

# The Pathological Processes

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The body can be attacked in a series of ways, which produce the system failures later in this book. The following paragraphs summarise the essential features of these generic kinds of faults, which can affect any system. The treatment of any one patient typically involves a mixture of two regimes, one aimed at the pathological process, the other aimed at the failure of the system which is affected.

It is very important to understand pathology. You will think me terminally sad for admitting this, but I read path books in bed at night (especially those of my former colleague Neville Woolf). They give you insight into what is happening to your patients.

These pathological processes are summarized in Table 1.

## 1.1. ATHEROSCLEROTIC

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We are all subject to a gradual deterioration in the condition of our arteries, which is accelerated by smoking, high blood pressure, diabetes and genetic susceptibility. The walls of the arteries become laden with lipid (in ‘plaques’), and later with calcium.

The blood plays its part in this pathology, since its clotting contributes to the clinical dysfunction. Sometimes the arteries are perfect and the thrombosis is entirely the fault of the blood, but most of the time it is the roughened arteries that are the major cause.

Atherosclerotic problems give three kinds of characteristic symptom stories. If the pathology affects an organ whose blood flow changes markedly in response to demand (muscle on exercise, gut digesting food) then there may be a stage in the narrowing process at which the organ has enough blood at rest but not under the increased demand. The patient complains of pain during exercise or, if it is mesenteric ischaemia, blood supply to the gut is compromised and pain comes on after eating. The pain is relieved when the demand for blood flow is reduced. Thus we get the characteristic symptoms of ‘angina’ (in the heart) and ‘intermittent claudication’ (legs). The second kind of symptom that can occur is that associated with intermittent arterial blockage caused by small emboli that presumably break up and fail to cause permanent symptoms. These are most evident when they occur in the blood supply to the nervous system (‘transient cerebral ischaemic attacks’). Lastly, sudden complete blockage by a major embolus or thrombosis can occur. This corresponds to ‘stroke’, ‘myocardial infarction’, ‘mesenteric infarct’ or ‘ischaemic limb’.

On physical examination and investigation, the stroke gives neurological signs consistent with the focal pathology. A myocardial infarct is easiest to diagnose on the ECG. A mesenteric infarct, in which a piece of gut becomes necrotic, causes abdominal pain and always takes the patient into ‘very seriously ill’ territory: low BP, weak pulse, shock. The ischaemic limb becomes painful and cold, and the peripheral pulses vanish.

Treatment of the failure in the system can be surgical, especially in the lower limbs; by percutaneous catheter intervention in the limbs, heart, sometimes in the renal arteries but rarely in the carotids; or by thrombolytic enzyme, especially for heart and carotid. Preventive treatment aimed at the underlying pathology can be lifestyle and medical treatment for hypertension, diabetes and high cholesterol. Or by never smoking.

## 1.2. CANCER

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Malignant change can happen in any tissue. Lung, breast, oesophagus, stomach, colon, prostate and ovary are the common sites of the localised ‘solid’ tumours. While the haematological cancers, leukaemias and lymphomas, tend to be spread throughout the marrow and lymphatic system from the outset.

Cancers are randomly occurring things that grow very slowly at first, but which then begin to grow exponentially quickly. As you know, they invade surrounding structures and can spread via lymphatics or the bloodstream (‘metastasise’) to sites away from the original ‘primary’ location.

In the solid tumours, the main presenting problems are typically due to the primary tumour, but it is when the metastases occur that the really serious problems begin. Each type of solid tumour has its preferred target destination for metastasis, but there is a lot of variation. When the tumour attains the metastatic stage, it is out of reach of curative surgery, it can have major organ-destroying capability, and it puts increasingly greater demands on metabolic activity.

In cancer there tends to be a gradual accumulation of symptoms. For a long time there is no detectable malignant mass, but the disease relentlessly progresses until it becomes overt in some way.

The treatment of cancer can be as damaging in medical terms as the original disease, taking one into ‘immune’ and ‘haematological’ failure syndromes.

There is more about cancer in Section 2.13.

### 1.3. INFECTION

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As organisms, we are very good at repelling invading pathogens, *when healthy*. We live in harmony with many of them, on the skin, in the upper airways and in the gut. It always amazes me how we do not continually suffer pneumonia, always breathing bacteria into our warm wet lungs. The culture of bacteria in the colon is separated from the bloodstream by less than a millimetre of delicate tissue. A biologist will tell you that there are zillions of microorganisms out there in Nature, the vast majority of which would be only too happy to feed on us, and yet only a small fraction have evolved to be true ‘pathogens’ that routinely cause human disease.

Apart from upper respiratory tract infections which affect us all, and perhaps urinary tract infection in females, the occurrence of infective illness is typically associated with less than perfect health: with sub-optimal nutrition — short on proteins, vitamins and energy; with abnormal anatomy in many forms; and sometimes with frank immunosuppression. Infection is also related to the infecting load of pathogen to which the patient is exposed. Occasionally a clean-living, healthy person is taken over by a catastrophic bacterial infection that just gets lucky and swamps the defences.

Diagnosis of infection can range from the trivial to the very difficult. There may be a large, red, hot swelling, oozing pus on the patient’s right cheek; or the patient may have a fever and be shivering with no swelling or pain anywhere. The treatment is often antibiotic-based, but some infections (in which localised bags of pus form) are amenable to surgical intervention.

In the syndrome of severe sepsis (Section 2.11), a massive inflammatory reaction can occur which results in failure of many systems in the body.

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## 1.4. AUTOIMMUNE AND INFLAMMATORY

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Autoimmune disease represents a molecular mistake by the immune system, in which the patient's own body becomes the target for immune attack. We cannot do without our immune system, but it has a very hard job to do: it is required to discriminate between self and invader quickly and precisely in order to avoid infection.

The victim of autoimmune disease is more commonly female and of child-bearing age, and this is probably not a coincidence. To the immune system, the foetus is a foreign invader, and the immune system must be modified to avoid it attacking the foetus.

Many organs and tissues can be targeted by autoimmune disease. A whole series of arthritis-type conditions can be seen in the musculoskeletal system. In nephrology, autoimmune attack against blood vessels ('vasculitis') causes renal failure, which often also affects the joints as part of a multi-system attack. In neurology, 'disseminated sclerosis' is the commonest autoimmune disease. In haematology, red cells and platelets can be attacked by 'auto-antibodies'. The 'anti-phospholipid' syndrome is a pro-thrombotic condition in which an antibody to membrane lipids is associated with recurrent thromboses. Autoimmune reactions in the skin are common. In all of these conditions, treatment is aimed at suppressing the immune activity.

The endocrine glands are a very common target (hypothyroidism was the first disease ever to be recognised as 'autoimmune', by Deborah Doniach at the Middlesex Hospital Medical School, sadly now closed). These autoimmune endocrine conditions tend to run their course and end up in destruction of the gland: the doctor's job is to treat the resulting endocrine deficiency. Immunosuppression is not necessary in these cases.

There are other diseases, notably the 'inflammatory bowel diseases', Crohn's and ulcerative colitis, where the clinical disease is due to excessive inflammation. However, that inflammation is not 'autoimmune' in origin, but is a manifestation of a subtle form of immunodeficiency.

## 1.5. METABOLIC AND ENDOCRINE

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The body's biochemistry can go wrong in very many ways. The root cause of the 'metabolic' problem can be genetic, endocrine, renal, hepatic, dietary, intestinal, drug-induced or even psychiatric. But somehow or another, some biochemical abnormality occurs and an organ or function somewhere suffers. I suppose the commonest such metabolic abnormality is atheroma. I am not going to say 'hypercholesterolaemia' here (important though the cholesterol is) because I think that it is more subtle than simple hypercholesterolaemia.

We can include the endocrine diseases under 'metabolic'. Right behind atheroma in the 'metabolic' collection is diabetes (Section 2.6.1), as you know associated with a high blood sugar. In other metabolic disorders, the thyroid can be abnormal, or one of the electrolytes sodium, potassium, acid-base, calcium. High plasma urate is associated with gout. The minerals such as iron, copper and zinc can cause trouble. Lipids are important.

## 1.6. CONGENITAL

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If we include both genetic conditions and acquired conditions that are present at birth, either through environment or accident of development, there must be about 5,000 congenital conditions. No one person can know about them all. It is the paediatricians who are experts here. Many of the inherited conditions are evident in adult medicine, and a very few genetic conditions first show themselves in adult life. Any system can be involved in genetic disease: there is sometimes, but by no means always, a family history; by and large the condition is symmetrical, meaning that it does not favour left over right. The most common in adult practice in the UK? It depends on the geographical locality, but inherited hyperlipidaemias, dominant otosclerosis, cystic fibrosis, thalassaemias and sickle cell anaemia are up there.

It is just now becoming possible to treat some of the recessively inherited disorders by gene therapy, but this is far from routine practice.

## 1.7. TRAUMATIC

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Trauma is the domain of the surgical specialists, especially orthopaedics. Major trauma results in damage to skin and bone and possibly head and spinal column and cord. Haemorrhage is a major problem, and later, infection may complicate trauma.

The internal organs can be affected, especially lung (traumatic pneumothorax), and spleen (which can be ruptured).

Trauma should be obvious as a cause of disease but sometimes the clinical problem can have its onset a long time after the traumatic event, e.g. a spleen rupturing two weeks after a car crash, or epilepsy or pituitary failure developing a year after a head injury.

## 1.8. DRUG-INDUCED

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Lastly we must admit to those diseases that are caused by our own treatment. No drug is perfect. Even penicillin, which can completely cure the patient of a life-threatening infection, can cause severe allergic reactions. Like genetic or metabolic conditions, drug-induced ailments are typically symmetrical in distribution. The liver is a common target of drug-induced disease, but the skin, the gut, kidneys, nervous system, heart and lungs can all be damaged by drug reactions. Some of these reactions are inevitable (neutropenia in chemotherapy), some are truly 'allergic', and some are 'idiosyncratic' toxic reactions. Obviously the key to diagnosis lies in the 'drug history', which will include both prescribed and self-administered medications, and always remembering to ask about known allergies.

**Table 1.** Pathological Process: Summary.

	<i>Pathology</i>	<i>Nature</i>	<i>Clinical Characteristics</i>	<i>Important Tests</i>	<i>Treatment</i>
1	Atherosclerotic	Patchy narrowing of arteries, $\pm$ sudden thrombosis.	Pain in some tissues on increased demand; sudden catastrophic event.	Scans of affected organ. Angiograms, Doppler US, ECG.	Surgical or radiologically based intervention with catheters. Thrombolytics.
2	Cancer	Exponential growth of unregulated cellular clone.	Insidious progression. Weight loss, $\pm$ abnormal bleeding. Pressure effects.	Scans, especially PET. Biopsy.	Surgery, chemotherapy, radiotherapy.
3	Infective	Pathological growth of unwelcome bacteria, viruses or other invaders.	History covering days. Fever, tachycardia, local symptoms.	White blood count, CRP, scans, cultures.	Antibiotics, $\pm$ surgery, fluid support.
4	Autoimmune and inflammatory	Mistaken immune reaction against own tissues.	Younger adult. Relapsing-remitting, painful condition with damage to affected organs.	CRP, autoantibodies $\pm$ biopsy.	Immunosuppression.
5	Metabolic, Endocrine	Biochemical damage to target organs.	Often of gradual onset. Symmetrical. Highly variable	Blood biochemistry.	Replacement therapy: endocrine or biochemical.
6	Congenital	Huge variety of problems.	Always symmetrical. Often, a family history.	Scans, biochemistry.	Support the damaged system.
7	Traumatic	Physically damaged tissues.	History usually known. Limbs are major target but by no means always.	X-rays, scans, circulatory assessment.	Surgery to repair if possible. Correct blood loss. Avoid infection.
8	Drug-induced	Toxicity of exogenous chemical.	Hopefully history will be known.	The best test is to withdraw the drug.	Withdraw drug. Support damaged system.