reflects the biological reality that bodies are a complex mixture of human and non-human cells, organisms and material. In Sect. 5.6, we have explained faecal transplantation. In this procedure, the donor gives away some of his/her tissues and associated bacteria to the recipient. The component responsible for treatment is bacterial, but without the tissue of the donor, the bacteria will not grow. One could imagine a scenario in some societies where the faecal material is bought and sold (as it is in some parts of the US). Would the donor be selling his/her tissues? Yes. Are the tissues responsible for treatment? Not really, because the bacteria are. Does the donor own the faecal material? The donor does own the tissues, but does the donor own the associated bacteria? As these questions indicate, it becomes impossible to draw a line between what belongs to the human and what does not.

An obvious response to what we have said so far may be that what we have said about bodies is true of many things which we readily accept as property. Land is constantly changing and materials fall off other lands onto it and vice versa. What we have said is just as true of animals too and yet we do not have difficulty in determining animals as property (but see Sect. 3.5). So, do our points add to the debate? We suggest two reasons why they do.

Firstly, many of the issues that arise involve very small parts of the body. The leading case of Yearworth involved a small sample of sperm. The Court of Appeal ruled that even though the sperm had left the appellants, it was still their property. Yet in relation to land, there is no dispute over tiny portions, especially not the parts which fall onto land from elsewhere, such as a leaf. The odd leaf on a garden lawn is of no interest or relevance to the purchaser of a house. The odd bit of sperm in a test tube can be hugely significant. So while in other areas of property law, problems over abandonment and tiny bits of property give rise to no real concern, they do when we are considering bits of bodies, because even tiny bits of bodies can carry great significance.

Secondly, and more significantly, our classification of bodies and parts of bodies is saying something about how we identify ourselves and parts of our bodies. Our description of what is property says something about its value and place in the world, as would a determination that something did not amount to property. We believe the leakiness, the interconnections,
the interchanges between bodies are a central aspect of our humanity, in biological, but also social and psychological senses. These are lost in the reduction of our bodies to property. This matters less in our discussion of the earth, where the relational aspects are not central to their identity or meaning. The debate over human nature and the regulation in dealings of bodies become restricted to a highly individualistic model when the debate is structured around property. That may or may not be appropriate, but it should not be fixed by the language used.

5.11 An Alternative Approach

So far we have argued that the debates over the legal attitude towards bodies and body parts have adopted a highly individualistic stance. Both those arguing from a property perspective and those arguing for a human rights approach overlook the relational aspect of the body: that bodies are biologically a mixture of dead material and live material, cellular and noncellular, human and non-human. Our bodies are marked by their interconnection with other bodies and with the environment. The models of seeing the bodies or parts of the body as ‘ours’ which need protection by property rights or rights of autonomy overlook these important relational interests and skew the debates over the correct regulation of the body and body parts in an individualistic approach.

A second point we would raise against the claim that our bodies are property is the following. We do not have the same interests in each part of our bodies. The kinds of interests and rights we would claim or wish to claim vary depending on the circumstances of the separation of the bodily material and the nature of the bodily part or product in question. People simply do not have the same kind of attitude towards the dry skin that drops off as they walk by, as they do towards a donated egg. The following points are particularly pertinent.

1. First, treating something as your property can carry with it burdens and responsibilities. If you leave your property on someone’s land, they can regard that as an interference in their rights. It can amount to the offence of littering. If your property damages another person’s property, you are liable to compensate them. If you leave a hair in a taxi, are we sure we want you to be responsible for that property? True, we might seek to rely on the defence of abandonment, but that may not entirely relieve you of responsibilities in relation to your property. In any event so much of our bodily material is dropped off in day-to-day activities and, in so many situations, we do not want to claim property rights in our bodily products and parts, that abandonment would need to be used in nearly every situation in which a bodily part is separated. Surely a more sensible approach would be to recognise that there are a few specific situations in which we might want to protect our interests in our bodies and legislate in favour of them, rather than claim property rights in all body parts, but rarely apply them.

2. Second, treating all your bodily parts as property can impose undue burdens on others. This means people have obligations to identify the owner in so far as is reasonable before removing the property, for fear that otherwise they may face a penalty for criminal damage or theft. Again, dishonesty or belief in consent can provide defences, but that is a strange way of looking at the situation. A person who throws away a hair left behind by a friend is not committing an offence to which they have a defence, but is not doing anything wrong at all.

3. Third, different parts of the bodies carry different meanings and different interests. Consider, for example, the issues raised in the Evans v UK[^30], which involved a couple who had donated their gametes to produce stored embryos, but then disagreed on how they should be used. The case raised complex issues over rights to reproduction, efficiency and consistency; state regulation of assisted reproduction; interests of the
embryo; gender discrimination; and we could go on (Lind 2006). Whether the sperm
and egg were property or not rather pales into significance in that case. Quite clearly,
the case would be utterly different if the two individuals had donated hair that had been
reduced to a piece of art. Even if you do support accepting property interests, this
example shows that property could only ever be the first tiny step in dealing with the
legal issues raised by body parts and does not deal with the host of other issues raised.

It seems to us, therefore, far more preferable to produce a statutory approach which can
provide appropriate rights over particular kinds of bodily material in particular kinds of
circumstances, which may indeed in some situations look like property rights, rather than
base the response of the law on the approach that bodies are property: the interests of the
individuals concerned, the interests of the state and other individuals vary enormously
depending inter alia on the part of the body we are talking about, the circumstances of the
removal and the use to which it is being put. It may well be that in some cases, the statute
would give rights which will look very much like property rights. In other cases, the proper
balancing of the interests will have nothing equivalent to a property interest. In some
circumstances we wish to disclaim any responsibility or rights over bits of the body (e.g. the
fallen hair), while in other circumstances we wish to have full control rights. The Human
Tissue Act 2004 is a fine example of a statute which seeks to balance the competing
interests of individuals, family members, researchers, educators, doctors and the wider
public. It provides a far more sophisticated approach than a straightforward property
approach ever could.

This is not to say that the Human Tissue Act 2004 is complete. The Act says nothing
about commensal micro-organisms on and in our body. As medicine improves, many things
consisting of a mixture of our own cells and commensal microbes) will find uses, and they
may well acquire commercial values. The Act has not dealt with them at all. We suggest that
these issues be examined by Parliament sooner rather than later, as medical advances will
soon present problems for the courts.

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Footnotes

2 Moore v. Regents of the University of California 793 P 2d 479 (Cal. 1990).


9 [1998] 3 All ER 714 at 749.


11 [1996] 4 All ER 474.

12 [1908] 6 CLR 906 at 914.


18 The Court of Appeal in Dobson v. Northern Tyneside Health Authority [1996] 4 All ER 474, at 478. obiter accepted that the general approach of the common law was that a body was a res nullius and therefore incapable of being property.


22 Moore v. Regents of the University of California 793 P 2d 479 (Cal. 1990). For a useful discussion of the issues arising from this case see Harrison (2002).


27 Human Tissue Act 2004, section 1 and Schedule 1.


30 *Evans v UK* [2007] 43 EHRR 21.
6. Sickness

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6.1 Introduction

‘Early to bed and early to rise makes a man healthy, wealthy and wise’ goes the common saying. This pre-supposes that people wish to be healthy, wealthy and wise, and that is probably a fair assumption. Health is becoming a modern-day obsession. Fit-bits and other activity trackers are worn to ensure one has sufficient exercise. The obsession over healthy eating has a long history. ‘How are you?’ is a standard opening pleasantry in many a conversation. Yet lurking behind this innocuous question is a more profound one. What is it to be well? How are we to understand the notion of health?

These questions are important. Lawyers have attached increasing weight to a ‘right to health’. In elections, health is nearly always recognised as a key theme. Most governments seek to promote health and will have a Department for Health (or some such body). Many employers these days want to be seen to encourage good health among employees. But, what is it, precisely, that these bodies are seeking to achieve? Not surprisingly such questions have produced a burgeoning literature on the definition of health (de Campos 2017; Foster and Herring 2016).

This chapter explores these issues. The academic literature, particularly the medical literature, is typically premised on assumptions about what a good human body is like or what a good life will be. It is assumed that our normal status is to be free of illness and impairment. The goal of medicine is to return the body to its natural ‘disease-free state’. Callahan (1998) describes well a standard understanding of health:

The goals of medicine encompass the relief of pain and suffering, the promotion of health and the prevention of disease, the forestalling of death and the promoting of a peaceful death, and the cure of disease when possible and the care of those who can not be cured.

By contrast Illich (1974) sees suffering and disease as part of health:

The ability to adapt to a changing environment, to growing up and to ageing, to healing when damaged, to suffering and to the peaceful expectation of death. Health embraces the future as well, and therefore includes anguish and the inner resources to live with that anguish.

In contemporary writing, especially from feminist and disability scholars, there are arguments that we should see impairment and vulnerability as part of the essence of being...
human (Herring 2016). Under that approach wellness involves being independent and self-sufficient, whereas being interdependent is inevitable and necessary for human flourishing. It is assumed that health is an individual characteristic, whereas our wellness is found in our relationship with others.

6.2 Definitions of Health

When the World Health Organisation (WHO) was first established, its founding statement defined health (World Health Organisation 1947) in the following way:

Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.

The WHO continued the work of classifying disease. Its International Classification of Diseases (ICD) seeks to provide standard definitions and a list of conditions which are recognised by the medical profession (World Health Organisation 2011). The original purpose of the ICD was to ‘classify causes of mortality as recorded at the registration of death’. Later, its scope was extended to include diagnoses in morbidity. The authors of the ICD admit:

Although the ICD is primarily designed for the classification of diseases and injuries with a formal diagnosis, not every problem or reason for coming into contact with health services can be categorized in this way. Consequently, the ICD provides for a wide variety of signs, symptoms, abnormal findings, complaints and social circumstances that may stand in place of a diagnosis on health-related records.

Therefore, there are two categories found in the ICD classification which address these factors directly found in chapter 18 ‘Symptoms, Signs and Abnormal Clinical and Laboratory Findings, Not Elsewhere Classified’ and chapter 21 as ‘Factors Influencing Health Status and Contact with Health Services’ (World Health Organisation 2013).

The WHO is well aware that disease or health does not depend on the diagnosis alone, but also on many factors external to the patient. The WHO International Classification of Functioning, Disability and Health (World Health Organisation 2002) explains:

Two major conceptual models of disability have been proposed. The medical model views disability as a feature of the person, directly caused by disease, trauma or other health condition, which requires medical care provided in the form of individual treatment by professionals. Disability, on this model, calls for medical or other treatment or intervention, to ‘correct’ the problem with the individual.

The social model of disability, on the other hand, sees disability as a socially-created problem and not at all an attribute of an individual. On the social model, disability demands a political response, since the problem is created by an unaccommodating physical environment brought about by attitudes and other features of the social environment.

On their own, neither model is adequate, although both are partially valid. Disability is a complex phenomena [sic] that is both a problem at the level of a person’s body, and a complex and primarily social phenomena. [...]
bodied. We shall impart two anecdotes to illustrate the difficulty of answering the question, ‘What is disease?’

One of us (PC) recalls as a medical student dealing with a patient who had proteinuria. After doing all the tests, up to taking biopsies from his kidney, nothing seemed to be wrong (this was before medical genetics was in widespread use; these days we would have done a genetic screen of this patient). The medical team reassured the patient that he was all right, and that some people might have proteinuria but live to 80, and it is just one of those quirks of Nature. They asked him to come back for tests once a year, and discharged him. Was this patient ill?

One of us (PC) once talked to a medical friend who had recently admitted a child of fourteen who presented with a fainting episode. On admission to hospital, the clinicians diagnosed a transient ischaemic attack (TIA), or a ‘temporary stroke’. A CT scan showed no abnormalities, and an NMR scan shows that in the right frontal lobe, there were some abnormalities in the white matter. A metabolic screen was ordered, and the results showed that the patient had marginally raised sulphites in the urine, and decreased blood levels of arylsulphatase A below the normal range, though not to a level which is normally seen in the disease state. A follow-up genetic screen was performed, and the patient was found to have three mutations in the two alleles of the arylsulfatase A gene which characterise metachromatic leukodystrophy. Two of these mutations were the recognised common pseudodeficiency variants, a pseudodeficiency being thought to be a variant that, although causes a lowering in enzyme activity, does not cause the disease itself. However, the patient was otherwise well; he had none of the ‘classical’ symptoms of metachromatic leukodystrophy, or at least he had not developed any of those symptoms yet. What should we do? The treatment for metachromatic leukodystrophy is a bone marrow transplant, which carries significant mortality and morbidity. Is it worth risking a bone marrow transplant for what seems to be a one-off incidental finding? While watchful waiting was adopted after discussion with the family, they were counselled that early bone marrow transplant had a far better outcome prognostically that one performed further into the disease. The continuing increased medicalisation of the patient continues in what could be an entirely healthy individual. Does he have a disease?

Precision in disease definition is of particular importance in the areas of newborn screening (see Sect. 2.6) and pre-implantation genetics (see Sect. 2.2.4). It is obvious that definitions of disease change over time.

6.3 Case Study 1: Epilepsy

We could find no better illustration of these changes by examining the history of epilepsy. This disease comes about because of abnormal activity in the brain (Goldberg and Coulter 2013). Some of the cases have genetic components (Noebels 2015), but others arise from trauma to the brain (Hunt et al. 2013). Epilepsy certainly is not infectious, and does not necessarily lead to cognitive impairment.

Epilepsy was probably first described by Sumerians. We are certain that between 718 and 612 BC, the Babylonians described it (British Museum tablet BM 47753, see Kinnier Wilson and Reynolds (1990)); they thought that this disease was caused by supernatural entities. Epilepsy was described slightly later in China during the Warring States Period (404–221 BC) (Huang Di Nei Ching; see Lai and Lai (1991) for a short discussion), but it was viewed as a disease, with acupuncture, herbal medicine and massage recommended as possible treatments. Ancient India also viewed epilepsy as a disease with possible treatments (Manyam 1992). ‘The Sacred Disease’, attributed to Hippocrates, also contains a description of epilepsy, but the author rightly claimed that this disease has no supernatural cause, is curable, and even correctly identified the cause of the disease to lie in the brain (Hippocrates ca. 400 B.C.).

Sadly, the Judaeo-Christian tradition propagated the misconception that epilepsy was caused by demons, and also the myth that this disease was contagious (Diamantis et al.)
2010). We had to wait until John Thompson Dickson to suggest that decreased ‘vitality’ in certain areas of the cerebral cortex caused epilepsy (Thompson Dickson 1869, 1870a,b). Subsequently, Thompson Dickson (1872a,b) clearly stated that

the manifestation of epilepsy was a concatenation of phenomena dependent upon various abnormal states of the surface grey matter of the cerebral lobes […] It will not therefore be difficult to grasp the fact, that if the spot on the surface which becomes the seat of the affection should be a centre presiding over a ganglion controlling muscular movement, convulsion or movement in the muscles so deprived of control will occur; but if, on the other hand, the spot on the surface not be associated with ganglia controlling muscles, muscular manifestations cannot occur. And what is true of the muscular manifestations is true of all other manifestations of epilepsy, and so definite and perfect are the relations to control of function that they can be brought into algebraic formulae.

At about the same time, Hughlings Jackson published his classic A Study of Convulsions (Hughlings Jackson 1870), where he stated: ‘A convulsion is but a symptom, and implies only that there is an occasional, an excessive, and a disorderly discharge of nerve tissue on muscles.’ Like Thompson Dickson, he thought that this discharge came from the cortex, when he wrote subsequently: ‘Epilepsy is the name for occasional, sudden, excessive, rapid, and local discharge of grey matter’ (Hughlings Jackson 1873). These ideas are very similar to modern ideas on epileptogenesis, and were subsequently confirmed by Penfield and Jasper (1954).

The next great advance came with efficacious drugs for treating epilepsy, potassium bromide and potassium iodide (Wilks 1861). In 1912, another anti-epileptic drug was discovered, phenobarbital or luminal. This drug was synthesised by Bayer, but was accidentally found to be useful for epilepsy (Hauptmann 1912), and became popular because it had fewer side effects. This was followed in the 1950s by benzodiazepines, many of them synthesised by Leo Sternbach when working for Hoffmann-La Roche (Sternbach 1979). Subsequent research shows that benzodiazepines act on a membrane protein, the γ-aminobutyric acid type A (GABA_A) receptor (Möhler and Okada 1977; Squires and Braestrup 1977), to exert their therapeutic effect. Nowadays in affluent societies, most people would view epilepsy as a non-transmissible physical illness, not infectious and certainly not caused by demons.

It would be easy for us to stand from where we are and laugh at people who see epilepsy as a curse or something caused by demons; this still happens in some places on the earth. And people in mediaeval Europe or ancient Babylon were probably convinced that they were right to see epilepsy coming from supernatural entities. It is through better scientific understanding that we came to realise the basis of epilepsy. But it took us over 26 centuries to come to where we are. Similarly, homosexuality was viewed as ‘unnatural’, but science discovered it in many animals (Poiani 2010; Sommer and Vasey 2006). These discoveries were referred to in the amici curiae brief of the American Psychiatric Association for Lawrence v. Texas [2003] 539 US 558, which struck down the sodomy laws in fourteen US states. Could we be holding beliefs about certain diseases or non-diseases which would seem irrational and nonsensical in 26 centuries’ time?

6.4 Case Study 2: Schizophrenia

The most likely candidates are probably the psychiatric illnesses, simply because their diagnoses rely mainly on symptoms, and can be subjective. Moreover, little is known about the pathogeneses and disease mechanisms of mental illnesses, simply because we know so little about how the brain functions. Another complicating factor is that there is a very large social dimension to psychiatric illnesses; indeed, some sociologists would go so far as to claim that mental illnesses are merely social constructs (Bowers 1998). However, even with
all these other complicating factors, a picture is gradually emerging that there is a biological and an environmental basis to most, if not all, psychiatric illnesses.

Take, for example, schizophrenia, a psychiatric illness characterised by distortions of thought and feeling for a prolonged period of time, in the absence of any known organic causes such as brain tumour. The International Classification of Diseases 10th edition (World Health Organisation 2011) contains detailed diagnostic criteria for mental illnesses, but those for schizophrenia are almost entirely based on symptoms. These diagnostic criteria can be traced to the clinical work of Kraepelin (1893) and Bleuler (1911). Kraepelin first described this illness on pp. 435–445 of the 4th edition of his textbook, naming it ‘dementia praecox’ (Kraepelin 1893). Bleuler (1911) first named it ‘schizophrenia’, to mean there is a separation of function between thinking, memory and affect. Sadly this name has later been borrowed to mean ‘split personality’, which is very different from schizophrenia. Although schizophrenia first made its appearance in the clinical annals in the nineteenth century, researchers suggest that it was also present much earlier, perhaps as early as the fourteenth century in Europe (Heinrichs 2003).

Scientists have attempted, for a long time, to put schizophrenia on a physiological basis, and avoid the somewhat subjective diagnostic criteria in use. Clinicians have known for a long time that schizophrenia has a high heritability of up to 80% (Sullivan et al. 2003). A large-scale analysis of over 3300 European schizophrenia patients with over 3500 controls show that there are two genetic components, one involving the major histocompatibility complex, and the other involving thousands of genes, each with a very small effect (International Schizophrenia Consortium 2009). These susceptibility genes appear to cause grey matter loss and neuron pathology (Bennett 2011), probably via neurotransmitter changes (Schizophrenia Working Group of the Psychiatric Genomics Consortium 2014) and an inflammation pathway (Najjar and Pearlman 2015). There are also brain connectivity changes (Konrad and Winterer 2008) and glial cell changes (Bernstein et al. 2015) in schizophrenia; some of these glial activity changes have been visualised by brain scans (Bloomfield et al. 2016). And the role of environmental factors such as social stress in the pathogenesis is gradually being defined (Mizrahi 2016).

A picture is thus slowly emerging that schizophrenia is linked to defined pathophysologies. Discrete observations are being connected together to form a concrete picture of how genetic and environmental factors combine to produce this disease. Science is reducing the social factors in clinical diagnosis. Indeed, a blood test has been proposed to improve the determination of psychosis risk (Perkins et al. 2015). In the future, we can look forward to more objective diagnostic criteria for even mental illnesses.

6.5 Autonomy and Interdependence

In this section we explore two understandings of health: one based on an individualised model of health where the healthy body is seen as one where a person is self-sufficient and has autonomy, and another where a person is vulnerable and depends on others. These are commonly presented as two alternatives, but the there are elements of truth in both models.

6.5.1 Independence and Autonomy as Health

This is the model of health most readers will be familiar with. A well person is one who is able to function independently from others and is able to have a large degree of control over his/her life. In short the traditional understanding of autonomous health is that a person should be ‘author of their life’. Life should be self-determined. As Berlin (1958) puts it:

I wish my life and decision to depend on myself, not on external forces of whatever kind. I wish to be the instrument of my own, not of other men’s act of will. I wish to be a subject, not an object; to be moved by reasons, by conscious purposes, which are my own, not by causes which affect me, as it were from outside.
Or as Pettit (2001) puts it:

We want to be the authors of our own stories, to be able to look on our works and say: ‘This bears my signature, this is me.’

Hence illness is typically seen as a time when we become dependent on others to meet our needs and require the services of health care professionals to make us better and return us to our autonomous lives.

This feeds into an understanding of health and the role of medicine which is individualised: the doctor will assess the patient’s body, determine what is wrong, apply the appropriate medication and return that body to full health. And, of course, in many ways that is how medicine works in practice. However, another way of understanding health can emerge.

**6.5.2 Interdependence and Vulnerability as Health**

In this approach vulnerability is an inherent part of being human (Butler 2004; Herring 2013). Fineman (2013) argues:

Throughout our lives we may be subject to external and internal negative, potentially devastating, events over which we have little control—disease, pandemics, environmental and climate deterioration, terrorism and crime, crumbling infrastructure, failing institutions, recession, corruption, decay, and decline. We are situated beings who live with the ever-present possibility of changing needs and circumstances in our individual and collective lives. We are also accumulative beings and have different qualities and quantities of resources with which to meet these needs of circumstances, both over the course of our lifetime and as measured at the time of crisis or opportunity.

This vulnerability comes from three primary sources. The first is that our bodily fleshy nature makes us vulnerable. We are in our nature corporeal beings. Second, our incapacities to make autonomous decisions make us vulnerable and, third, our emotional state is not, and should not be, stable.

1. **The body**

   We are in our nature corporeal beings. And it is in the nature of human bodies that they are susceptible to sickness, illness and injury. As Fineman (2013) puts it: ‘[W]e are born, live, and die within a fragile materiality that renders all of us constantly susceptible to destructive external forces and internal disintegration.’

   Further, our bodies are ‘profoundly leaky’ (Shildrick 1997). People tend to imagine their bodies as statistic, immutable and a barrier against the world. In fact our bodies are constantly changing, with new material being added to them and old material being discarded. By the end of each day we have lost a whole host of cells and grown new ones. By our deaths there is little of us that is biologically the same as when we were born (see Sect. 5.7). Further, our bodies are not all human. Inside, they are dependent on a wide range of non-human organisms to survive. Outside, they are constantly interacting with the environment (see Herring and Chau (2014) and Sect. 5.6). Micro-organisms are passed from one person to another. Pollution can have devastating impacts on bodies. It is well known that a broad range of socio-economic factors impact on life expectancy (MacInnes 2013). The truth is our bodies are in a constant flux, are profoundly leaky and deeply dependent on other bodies and the broader environment (Herring and Chau 2007).

2. **Autonomy**

   The ideal person against which the ill or disabled are measured is the autonomous person. We like to think we make our own decisions on issues and act in a rational way. Impairments in rational thought are deemed mental disorders or learning difficulties.
Impairments in rational thought are deemed mental disorders or learning difficulties. But few of us have the capacity to be genuinely autonomous. To be autonomous, a person must not only understand the information about a decision but must be able to use it. Most of us make decisions with an awareness of few of the relevant facts about the decisions we make. Even if we do know the facts, Drobac and Goodenough (2015), in their analysis of the psychology of decision making, list the following requirements for rational use of information:

- parties with stable, well-ordered preferences;
- choices that are fully voluntary and unconstrained;
- relatively equal, and ideally complete, information;
- relatively equal bargaining power and experience;
- sufficient cognitive capacity to evaluate the transaction and to exercise voluntary control over the conflicting factors and emotions involved;
- the absence of monopoly power or other distortions of the market;
- the presence of good faith and absence of fraud in both parties;
- a level of consequence for a mistake that is not disastrous to the party.

The authors, after examining the latest neuroscience and psychology, suggest that few people have these capacities. They are not alone in their analysis. Levy (2014) refers to a wide range of psychological studies which reveal ‘fallibilities of human reasoning’ (including ‘myopia for the future’, ‘motivated reasoning’ and ‘biases in assessing probabilities exacerbated under cognitive load’). He concludes that ‘human beings are, under a variety of conditions, systematically bad reasoners, and many of their reasoning faults can be expected to affect the kind of judgements that they make when they are called upon to give informed consent’. Kahneman (2011) has listed these cognitive biases and explained how we often fail to reason logically (see Sect. 3.3.3).

3. Emotional instability

We assume that health is tied to a happy state of mind. But happiness is not always commensurate with well-being. There are times when it is right to be sad. Grief may be an unhappy emotion, but it is not an illness; indeed not experiencing grief at the loss of a loved one is more likely to be indicative of a problem.

The importance of our emotional state depends upon the support of others and this creates vulnerability. Neale (2012) puts it the following way:

Even the least vulnerable human being is still fundamentally, and inescapably, vulnerable in the negative sense, since none of us can meet her basic needs and satisfy her core desires without the co-operation of others; and even the most capable adult is vulnerable to hurt and harm, both physical and emotional.

She goes on to explore how striking a balance between positive and negative emotions is part of having dignity:

Take the example of a bereaved relative at a funeral, or in court during the trial of someone accused of her loved one’s murder. She bears herself with restraint and self-control, and is moderate in her utterances. She may even express forgiveness, call on her community not to retaliate, or request mercy for the perpetrator. All of this impresses us because we assume her to be suffering great pain and distress, and to be conducting herself in this way despite the way she is feeling. In other words, her vulnerability is a necessary and integral part of what we value when we value her dignified conduct. [...] Vulnerability is thus an ontological condition of our humanity.
Given our vulnerable nature, we need others to provide us with food and emotional support. We are all profoundly dependent on others for our physical and psychological well-being. In a powerful article Lindemann (2003) contrasts the emphasis on ‘accommodations’ made to assist disabled people with the lack of appreciation of how much accommodation there is for the able-bodied:

Colleagues, professional staff members, and other adults are unconscious of the numerous accommodations that society provides to make their work and life style possible. ATM’s, extended hours in banks, shopping centres and medical offices, EZpass, newspaper kiosks, and elevators are all accommodations that make contemporary working life possible. There are entire industries devoted to accommodating the needs of adult working people. Fast food, office lunch delivery, day time child care, respite care, car washing, personal care attendants, interpreters, house cleaning, and yard and lawn services are all occupations that provide services that make it possible for adults to hold full time jobs.

The able-bodied need the provision of stairs to get to the first floor as much as the wheelchair user needs the lift. Yet it is the provision of the lift for which we pat ourselves on the back for making such excellent provision for the disabled. In fact, we all depend on a wide range of social provisions to live in our society, from sewerage to supermarkets, from banks to buses. Our self-sufficiency is a myth (Herring 2013).

Our health too must be seen as a relational thing. Our well-being depends on the well-being of others around us. Covid-19 has made that abundantly clear. The illness of our family members or of those in our community makes us ill. We are denied our autonomy because of the health of others.

That is why relationships must be at the heart of an understanding of health. There is great wisdom in the National Aboriginal Health Strategy Working Party (Boddington and Raisanen 2009):

Aboriginal health is not just the physical well-being of an individual but is the social, emotional and cultural well-being of the whole community in which each individual is able to achieve their full potential thereby bringing about the total wellbeing of their community. It is a whole-of-life view and includes the cyclical concept of life-death-life.

Rather than seeking to make healthy bodies we may be more effective trying to create health communities and health societies.

### 6.6 Legal Significance of the Different Understandings of Health

The view taken of health as an individual thing or a relational/communitarian thing can have profound effects on the way the law responds to a range of different medical decisions (see Herring (2013) for a description of the legal significance of a vulnerability-centred understanding of the self). Here are some examples:

1. **Mental Capacity**
   
   The standard presentation of the law is that if a person has mental capacity, then their decision must be respected. So, a patient who refuses medical treatment cannot be given it against their will. That is so even if that refusal is seen as one that harms others (S v. St George’s NHS Trust [1998] 3 All ER 673). Autonomy has become a key principle within medical law.
   
   This seems very much in line with the independence and autonomy view of health. Our bodies are our own and we can decide what happens to our bodies. However, this presentation is not as straightforward as it appears. That is because it is not true that
the law allows us complete authority over what happens to our bodies. Obviously, a patient cannot demand a particular treatment from a doctor (R(Burke) v. GMC [2005] EWCA Civ 1003). However much a patient may insist that they can make decisions about their bodies, the doctor is still entitled to refuse treatment. This is, in part, a recognition that we live in a community. The NHS cannot be expected to provide every treatment that every patient wants. But it also requires us to respect the views of others. If doctors in their professional opinion think a treatment is not appropriate, we have no right to demand it of them. So there are relational and communitarian values found in the law, alongside a recognition of the right to refuse medical treatment.

We also find that traditional assessment of capacity tends to be carried out on a highly individualistic basis. Typically the person is sat down in front of a medical professional and asked a series of questions. Their answers are used to determine their mental capacity. People are assessed and treated in isolation, and not seen as relational people, in mutually interdependent relationships. The focus is on whether the individual on their own can understand the relevant information, weigh it up and make a decision (Breden and Vollmann 2004; Stoljar 2011).

This reflects a very particular understanding of what it means to have the capacity to make a decision. It is not how most people make decisions. Most think it through with others and rely on their insights, or at least interact with others on the internet. The friends chatting through a topic with a cup of tea might be the archetype of decision making, rather than the philosopher alone in his study (Gilbar 2011). As Ho (2008) argues:

We are socially-embedded beings, such that autonomy often incorporates intrinsically relational or social content, and it is thus impossible to assess patient autonomy without critically evaluating how or whether the interconnected social, political, and health-care structural frameworks often foreclose certain opportunities or pre-determine how individuals approach various health-care situations.

A relational approach would recommend that assessment of capacity should be of an individual located with their network of family, friends and caregivers (Chan 2004). The courts are beginning to recognise this. The Mental Capacity Act 2005, section 1(3) specifically states:

A person is not to be treated as unable to make a decision unless all practicable steps to help him to do so have been taken without success.

This may well involve family and friends supporting the decision-maker. Further in Montgomery v. Lanarkshire [2015] UKSC 11, the Supreme Court acknowledged the importance of patients and doctors working together to make decisions about medical treatment. We are beginning to see the acknowledgement that mental capacity and medical decision making is not to be understood simply as an individual thing, but as a relational one.

2. Confidentiality

Traditionally, the law has treated protected information about a person’s body as confidential. It is private and belongs to the individual concerned. However, this understanding of the law is increasingly coming under challenge, particularly in the area of genetics, as shown in the case of ABC v. St George’s [2015] EWHC 1394 (QB), [2017] EWCA Civ 336, [2020] EWHC 455 (QB), as discussed in Sect. 5.9.2.

Some care needs to be taken with this decision. It should be remembered that the claim was in negligence and so the question was not what the doctors ought to have done, but rather whether in not telling the claimant, this act of the doctors fell below the duty of care and therefore generated legal liability. There is nothing in the
judgement to suggest it would have been unlawful if the disclosure had taken place (although there is no clear statement that it would have been lawful). What the case highlights is that the notion that information is simply about one body is no longer a helpful concept. The state of our bodies’ health is highly relevant for those around them. In this context there is a strong argument for saying that genetic information is ‘family information’ (Gilbar 2011); it is about a group of people and does not belong to only one person. It is not simply information that belongs to the concerned individual and of relevance only to them. It is relevant to all around them.

It is not that the law is indifferent to the claim that people must be aware that their bodies can impact on others. It is well established (e.g. see R v. Dica [2004] EWCA Crim 1103) that if someone is aware they may be HIV-positive and has sex with another person, passing on the virus without informing them of their status, they can be convicted of the offence of inflicting grievous bodily harm under section 20, Offences Against the Person Act 1861. Indeed, it would appear to follow from this that if a patient diagnosed as being HIV-positive told their doctor that they were going to continue having unprotected sexual relations with their partner without disclosing their HIV status, it would certainly be permissible for a doctor to disclose the status to the partner because that would be needed to prevent a serious crime (something which is a well-established exception to the requirement of confidentiality). This issue is less straightforward in ABC v. St George’s because, by not telling the family of his diagnosis, the man was not performing a crime.

6.7 Conclusion on Understanding Health

Dependency is an inevitable facet of human life (Herring 2013). And because we are dependent we need care. True, there will be times during our lives when our dependency on others is more obvious. In early years and in times of sickness, perhaps particularly towards the end of life, we will need overt care. However, at all times in our life, we need the care of others to meet our practical and emotional needs. Indeed the care we provide for others is an important part of our well-being too. Kittay (1999) wrote of our interdependence:

My point is that this interdependence begins with dependence. It begins with the dependency of an infant, and often ends with the dependency of a very ill or frail person close to dying. The infant may develop into a person who can reciprocate, an individual upon whom another can be dependent and whose continuing needs make her interdependent with others. The frail elderly person […] may herself have been involved in a series of interdependent relations. But at some point there is a dependency that is not yet or no longer an interdependency. By excluding this dependency from social and political concerns, we have been able to fashion the pretence that we are independent—that the cooperation between persons that some insist is interdependence is simply the mutual (often voluntary) cooperation between essentially independent persons.

In relationships of caring and dependency, our interests become intermingled (Herring 2013). We do not break down into ‘me’ and ‘you’. To harm a caregiver is to harm the person cared-for; to harm the person cared-for is to harm the caregiver. An illness of one person can be an illness for a whole community.

The definition of health, therefore, is a complex issue. We live in our bodies and we live in our society. Health is found in a healthy body and a healthy community. Illness and disease can bring both blessing and curse. Society’s response to certain conditions and provision from them can exacerbate or limit the impact of the condition. What makes health is a complex interplay between our bodies, others’ bodies and the resources offered by a community.
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7. Death

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7.1 Hypotheses of Ageing and Death
One of the puzzles of life is death. Why do living organisms grow old and die?

The first scientist to consider ageing and death in the light of evolution was August Weismann. In an essay translated into English in 1891 (Weismann 1891a), he hypothesised a species of immortal living organisms which can reproduce. Over time, these organisms accumulate environmental injuries from which the organisms may not fully recover; indeed some individuals of these species may die from external forces. The older the organism, the more injured and thus weaker it becomes. It is thus necessary that new and perfect individuals should continually arise and take their place. The old and injured organisms are deleterious to the species; natural selection operates and these organisms evolve to die.

He further explained that ‘in regulating duration of life, the advantage to the species, and not to the individual, is alone of any importance … It is of no importance to the species whether the individual lives longer or shorter, but it is of importance that the individual should be enabled to do its work towards the maintenance of the species. This work is reproduction, or the formation of a sufficient number of new individuals to compensate the species for those which die.’ Once this has been achieved, the individual is of no value to the species and may die (note that, by reproduction, he included care for the young, so those species which do so tend to outlast the period of reproduction). These two strands of thinking combine to explain the necessity of reproduction and the utility of death.

The work of Weismann (1891a) emphasises the necessity of reproduction. In order that the new organisms be allowed adequate living resources, it is evolutionarily advantageous for the old organisms to die.

Haldane (1941) considered the effect of genes on different times of the life of a living organism, especially before and after its reproductive age. A gene deleterious to early survival of the living organism will be rapidly eliminated from the gene pool, especially when this gene acts before the reproductive age. Genes which are deleterious at old age are less important, as the organism is probably dead before these genes exert their effects. These genes will be passed on before their effects are manifest, and will thus not be easily eliminated from the gene pool. Stated simplistically, ageing comes from the deleterious effect of genes which are beneficial at an early age, especially before and at reproduction. Medawar (1952) also suggested that, as natural selection becomes less forceful in old age, genes which are beneficial in early age but harmful in old age can accumulate. These deleterious mutations accumulate over time and the living organism ages, and dies. This hypothesis is subsequently known as the ‘mutation accumulation’ theory.
Williams (1957) built on Medawar’s work and suggested the idea of ‘antagonistic pleiotropy’. Pleiotropic genes are genes with opposite effects on fitness in different somatic environments (or, in this case, different times). He postulated that these pleiotropic genes are beneficial to the organism at an early age, but become harmful at old age. Williams (1957) identifies the beginning and cessation of reproduction as key events in this theory. Genes which confers fitness before and during reproduction would be selected for even if they are deleterious to the species post-reproduction. These genes are not eliminated by natural selection because of the declining force of selection as the organism becomes sterile.

These hypotheses were combined and given a mathematical basis by Hamilton (1966). He extended Williams’ idea of antagonistic pleiotropy, and suggested that any genes which have age-specific actions are pleiotropic. He started the paper by suggesting this scenario: there exists an organism which stops reproduction before age 45, and there are genes which protect the organism from all lethal diseases at age 15, 25, 35 and 45. There is no selective advantage for the fourth gene, but varying degrees of selective advantage for the first three genes. In this sense, although these three genes have null effects at old age, they are pleiotropic. The author also shows that any mutation causing an improvement in early fecundity at the expense of an equal detriment later will give rise to mutants which will gradually become numerically preponderant. His conclusion is that, for organisms that reproduce repeatedly, senescence is to be expected as an inevitable consequence of the working of natural selection (original author’s italics).

Both the mutation accumulation and antagonistic pleiotropy hypotheses examine the necessity of ageing from the point of view of interaction between the living organism and the external environment. Orgel (1963) examined this problem from the point of view of protein synthesis without considering the external environment. He explained that the production of proteins from RNA (which in turn is produced from DNA) cannot be completely accurate. If too many errors accumulate, the cell may fail to replicate. However, not all errors are deleterious. Some of these synthesis errors lead to errors in DNA replication, and thus cause variation in the next generation. This variation is essential for the evolution of the species.

If DNA replication becomes too inaccurate, then the survival of the species would be endangered. If it is completely accurate, it could reduce natural variation and thus reduce the evolutionary success of the species. The accuracy of DNA replication and of protein synthesis has to be kept within narrow limits. The accumulation of deleterious changes in some cells is the price paid for enabling natural variation. These considerations by Orgel (1963) thus suggest that this accumulation of errors is one possible source of progressive deterioration of cell lines. Kirkwood (1977) built on this hypothesis and explained that the process of error regulation may underlie ageing. As errors accumulate, the living organism has to decide whether to channel the limited resources to reproduction or to cellular repair. This hypothesis is called the ‘disposable soma’ hypothesis. As opposed to the mutation accumulation or antagonistic pleiotropy hypothesis, the disposable soma hypothesis is more centred on the internal cellular machinery of the living organism.

A recent review has examined these hypotheses (Johnson et al. 2019) in the light of experimental findings, and noted that these theories, together or combined, are successful in explaining observed experimental findings. These scientists also explained how some observations challenge these three hypotheses.

For example, in the mouse, mutants which do not express the growth hormone receptor (GHR -/-) live at least 25% longer than wild-type mice, but these mutants are only about three-eighth the weight of the wild-type, and they consume about half the weight in food. They also express lower levels of insulin-like growth factor-1 (IGF-1) (Coschigano et al. 2003). Though these mutant mice are fertile, the females have impaired follicle development and ovulation rate, sexual maturation, and production and responsiveness to sex hormones (Zaczek et al. 2002). It is thought that these smaller-sized GHR -/- male mice would not be able to establish and defend territories against larger wild-type males and would thus have
fewer mating opportunities. Moreover, they are less likely to survive harsh winters in temperate climates, as they have an unfavourable surface-to-mass ratio (Bartke et al. 2013).

Interestingly, some mutations of the IGF-1 receptor in human populations have been shown to promote longevity (Suh et al. 2008) in Ashkenazi Jewish populations, but not in Han Chinese populations (Xie et al. 2008). Thus, there are some parallels in how ageing develops in different species, but the parallel is not complete. So far, scientists have not been able to identify deleterious effects of these mutant genes which cause longevity in humans. There are two reasons for this: one is that these deleterious effects have not been found, the other is that these effects are of less importance in human societies, as we no longer live in the wild, and are less subject to the vagaries of the environment.

Over the years, scientists have developed some understanding into the evolutionary advantages of ageing and death, but this understanding is by no means complete. But it does appear that death is an inevitable consequence of life, and attempts to prolong life can only work so far before one hits the wall of self-limiting factors such as antagonistic pleiotropy. Or, to put it simplistically, there is no such thing as a free lunch. Whatever one gains to achieve longevity, one has to pay back somewhere else. The rest of this chapter builds on our previous work (Chau and Herring 2007).

7.2 What Is Death?

From a biomedical point of view, death can be defined simply. Any living organism carries out metabolic functions, respiration and excretion; in some phases of its life, the living organism reproduces and grows. Any living organism maintains a barrier to cause an entropy decrease locally, at the expense of a global increase in entropy. When these functions cease, the living organism is dead.

Usually, there are no difficulties in deciding whether a person is dead or not, even if there is disagreement over when death occurred. In the absence of medical intervention, the process of death is relatively simple and quick. As people age, the cells of their body show a reduced capacity to proliferate, and so tissues show impaired cellular regeneration in response to normal ‘wear and tear’ or to injury, and indeed cells are also more likely to die (Khan et al. 2017; Oh et al. 2014). With fewer and fewer cells, organs such as kidneys, heart or liver ultimately fail and the person dies ‘naturally’. In the case of disease, a specific major organ system fails, and its cells and tissues start to die (Borutaite et al. 2003; Qiao et al. 2005). In both ageing and disease, the final common pathway is that cells of an organ die in quick succession, leading to other organ systems failing; e.g., heart failure quickly leads to kidney failure. Death of the whole organism is concomitant with massive cellular death in major organs.

Consider the disease progression of one of the commonest causes of death in affluent societies: death due to the failure of the cardiovascular system. A blood clot may come to block one of the coronary arteries, and parts of the heart muscle suffer a restricted blood supply (ischaemia) and become starved of oxygen and nutrients. This leads to increases in the acidity of the tissue (lowering of pH), the potassium levels around the heart cells, and the calcium levels within them, all of which lead to electrical instability of the heart, and so to an irregular heart beat (or cardiac arrhythmia; see Mehta et al. (1997) and Zipes and Wellens (1998)) or even cessation of beating, both of which prevent effective pumping of blood round the body. The tissues of the body are therefore also starved of oxygen and nutrients, and their cells begin to die, with their membranes disintegrating and their genetic material, the DNA, degrading. For example, in the case of nerve cells, ischaemia leads to damage and then death within half an hour of total heart failure (Hayashi and Abe 2004). In the kidney a restriction in blood supply leads to cell death (Padanilam 2003), so the excretory function is severely compromised. General ischaemia caused by cardiac insufficiency thus leads to massive cell death in all tissues. The patient can no longer maintain physiological functions such as digestion or excretion, and dies.
What we have described above is the process of death in the absence of any medical intervention. However, the matter becomes more complicated if medical procedures are applied. For example, if the heart fails, restriction of blood flow in the brain will set in within a matter of minutes, and after about 15 min a large proportion of cerebral cortical neurons will have died. Should the patient be resuscitated before total brain death occurs, the brain stem (which controls breathing, blood pressure and body temperature) may remain functional when the cerebral cortices are dead. These patients are in a ‘persistent vegetative state’ (‘PVS’) (Multi-Society Task Force on PVS 1994a, b). A PVS patient is unaware and insensate, cannot self-feed and has lost all language capabilities, but is capable of some degree of movement and is not comatose (but see Sect. 3.3.1 for difficulties with the diagnosis of PVS and related states). However, even with medical intervention, the cerebral cortices and the brain stem might both die. In this case, the patient is defined as ‘brain-dead’, but the other major organ systems of that individual can be intact, since the brain is one of the organs most sensitive to interruption of blood flow. The difference between PVS and brain death is that, in the former, the patient is ‘awake’ and can execute some motions, although lacks consciousness, but in the latter, the patient is comatose.

PVS patients present a major challenge to the notion of death. The cerebral cortices of PVS patients are not functioning, so their personalities are totally absent; they have no consciousness. They can often breathe spontaneously, their blood pressure is under physiological control, but they have to be fed and exercised by carers. In brain-dead patients, they can be kept alive (often for years) but only with total parenteral nutrition (where food is usually given to the patients through their veins), artificial respiration and special medical procedures to prevent pressure ulcers and muscle degeneration.

This ability to ‘keep alive’ people who, in the past, would have died causes problems in defining death. And this problem will only get worse when looking to the future if even more remarkable medical procedures should become available. Transplants of bone marrow (Mathé et al. 1963), kidneys (Merrill et al. 1956), livers (Calne and Williams 1968; Starzl et al. 1968), hearts (Barnard 1968), lungs (Hardy et al. 1963), hands (Dubernard et al. 1999), or even faces (Spurgeon 2005) are now possible. And this list may well expand. The most challenging organs to keep alive in this respect are probably the head and brain. Although human brain transplants are not yet possible, animal head transplants have been performed for some time with variable survival rates and with evidence of functional brain activity such as pupillary light reflexes, noise-responsive eye winking, facial movements on electrical stimulation of the motor-sensory region of the cerebral cortices, and breathing, sleeping, biting and eating (Chute and Smyth 1939; Demikhov 1962; Heymans 1912). These experiments have shown that, under appropriate conditions, it is possible to keep even the head of a higher mammal alive for a prolonged period of time.

Machines that replace parts of the human body are also becoming increasingly common. Dialysis techniques can replace the human kidney to some extent (Alloatti et al. 2000), liver dialysis can replace some functions of the liver on a very short-term basis (van de Kerkhove et al. 2004) and artificial hearts have been placed in humans (Gray and Selzman 2006). With further scientific progress, it would not be inconceivable that any part of a human being could be kept alive using machines for the course of its cells’ natural lives. What, then, is the meaning of death under those circumstances?

### 7.3 Legal Definition of Death

It is surprising that the legal definition of death has received very little attention from the courts (Herring 2007). Rarely has the judiciary felt the need to pronounce on the issue. In *Airedale NHS Trust v Bland*, Lords Brown-Wilkinson, Goff and Keith accepted that brain stem death was the definition of death for the purposes of medicine and law. Lord Keith in *Bland* held:
In the eyes of the medical world and of the law a person is not clinically dead so long as the brain stem retains its function.

Tony Bland, although suffering PVS, was not brain stem dead and so was still alive. In Re A, Johnson J held that a child who was on a ventilator and certified as brain stem dead was also legally dead. This was in line with the medical expert opinion, even though the parents took the view that the boy was still alive.

Perhaps the safest statement to make is that at present the legal definition of death is taken to coincide with the medical one. Traditionally, death is equated with failure of the heart (Harvey 1653) and cessation of breathing (Lancisi 1707), and this concept of cardiopulmonary death was widely used as a medical definition of death all over the world until the 1960s. Patterson (2006) has argued:

The term ‘death’ is not restricted to the absence of any biological life, but used as shorthand for the legal acceptability of certain conduct.

However, the author cites no cases to support this proposition, and it is not clear that such cases exist! In the Bland case, for example, the easy route would have been to declare Tony Bland dead, thereby to justify turning off the life support machine—not the line of reasoning taken by the judges. That said, what might be appropriately claimed is that the legal definition of death is so fluid that it is open to manipulation by a judge to achieve the desired result. In fact, in the few cases where the issue arises, a court is very likely to follow the expert medical opinion (Bennion 1994; Miller and Parrott 2007; Skegg 1984). Section 26(2) of the Human Tissue Act 2004 authorises the Human Tissue Authority to issue codes of practice that will set out how it will be determined whether a person has died in cases involving transplantation. None has been produced yet, but an early publication from the Human Tissue Authority (Human Tissue Authority 2006b) suggests that brain stem death will be the test.

So, lawyers may seek to pass the hot potato of defining death over to the doctors. The problem is that it there is some disagreement over what the medical definition of death is. More significantly, it is far from clear that the definition of death is entirely, even predominantly, a medical issue. The next section will consider some of the definitions of death that have been used.

7.3.1 Brain Stem Death

Definition

As already indicated, brain stem death is widely accepted in the United Kingdom and many other European countries as the medical definition of death (Pallis and Harley 1996). The brain stem is the most caudal or lowest part of the brain, and connects the spinal cord with the rest of the brain. It contains the medulla oblongata, midbrain, pons and cerebellum (see Fig. 3.8). These structures are responsible for general wakefulness and for controlling blood pressure, body temperature and breathing. Normal spontaneous breathing will be impossible if the brain stem is injured.

Before the advent of mechanical ventilators and associated techniques to keep immobile patients from muscle wasting, pressure ulcers etc., a patient with brain stem death would be unable to breathe, and would thus die within a matter of minutes. Advances in mechanical ventilators and related methods made it possible for patients suffering from brain stem death to survive, and in this way these patients could be kept alive for a considerable period of time. The problem thus arises of whether these patients are dead or not, because they cannot sustain life on their own, but are obviously not dead provided the machines are working.

In the late 1950s and early 1960s, clinicians began to use electroencephalography (EEG) as a diagnostic tool to decide if the brain of a patient was dead (Jouvet 1959). The EEG
records electrical activity from the cerebral cortices of the brain, and cessation of EEG activity was interpreted to mean that the patient was brain-dead. Around the same time, organ transplantation was making rapid progress. Less invasive surgical techniques and more effective immunosuppressive drugs were making transplantations safer. The first kidney transplantation was performed in 1954, albeit between genetically identical twins (Merrill et al. 1956). The first successful liver transplant was performed in 1967 (Calne and Williams 1968; Starzl et al. 1968); the same year witnessed the first successful heart transplant (Barnard 1968).

The success in human organ transplantation meant that there was a demand for viable cadaveric organs. Notably, one month after the first successful heart transplant, a committee was convened at Harvard Medical School to study the problems of the hopelessly unconscious patient, and concluded that irreversible coma should be the criterion of death of such patients (Harvard Medical School 1968). It is hard to avoid the suspicion that ensuring that organs could be used for transplantation played an important part in their deliberations. In the United Kingdom, brain stem death was first recommended as a criterion for death in 1976 (Conference of the Medical Royal Colleges 1976), although it was first called ‘brain death’. The nomenclature ‘brain stem death’ was formally adopted later (Royal College of Physicians Working Group 1995).

At present the Department of Health’s A Code of Practice for the Diagnosis of Brain Stem Death (Department of Health 1998) sets out in detail the definition of brain stem death, which outlines three requirements that must be met before a doctor makes such a diagnosis: first, it must be concluded that the coma is not due to reversible causes, such as a drug overdose; secondly, it must be demonstrated that several components of the brain stem have all been permanently destroyed (significantly, this includes the respiratory centre); and thirdly, it must be proved that the patient is unable to breathe spontaneously. The code suggests that two medical practitioners who have been registered for more than five years and are both specialists in the field should agree that there is brain stem death before pronouncement.

**Justification for Brain Stem Death**

The primary justification for using brain stem death as the decisive criterion is that a person whose brain stem is dead has ceased to live in anything but a mechanical way (Dubois 2002). The ‘integrative unity’ of body and mind has come to an end (Potts 2001). The reasons for preferring the brain stem test as opposed to the whole brain test are as follows: first, that without the brain stem, the patient will be rendered comatose; and secondly, that clinically, it is easier to ascertain brain stem death than total brain death.

**Objections to Brain Stem Death**

A fundamental attack on the concept of brain death is that it elevates the brain to being the sole component of personhood—too narrow a view (Potts et al. 2000; Russell 2000; Shewmon 1998). Veatch (1989) imagined a time in the future in which it would be possible to give a person a brain transplant. He suggested that if a brain stem test were used, this would lead to such a person being classified as dead, even though they would patently be alive. One response to this argument, though, is that we can say that the body is not dead but the person is dead. His example also raises the issue, in the case of a head transplant: Who now exists? Is it the person who had the head, or the person who had the body, or both?

It has also been objected that under the brain stem criterion, a person can be classified as dead, even though their body is warm and breathing (Evans 2002). This creates too big a gap between the legal meaning of death and its understanding by people on the street (Byrne and Rinkowski 1999). Shewmon (2001) states that homeostasis (maintenance of the internal environment of the living organism, for example, energy balance, wound healing, fighting off infections, development of a febrile response), successful gestation of a fetus,
sexual maturation and proportional growth are all capable of occurring in people who are ‘brain-dead’.

Others have expressed concerns about the reliability of the tests used to determine brain stem death (Karakatsanis and Tsanakas 2002; Mejia and Pollack 1995; Wang et al. 2002). If it is not possible to provide a reliable test of brain stem death, then doubt is created over the efficacy of it as a criterion of death.

7.3.2 End of Consciousness

Definition
This approach is based on a person’s capacity for consciousness (DeGrazia 2004): once that is lost irreversibly, then the person should be regarded as dead. Sometimes this is known as ‘higher brain death’. Note that brain stem death is different from higher brain death. In the former, usually only the brain stem and the rest of the brain is dead, but in the latter, only the cerebral cortices are dead. Its use would mean that PVS patients would be regarded as dead, and so Engelhardt (1999) is able to refer to the permanently unconscious as ‘biologically living corpses’.

Justification of End of Consciousness
To some commentators the definition of death should depend on what we understand it is to be human (Rich 1997). To some people this is a consciousness of one’s self or others and an ability to interact with other people. Supporters of such an approach would argue that a person who has permanently lost the ability to communicate or relate to other people and/or a person who has permanently lost a conscious awareness of themselves and their surroundings has lost what is essential to being a human and should therefore be regarded as being dead. As Savulescu (2003a) puts it, ‘[I]t is our mental life which constitutes who we are, not the machine that supports it.’ Indeed, this view has led some commentators to suggest that we should see a difference between biological death (of the organism) and the death of the person (the permanent loss of consciousness). It is the latter that matters in moral terms, supporters argue (Engelhardt 1999).

Objections to End of Consciousness
A loss of consciousness criterion for death would lead to a far wider classification of death than that used at present. Most directly, those suffering from PVS would be regarded as dead (but see Sect. 3.3.1 for difficulties with the diagnosis of PVS). Even more dramatically it could classify as dead (or at least non-human) large numbers of people with severe mental illness or disability. However, it may well be argued that most people with severe mental disability have some form of self-awareness and are not therefore categorised as lacking consciousness. That said, the possibility that there is a question mark hanging over whether a very mentally ill person is dead may lead one to doubt the wisdom of the approach.

An alternative critique of an approach emphasising consciousness is to challenge that concept itself. Neurophysiological progress is making us realise that what is uniquely human is shared by many other species, and that what in the past we thought to be metaphysical can be explained by biology. Many people think that there is a mind-matter dichotomy, and that the seat of consciousness could not be located in the brain. Over the years, neurophysiology has shown us that thinking, learning, emotions and other kinds of complex behaviour are most probably changes in the brain state (see Sect. 3.3). It is not inconceivable that our feeling that there is an external existence outside of our body which is ‘us’ (religious people would probably call it the soul) is an illusion our brain cells gives us, so that we think there is something called ‘us’ outside our bodies when there is not. In short, science may be coming to the view that we humans are a form of a very complex physiological machine, like many other animals. In that case a more mechanistic definition of death than that based on consciousness may be appropriate.
7.3.3 Ending of Cardiac Function

**Definition**
If the heart stops beating irreversibly, then this definition concludes that the patient is dead. It is important to stress the irreversibility of this definition, because the heart can stop but the patient can be resuscitated; clearly it would be nonsensical to define a person as dead every time his or her heart stops.

**Justification of Ending of Cardiac Function**
One prominent supporter of the loss of cardiac function test is the Danish Council of Ethics, which preferred it to brain death (Kamm 2001; Shewmon 2001, 2004). The Council took the view that the definition of death is not a technical question, but must be decided in terms of how the community as a whole understands death. It argued that the person in the street would view the stopping of the beating heart as the criterion for death because the heart is widely seen as a symbol of life (Truog 1997). So, even if the notion of the beating heart as the key to life is not logically or philosophically justifiable, it is intuitively felt to be the essential mark of life.

**Objections to Ending of Cardiac Function**
One difficulty with using the cessation of the heartbeat as the criterion for death is that even if a patient’s heart has stopped beating, medical intervention may still enable the patient’s resuscitation. This requires the ‘end of cardiac function’ criterion to rely on the concept of an irreversible end of breathing. That is problematic because, in respect of a particular patient, it might not be known whether the cessation of cardiac function is irreversible until further medical intervention has been carried out. Another difficulty is that it is also now clear that the stopping of the heart does not immediately lead to an end of brain activity (Mason and Laurie 2006). This, then, could lead to a person being treated as dead even though there is some form of consciousness.

7.3.4 End of Organism

**Definition**
If the body is seen as a ‘working organism’ with various functions, then it might be possible to define death as when that organism ceases to achieve those functions (Lamb 1985). The functions of the body might include metabolism, reproduction, sensation and locomotion. Only when all of these functions are no longer being performed should the body be said to have died.

**Justification of End of Organism**
This approach is supported by those who criticise the brain death criterion because it elevates the brain over the rest of the body. It would argue that a human being performs many functions, some of which, but not all, relate to the brain. Using the end of the organism as the criterion for death recognises that bodies are made up of many parts and perform many functions. The brain and its functions are only part of what the body does.

**Objections to End of Organism**
To its opponents, this view treats the body like a piece of machinery, and yet most people regard their bodies as more than an organism that, for example, simply takes in and expels air. Such an approach overlooks what most people regard as most important about their bodies: feelings, thoughts, emotions and the like. The counter-argument is that, as far as we know, our feelings, thoughts and emotions are correlated with changes in the state of the brain. In short, we are a machine that eats, sleeps, feels and thinks—though an extremely elaborate one—so to view our body as a machine is quite acceptable.
The other problem with this approach is that, as we have seen, in due course, it should be possible to replace some of our organs with artificial ones, including the brain. The patient then could be defined as living until all the original parts and replacement parts fail. Ultimately, we might end up with a living patient having none of the body parts from the original person, but who is defined as dead!

7.3.5 Death of Every Cell

Definition
An extreme view would declare that a person has not died until every cell in the body has ceased functioning. This would place the point of death at the state when the body has begun to putrefy.

Justification of Death of Every Cell
This approach could be the ‘safest’. If you believe that treating a live body as if it were dead is an appalling evil, then one would seek to avoid that at all costs. If you believe that one cannot be certain when death occurs, then this has the benefit of being the point in time at which we can be sure the person is dead.

Objections of Death of Every Cell
The practical implications of this approach are its main difficulties. It would mean that bodies could not be disposed of until they are ‘some kind of smelly porridge’ (Kennedy 1988). Until then they would need to be treated as live bodies. It would be an approach very much out of tune with the understanding of death of the person in the street. It is unlikely to be regarded as an acceptable notion by most people, especially those for whom religious belief or cultural practice requires burial soon after death. Pattinson (2006) explains that it would involve diverting finite health care resources, extending the grieving process, undermining health care staff morale, and preventing the use of any human organ or tissue for virtually all beneficial purposes from transplantation to teaching and research.

7.3.6 Desoulement

Definition
For those of a religious persuasion death is often defined as the moment the soul leaves the body and moves on to the afterlife (desoulement). The concept of a ‘soul’ is not easy to define. Roughly speaking the soul is the spiritual essence of a person that continues after death (Eberl 2005). For example, the Catholic Encyclopedia (Herbermann et al. 1912) suggests:

The soul may be defined as the ultimate internal principle by which we think, feel, and will, and by which our bodies are animated.

although the definition of the soul is a matter of heated and complex debate among theologians (see, e.g. Moreland and Rae 2000).

Justification of Desoulement
If the soul exists and if it is what is our essence, our eternal essence and is what makes a body a person, then its presence its crucial. Hence, in many theological circles the entry of the soul into the body is the start of life and its departure is the end in the sense that it marks the point in time when the individual’s life in their body ends and their afterlife begins.

Objections to Desoulement
Of course such a definition will be rejected by those who deny the existence of a soul. Even if the existence of a soul is accepted, there is the problem that the moment of desoulement is not apparent to humans. It cannot therefore readily provide a basis of a legal or medical test. Eberl argues that once a body is brain stem dead the soul cannot function, and leaves it. He therefore supports a brain stem death test, albeit from a desoulement perspective (Eberl 2005).

7.3.7 Death as a Process

Definition
All the approaches defined so far have sought to indicate the point in time at which death occurs. An alternative approach argues that death is better seen as a process that occurs over time (Haley 2001). Occasionally there will be a clear instant of death, where, for example, a person is destroyed physically in an accident. But otherwise there is no easy cut-off point at which we can mark the line between a person who is alive and a person who is dead. As one dying patient put it, ‘death keeps taking a little bit of me’ (Kafetz 2002).

Justification of Death as a Process
The argument in support of this approach is that at different points in time a person can be regarded as dead according to some understandings of that concept, but not according to others. Death is therefore better regarded as a process during which different aspects of death may be apparent. We can be sure by the time of putrification that a person is now dead, but to select one point of the process as the moment of death is artificial.

Objections to Death as a Process
Although there is much to be said in favour of this approach biologically, it is not a practical one. Ariès (1974) has argued:

Death in the hospital is no longer the occasion of a ritual ceremony, over which the dying person presides amidst his assembled relatives and friends. Death is a technical phenomenon obtained by a cessation of care ... Indeed in the majority of cases the dying person has already lost consciousness. Death has been dissected, cut to bits by a series of little steps, which finally makes it impossible to know which step was the real death, the one in which consciousness was lost or the one in which breathing stopped. All these little silent deaths have replaced and released the great dramatic act of death, and no one any longer has the strength or patience to wait over a period of weeks for a moment which has lost part of its meaning.

The law, relatives and professionals require a clear point at time at which someone has died (Stanley 1987). Proponents of seeing death as a process could, however, suggest that a person could be treated as dead for different purposes at different times. There could be one point in time in the process where a person is declared dead for the purpose of removal of organs for transplant, but another where they are dead for the purposes of burial or cremation.

7.3.8 No Definition

Definition of ‘No Definition’
This approach argues that to seek to define death is an impossibility. We are better off not seeking to do so. It is more profitable to focus on particular questions: At what point is it appropriate to authorise burials of bodies? When can organs be removed from a body for transplant to another? When can a person whose body is being artificially ventilated have the machine switched off? It would be possible to have different answers to these questions (Youngner and Arnold 2001).
Justification of ‘No Definition’
This approach is based on the notion that we cannot define the moment of death. There is no ‘correct’ answer. It is the kind of question to which one can answer, ‘Death means whatever you want it to mean.’ Disputes over what death means are likely to lead to high-minded disputes between theologians, philosophers, lawyers and medical scientists, which are, to be frank, likely to get nowhere. Better to focus the mind on the more concrete questions specified in the previous paragraph (Zamperetti et al. 2003).

Objections to ‘No Definition’
To many people there is a fundamental difference between a dead person and one who is not. We are willing to treat dead bodies in a way that would be utterly unacceptable were the body alive. Morally, the loss of personhood is a fundamental change of status (Veatch 2005). It is of crucial importance to relatives and medical staff that we can declare a point of death. It is impractical not to define death. For lawyers too, a definition of death is used in the way the criminal and medical law is structured. That said, it would not be impossible for the law to dispense with the notion of death. It would be possible, for example, for the law to list what can or cannot be done to a body demonstrating certain characteristics, without having to declare whether that body is dead or not.

7.4 Choosing Between the Definitions
We will now highlight some of the differences between the definitions, and summarise the key issues which have led people to define death in such different ways.

7.4.1 Safety First?
In choosing between these different definitions, consider the claim by Lamb (1994), ‘It is as wrong to treat the living as dead as it is to treat the dead as alive.’ The argument here is that it is as important not to put the point of death too early, as it is to put it too late. But not everyone will agree with Lamb’s suggestion. Treating a dead person as alive may be a waste of resources or may delay improperly the grieving process for the family; but is it really as serious as burying a person who is alive?

7.4.2 Death of the Body or of the Person?
The different definitions of death tend to group into two categories: those that emphasise life as being about conscious awareness and those that understand the body as a living organism. The problem is that many people regard both understandings of our bodies and lives as valid (Holland 2003). One solution could be to accept that we die twice: once when we lose consciousness and once when our biological organism comes to an end. This solution would be supported by those who argue that we are not just minds, nor are we just bodies, we are ‘embodied minds’ (McMahan 2002). McMahan further suggests:

An organism dies in the biological sense when it loses the capacity for integrated functioning. The best criterion for when this happens is probably a circulatory respiratory criterion ... What it is important to be able to determine is when we die in the non-biological sense—that is, when we cease to exist. If we are embodied minds, we die or cease to exist when we irreversibly lose the capacity for consciousness—or, to be more precise, when there is irreversible loss of function in those areas of the brain in which consciousness is realized. The best criterion for when this happens is a higher-brain criterion—for example, what is called ‘cerebral death’.

7.4.3 Perspective of Death
Another difference between the definitions may be the viewpoint from which death is appreciated: the dying person or his/her carers. Arguably brain death will be the point at which the dying person will lose all appreciation of their life, but cessation of breathing will
be the point at which the person will appear to have died to an on-looker. However, it should be noted that the stopping of breathing is the most common cause for the brain stem function to cease (Pallis 1990). Indeed, Mason and Laurie (2006) suggest it would be wrong to see brain stem death and non-breathing as two competing definitions of death. They prefer

to visualise the brain, the heart and the lungs as forming a ‘cycle of life’ which can be broken at any point; looked at in this way, there is no need to speak of two concepts of death—that is, cardiorespiratory death or brain death; it is simply that different criteria, and different tests, can be used for identifying that the cycle has been broken.

Similarly, the American Uniform Determination of Death Act 1981 states:

[A]n individual who has sustained either irreversible cessation of circulatory and respiratory functions, or irreversible cessation of all functions of the entire brain, including the brain stem, is dead.

The advantage of this viewpoint is that it does reflect the biology of death. Different parts of the body cease to function irreversibly at different times, so having a cycle of death would allow lawmakers to decide at what point organs can be harvested, and at what point the person is no longer considered to be in control of his or her higher faculties, etc.

7.4.4 Is Death a Medical, Legal or Philosophical Question?
A further key issue is who should define death. As already mentioned, so far the English courts have in recent times tended to follow the medical definition of death. Although this is approved of by some lawyers (Kennedy 1969), others have argued that the philosophical and moral arguments must also be taken into account and therefore the courts should not slavishly follow medical opinion (Lizza 2006; Skegg 1974).

For some scholars, death must be regarded as a basic biological phenomenon. Bernat (2006) argues:

Accepting that death is a biological phenomenon neither denigrates the richness and beauty of various cultural and religious practices surrounding death and dying, nor denies societies their proper authority to govern practices and establish laws regulating the determination and time of death. But death is an immutable and objective biological fact and not fundamentally a social contrivance.

7.4.5 Relevance of Practicality?
In producing a legal definition of death it is necessary to consider not only philosophical considerations, but also whether it is ‘usable’ and acceptable, i.e., in accordance with the general public’s understanding of death. In other words, it may be that the philosophically most desirable definition of death is not usable because it cannot be transformed into a clear and practical test. But should convenience affect the definition of such a fundamental concept?

7.4.6 Problem of Irreversibility
For many definitions there is a problem concerning irreversibility (Hershenov 2003; Lizza 2005). Do the definitions require that the condition in question be ‘irreversible’? Let us take, by way of example, the suggestion that loss of consciousness be the definition of death. If there is no need for this to be an ‘irreversible’ state, then whenever people temporarily lose consciousness they die and are then brought back to life. This seems implausible. However, if we insist that the condition be irreversible, this is problematic. We have already outlined earlier the experiments in which separate body parts (including the
head) were kept alive with appropriate technology. Another example would be patients apparently suffering from PVS who have been aroused from that state with the use of drugs (Clauss and Nel 2006). Using irreversibility as a criterion would mean that the boundary is constantly changing, so any socio-legal definition would have to update itself frequently. Further, it raises the question of whether the condition can be reversed by the use of any available technology. If so, if a person is in a state of unconsciousness and there is somewhere in the world a piece of machinery which could revive consciousness, then that person is not dead, even though it is implausible that the machinery could be used in their case. Or what about the freezing of bodies, in the hope that at some point in the future technology will have advanced to allow their revival?

7.4.7 Religion
We suggest that there is no getting away from the interconnection of religious belief and the definition of death. If there is a God or Gods, then a plausible definition of a person is ‘a human being recognised as such by God’. The value and meaning of life depends on God’s or the Gods’ perspective, which may include criteria not observable to humans, or not valued by them. By contrast, if there is no God, then the value and meaning of life depends only on what we can experience of the material world. Atheists tend, therefore, to be attracted by those views that emphasise the connection between an individual and the observable: namely, consciousness or the functions of organisms. Believers in God or Gods, however, might accept that a person is recognised as alive by God even though there is no way for that individual to relate to the world. They may prefer a definition of death which focuses on the death of the whole body (Jones 1999) as a point at which it might be assumed that even God or the Gods cannot regard there to be life in the body. There is no easy reconciliation between such approaches. One solution may be to allow the deceased and/or their relatives to select their own definition of death (Appel 2005). This approach has been adopted in Japan. One author has written of the right to choose which concept of human death will be applied to ‘our’ death (Morioka 2001). A difficulty with this approach is whether a patient should be entitled to insist on highly expensive treatment, keeping them ‘alive’ when they are in fact ‘dead’ according to the generally accepted medical standard (Evans 2002).

Another solution is to declare that the law cannot be based on unverifiable religious beliefs and we must reach the answers on the basis of the best scientific evidence available. The problem is that it is not clear that science provides us with a clear answer anyhow.

7.4.8 Role of Policy
It can be difficult to separate out the issue of defining death and the controversial ethical issues which can arise as a result, especially concerning euthanasia and organ transplantation (Kerridge et al. 2002). Bernat (2006) suggests:

Some scholars have gone astray by not attempting to capture our consensual concept of death and instead redefining death for ideological purposes or by overanalyzing death to a metaphysical level of abstraction—thereby rendering it devoid of its ordinary meaning.

Although it is tempting to suggest that a particular definition of death is unacceptable because the costs of adopting it would be too high for the National Health Service, surely a far more honest way of addressing the issue would be to determine the definition of death and then determine whether the spending of money on this patient is appropriate.

7.4.9 Public Opinion
How important, if at all, is it that the definition of death matches that understood by the general public? Some commentators insist that any acceptable definition of death must accord with the general understanding of death. This has formed part of the criticism of
those approaches that regard PVS patients or severely mentally disabled people as dead (Bernat 2006).

7.5 Conclusion

It is interesting that defining the exact moment of death has become such a topical issue for lawyers and doctors. Death in the absence of medical intervention can be seen as a relatively straightforward biological process. Untreated, the failure of major organ systems will lead to death quickly. For example, if the circulatory system is compromised by ventricular fibrillation, there will be widespread cellular death, and within a few minutes, the subject will be dead. Respiratory collapse due to, for example, drowning will also cause widespread cellular death in a few minutes. However, with medical intervention, the situation becomes much more complex. Medicine has made progress in keeping part(s) of the body alive for long periods of time. Indeed, it is not inconceivable that in the future most body parts will be able to be kept alive well beyond the ‘natural’ course of their lives. Furthermore, the possibility of organ donation and concern about expenses have generated greater public interest in the exact timing of death.

We have attempted in this chapter to outline a variety of ways of seeking to define death and to give an overview of their advantages and disadvantages. An attempt has been made to indicate some of the key issues that need to be addressed in seeking to reach a definition. We suggest that to produce a single definition of death with medical intervention is impossible and perhaps undesirable. One could see a justification for each of the foregoing definitions. There is much truth in the claim that death occurs as a process, with death occurring at different times and in different ways, and is experienced and understood differently by the various parties to the process. The search for a definition for a point of death is, we suggest, futile. The best we can do is to point out as clearly as possible the different ways in which, in a different sense, we die. Certainly in the process of death there are some significant milestones: the disappearance of higher neural functions, the cessation of breathing and the death of the body as a whole organism.

The question of when a person dies might, therefore, not be a useful one. It might be preferable, rather than asking when does a person die, to ask a series of different questions. How is it appropriate to treat the body of a person who is in a PVS? How is it appropriate to treat the body of a brain stem-dead person? When should relatives be informed that a person is dead and the body treated as a dead body? These questions are no easier to answer than asking what death is, but they make clear the reasons for which we are asking the question. They may bring out the medical, philosophical or theological questions more clearly than asking what death is in the abstract. They also recognise that death is not a straightforward event, but a process. Death, like life, can be a long journey.

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**Footnotes**


8. Conclusion

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Medicine is changing very quickly, and the law is trying to catch up with medical advances. In this book, we aim to explain the technological advances and discuss how the law could deal with them. We aim not to be prescriptive. We live in a liberal democracy, where each citizen is supposed to be a rational and thinking human being (whether that is true or not is another matter). Our aim is to explain the science and medicine; we then enumerate the different legislative options and discuss the consequences of these options. It is up to the citizens to decide, via their representatives, what the law of the land should be.

We emphasise that we need to base our legislation on facts and a sound understanding of the science behind medical advances. All too often, this is replaced by rhetoric. For this and other reasons, we would like to reiterate the importance of using system 2 thinking when considering...
complex matters of great import like these. It is tempting to go back to system 1 thinking because it is familiar and easy, but we are no longer hunter-gatherers living in the African savannah and system 1 thinking can be dangerous. In a complex society, where our actions have far-reaching consequences in time and space, it is imperative to use system 2 thinking to logically consider the situation and arrive at a conclusion about what to do using reasoning and not instinct.

This is not limited to legal matters. We humans have indeed built up complex cultures and civilisations, but part of us still retains the instincts of hunter-gatherers; for example, in affluent countries, our urge to eat is still that of hunter-gatherers but our food supply is much more abundant. In many matters in life, it is important to use system 2 thinking as much as possible, as system 1 thinking is becoming less and less relevant to our modern world. We hope that more widespread use of system 2 thinking followed by appropriate action will allow us to share our planet with other living organisms in a responsible manner, and ensure the survival of this world for years to come.
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- Theft Act 1968 in the UK p. 162
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