# 2 Basic Anatomy and Physiology of the Human Brain

This chapter contains some basic background on the anatomy and physiology of the human brain relevant to this project. The final section focuses on the neonatal brain and some common pathologies.

2.1 Anatomy of the head

The human *nervous system* consists of the *central nervous system* (CNS) and *peripheral nervous system* (PNS). The former consists of the brain and spinal cord, while the latter composes the nerves extending to and from the brain and spinal cord. The primary functions of the nervous system are to monitor, integrate (process) and respond to information inside and outside the body. The brain consists of soft, delicate, non-replaceable neural tissue. It is supported and protected by the surrounding skin, skull, meninges and cerebro-spinal fluid.
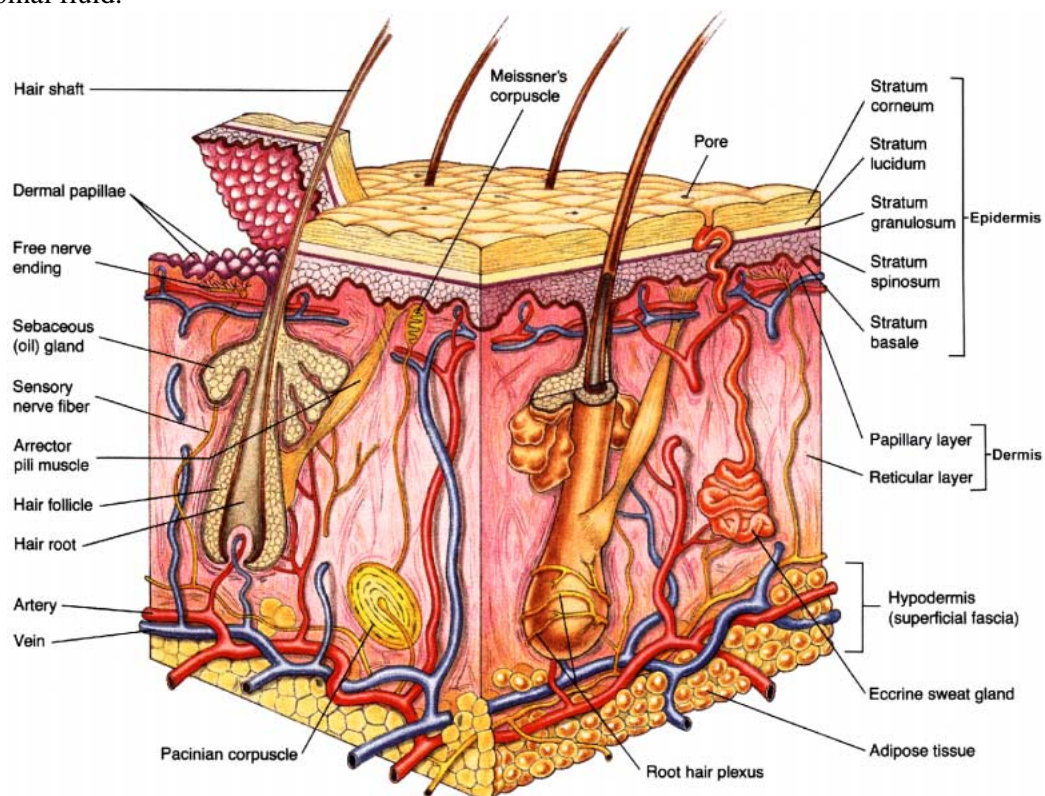

Figure 2–1 Skin and underlying subcutaneous tissue. (Reproduced from [Marieb 1991]).

Skin

The skin constitutes a protective barrier against physical damage of underlying tissues, invasion of hazardous chemical and bacterial substances and, through the activity of its sweat glands and blood vessels, it helps to maintain the body at a constant temperature. Together with the sweat and oil glands, hairs and nails it forms a set of organs called the *integumentary system*. Figure 2–1 shows a cross-section of the skin and underlying subcutaneous tissue. The skin consists of an outer, protective layer, the *epidermis* and an inner layer, the *dermis*. While the top layer of the epidermis, the *stratum corneum*, consists of dead cells, the dermis is composed of vascularised fibrous connective tissue. The *subcutaneous tissue*, located underneath the skin, is primarily composed of *adipose tissue* (fat).

Skull

Depending on their shape, bones are classified as long, short, flat or irregular. Bones of different types contain different proportions of the two types of osseous tissue: compact and spongy bone. While the former has a smooth structure, the latter is composed of small needle-like or flat pieces of bone called *trabeculae*, which form a network filled with red or yellow bone marrow. Most skull bones are flat and consist of two parallel compact bone surfaces, with a layer of spongy bone sandwiched between. The spongy bone layer of flat bones (the diploë) predominantly contains red bone marrow and hence has a high concentration of blood.
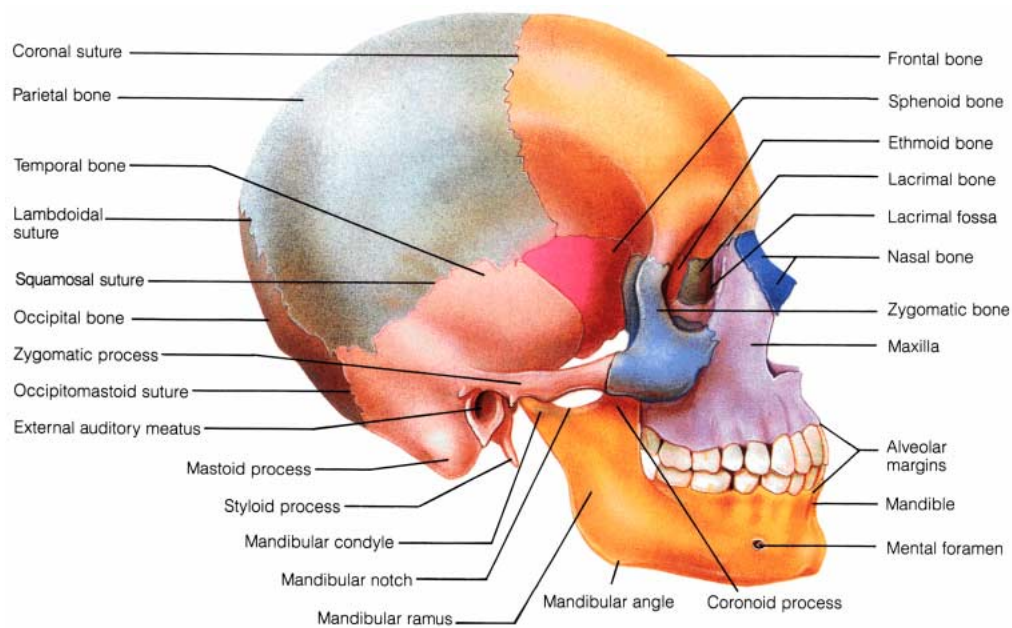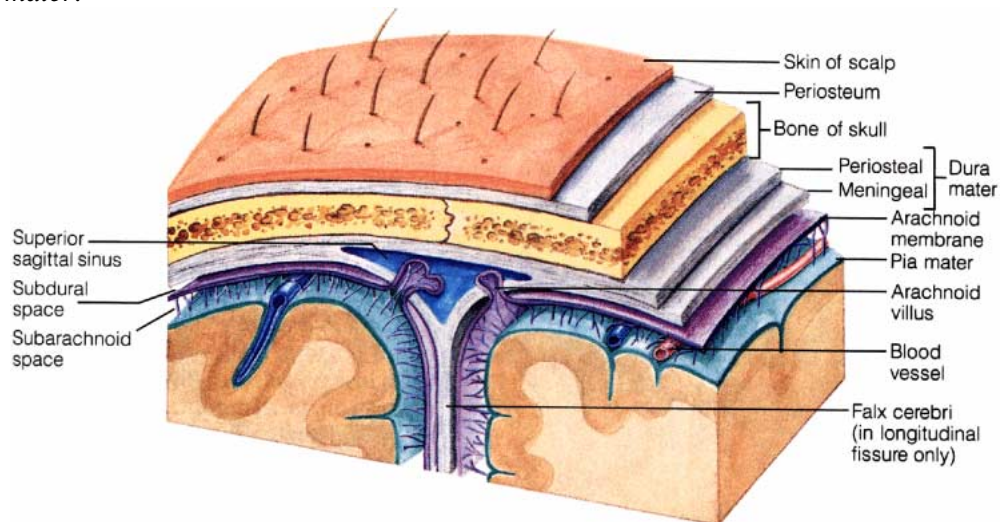

Figure 2–2 Skull. (Reproduced from [Marieb 1991]).

The skull is a highly complex structure consisting of 22 bones altogether. These can be divided into two sets, the *cranial bones* (or *cranium*) and the *facial bones*. While the latter form the framework of the face, the cranial bones form the *cranial cavity* that encloses and protects the brain. All bones of the adult skull are firmly connected by *sutures*. Figure 2–2 shows the most important bones of the skull. The *frontal bone* forms the forehead and contains the *frontal sinuses*, which are air filled cells within the bone. Most superior and lateral aspects of the skull are formed by the *parietal bones* while the *occipital bone* forms the posterior aspects. The base of the occipital bone contains the *foramen magnum*, which

is a large hole allowing the inferior part of the brain to connect to the spinal cord. The remaining bones of the cranium are the *temporal*, *sphenoid* and *ethmoid bones*.

Meninges

The *meninges* (Figure 2–3) are three connective tissue membranes enclosing the brain and the spinal cord. Their functions are to protect the CNS and blood vessels, enclose the *venous sinuses*, retain the *cerebrospinal fluid*, and form partitions within the skull. The outermost meninx is the dura mater, which encloses the *arachnoid mater* and the innermost *pia mater*.

Figure 2–3 Meninges. (Reproduced from [Marieb 1991]).
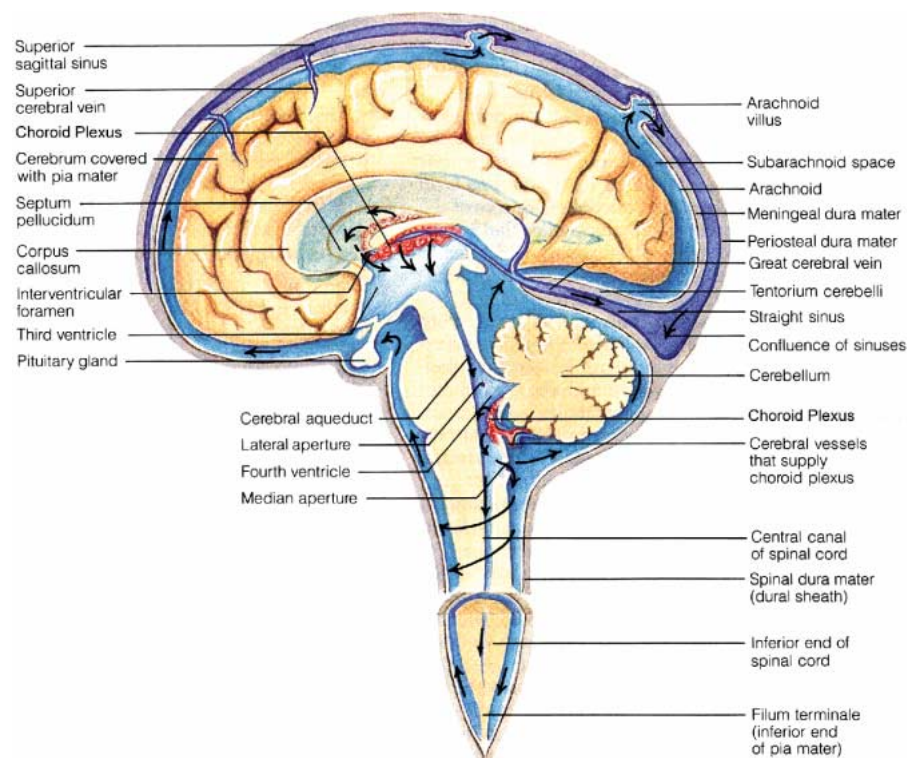
**Figure 2–4** Cerebrospinal Fluid. (Reproduced from [Marieb 1991]).

Cerebrospinal fluid

Cerebrospinal fluid (CSF) is a watery liquid similar in composition to blood plasma. It is formed in the *choroid plexuses* and circulates through the ventricles into the *subarachnoid space*, where it is returned to the dural venous sinuses by the *arachnoid villi*. The prime purpose of the CSF is to support and cushion the brain and help nourish it. Figure 2–4 illustrates the flow of CSF through the central nervous system.

2.2 Major regions of the brain and their functions

The major regions of the brain (Figure 2–5) are the *cerebral hemispheres*, *diencephalon*, *brain stem* and *cerebellum*.
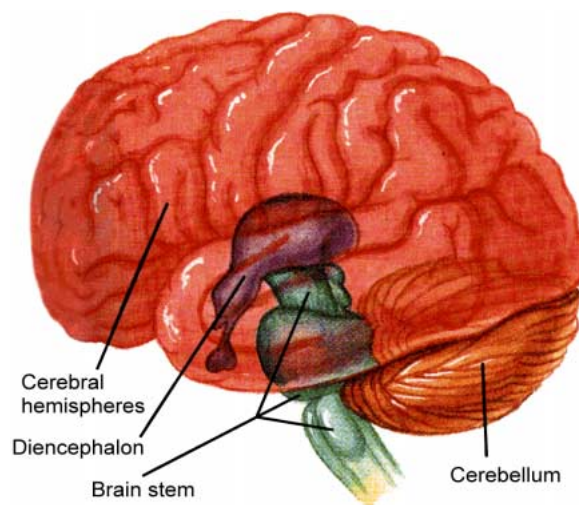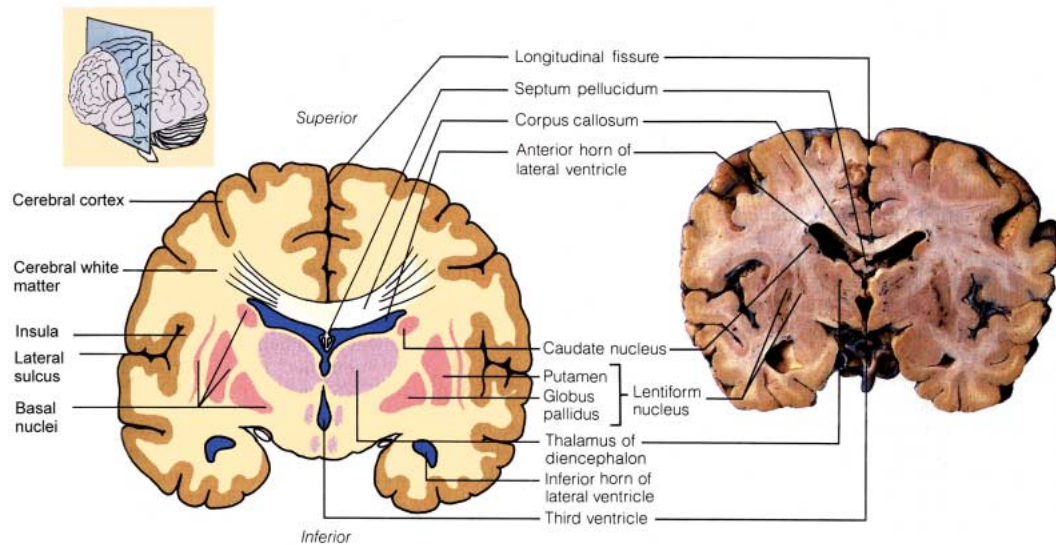

Figure 2–5 Major Regions of the Brain. (Reproduced from [Marieb 1991]).

Cerebral hemispheres

The *cerebral* hemispheres (Figure 2–6), located on the most superior part of the brain, are separated by the *longitudinal fissure*. They make up approximately 83% of total brain mass, and are collectively referred to as the *cerebrum*. The *cerebral cortex* constitutes a 2-4 mm thick *grey matter* surface layer and, because of its many convolutions, accounts for about 40% of total brain mass. It is responsible for conscious behaviour and contains three different functional areas: the *motor areas*, *sensory areas* and *association areas*. Located internally are the *white matter*, responsible for communication between cerebral areas and between the cerebral cortex and lower regions of the CNS, as well as the *basal nuclei* (or *basal ganglia*), involved in controlling muscular movement.

Diencephalon

The *diencephalon* is located centrally within the forebrain. It consists of the *thalamus*, *hypothalamus* and *epithalamus*, which together enclose the third ventricle. The thalamus acts as a grouping and relay station for sensory inputs ascending to the sensory cortex and association areas. It also mediates motor activities, cortical arousal and memories. The hypothalamus, by controlling the autonomic (involuntary) nervous system, is responsible for maintaining the body's homeostatic balance. Moreover it forms a part of the *limbic system*, the 'emotional' brain. The epithalamus consists of the *pineal gland* and the CSF-producing *choroid plexus*.

Figure 2–6 Major Regions of the cerebral hemispheres. (Reproduced from [Marieb 1991]).

Brain stem

The brain stem is similarly structured as the spinal cord: it consists of grey matter surrounded by white matter fibre tracts. Its major regions are the *midbrain*, *pons* and *medulla oblongata.* The midbrain, which surrounds the cerebral aqueduct, provides fibre pathways between higher and lower brain centres, contains visual and auditory reflex and subcortical motor centres. The pons is mainly a conduction region, but its nuclei also contribute to the regulation of respiration and cranial nerves. The medulla oblongata takes an important role as an autonomic reflex centre involved in maintaining body homeostasis. In particular, nuclei in the medulla regulate respiratory rhythm, heart rate, blood pressure and several cranial nerves. Moreover, it provides conduction pathways between the inferior spinal cord and higher brain centres.

Cerebellum

The *cerebellum*, which is located dorsal to the pons and medulla, accounts for about 11% of total brain mass. Like the cerebrum, it has a thin outer cortex of grey matter, internal white matter, and small, deeply situated, paired masses (nuclei) of grey matter. The cerebellum processes impulses received from the cerebral motor cortex, various brain stem nuclei and sensory receptors in order to appropriately control skeletal muscle contraction, thus giving smooth, coordinated movements.

2.3 The cerebral circulatory system

Blood is transported through the body via a continuous system of *blood vessels*. *Arteries* carry oxygenated blood away from the heart into *capillaries* supplying tissue cells. *Veins* collect the blood from the capillary bed and carry it back to the heart. The main purpose of blood flow through body tissues is to deliver oxygen and nutrients to and waste from the cells, exchange gas in the lungs, absorb nutrients from the digestive tract, and help forming urine in the kidneys. All the circulation besides the heart and the pulmonary circulation is called the *systemic circulation*.

Since it is the ultimate aim of this research project to image cerebral oxygenation and haemodynamics some aspects of the cerebral circulatory system are described below.
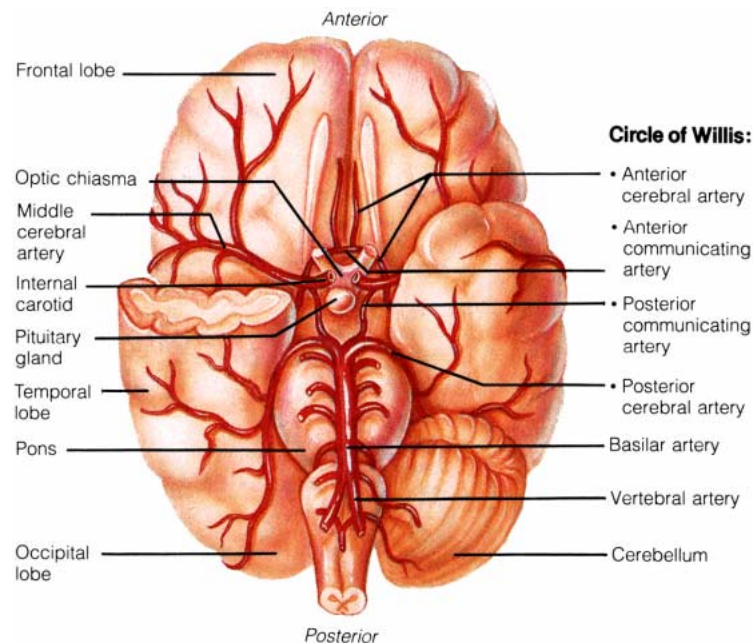
Figure 2–7 Major cerebral arteries and the circle of Willis. (Reproduced from [Marieb 1991]).

Blood supply to the brain

Figure 2–7 shows an overview of the arterial system supplying the brain. The major arteries are the *vertebral* and *internal carotid arteries*. The two *posterior* and single *anterior communicating arteries* form the *circle of Willis*, which equalises blood pressures in the brain's anterior and posterior regions, and protects the brain from damage should one of the arteries become occluded. However, there is little communication between smaller arteries on the brain's surface. Hence occlusion of these arteries usually results in localised tissue damage.

Cerebral haemodynamics

The cardiac output is about 5 l/min of blood for a resting adult. Blood flow to the brain is about 14% of this, or 700 ml/min. For any part of the body, the blood flow can be calculated using the simple formula

$$\text{Blood flow} = \frac{\text{Pressure}}{\text{Resistance}} \qquad (2.1)$$

Pressure in the arteries is generated by the heart which pumps blood from its left ventricle into the aorta. (Since pressure was historically measured with a mercury manometer, the units are commonly expressed in terms of [mm Hg], although the official SI unit is the Pascal [Pa].) Resistance arises from friction, and is proportional to the following expression

$$\text{Resistance} \propto \text{Viscosity} \times \frac{\text{Vessel Length}}{(\text{Vessel Diameter})^4} \qquad (2.2)$$

Hence blood flow is slowest in the small vessels of the capillary bed, thus allowing time for the exchange of nutrients and oxygen to surrounding tissue by diffusion through the capillary walls.

Approximately 75% of total blood volume is 'stored' in the veins which, because of their high capacity, act as reservoirs. Their walls distend and contract in response to the amount of blood available in the circulation. However, the function of cerebral veins,

formed from sinuses in the dura mater, is somewhat different from other veins of the body, as they are non-collapsible.

<div align="center">**Autoregulation**</div>

[Panerai 1998] describes *autoregulation* of blood flow in the cerebral vascular bed as the mechanism by which cerebral blood flow (CBF) tends to remain relatively constant despite changes in cerebral perfusion pressure (CPP). With a constant metabolic demand, changes in CPP or arterial blood pressure that would increase or reduce CBF, are compensated by adjusting the vascular resistance. This maintains a constant O_2 supply and constant CBF. Therefore cerebral autoregulation allows the blood supply to the brain to match its metabolic demand and also to protect cerebral vessels against excessive flow due to arterial hypertension. Cerebral blood flow is autoregulated much better than in almost any other organ. Even for arterial pressure variations between 50 and 150 mm Hg, CBF only changes by a few percent. This can be accomplished because the arterial vessels are typically able to change their diameter about 4-fold, corresponding to a 256-fold change in blood flow. Only when the brain is very active is there an exception to the close matching of blood flow to metabolism, which can rise by up to 30-50% in the affected areas. It is an aim of PET, functional MRI, near infrared spectroscopy (NIRS), and, possibly, near infrared imaging, to detect or image such localised changes in cortical activity and associated blood flow.

2.4 Structure and pathologies of the neonatal brain

Having introduced some basics of the anatomy and physiology of the adult brain, this section focuses on the specific differences in the neonate, as well as common neonatal pathologies which have motivated the construction of an instrument capable of imaging cerebral oxygenation, blood volume and, possibly, myelination.

The embryonic brain and spinal cord develop from the neural tube, which is formed by the fourth week of pregnancy. The brain grows immensely in both size and complexity during pregnancy and even soon after birth. Because a membranous skull restricts expansion, the forebrain is bent towards the brain stem, and the cerebral hemispheres almost completely envelop the diencephalon and midbrain. Moreover, the spatial restrictions cause the cerebral hemispheres to increase their surface area by becoming highly convoluted such that about two thirds of its surface are hidden in its folds. The skull bones of the foetus and neonate are soft and the sutures are not yet fused. Hence the skull is very flexible and deforms under light pressure. Brain development of the foetus, neonate and infant are more thoroughly reviewed by [Herschkowitz 1988].

Compared to the adult, neonates have a smaller head size (ca. 6-12 cm in diameter), thinner surface tissue, skull and CSF layers, lower scattering coefficients of grey and white matter (due to lesser myelination in the case of white matter), as well as a comparatively small mismatch between the two (see also Table 4–1). These anatomical features are all favourable to NIR imaging. The neonatal skull, because it is less mineralised, may also have a lower scattering coefficient, but there is no data at present. All these factors greatly benefit penetration of light deep into the white matter and enable measurements to be made across the head, which is essential for tomographic imaging.

Arterial and venous haemoglobin saturation values for the foetus in utero are relatively low at 56 % and 18% [Rooth 1963], respectively, compared to about 97% and 67% for adults. This is because there is a gradient in oxygen concentration across the placenta which ensures diffusion of sufficient amounts of oxygen from maternal blood into the foetal bloodstream. A higher oxygen affinity of neonatal haemoglobin (dissociation curve shifted to the 'left', c.f. Figure 4–3) compensates for this. Over a period of about 6 months after

delivery the neonatal haemoglobin is gradually substituted by the adult haemoglobin, which has a lower oxygen affinity.

The autoregulation mechanism of the (adult) brain was discussed in the previous section. However, in the newborn infant, and particularly in the very preterm infant, there is no consensus on whether, or to what extent, autoregulation in the brain occurs. It is also not clear what effect ischaemia has on cerebral blood flow and the evolution of haemorrhage.

Neurodevelopmental disorders in some *preterm* infants are due to either hypoxic-ischaemic damage to the periventricular white matter, or to intraventricular haemorrhage and its consequences. The period of highest risk is between 26 and 32 weeks of gestation. In preterm infants the majority of haemorrhages occur into the ventricles and the surrounding white matter, the periventricular region. Hypoxic-ischaemic damage is caused by cerebral underperfusion, often combined with a global oxygen deficiency due to an impaired lung function. It also affects the periventricular white matter, which is thought to be a result of the following two effects:

- Increased vulnerability due to high metabolic demands at this phase of the brain development.
- The area is at a 'watershed' of perfusion from the territories of the posterior and middle cerebral arteries (c.f. Figure 2–7).

Enduring neurodevelopmental disorders can lead to diminished neurological function in later life, and in particular spasticity, since motor fibres run through this region of the white matter. Given the potential of the premature infant's developing brain to repair some damage, spasticity is often restricted to stiff limbs and/or subtle learning disabilities.

Cerebral damage in the *mature* infant is most commonly a result of perinatal ('birth') asphyxia, leading initially to cerebral oedema (resulting in compressed ventricles and flattening of the convolutions of the brain), and later to tissue necrosis (tissue death) and apoptosis (cell suicide). The subcortical white matter, basal ganglia, cerebellum and brainstem are the areas predominantly affected, frequently leading to learning disabilities or global developmental delay and cerebral palsy.

Sample neonatal brain images, including that of a patient with hypoxic-ischaemia (Figure 3–4), can be found in chapter 3, which describes various conventional imaging modalities. A comprehensive review of common neurologic disorders is given by [Hill 1996].

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