

Defences: the integumentary system

Components

The integumentary system consists of the skin and its derivatives, including hairs, nails, sweat glands and sebaceous glands.

Functions

The defence of the body against invaders involves two systems, the integumentary system and the immune system. These systems interact to defend the body.

The skin acts as a barrier between the external environment and the rest of the body. It retains body fluids and defends against the entry of invaders such as viruses, bacteria and parasites. It also helps to maintain a constant body temperature.

Skin contains receptors that sense, for example, temperature, touch and pain. In sunlight vitamin D is synthesised in skin.

Recent research has shown that the skin plays an important role in immunity.

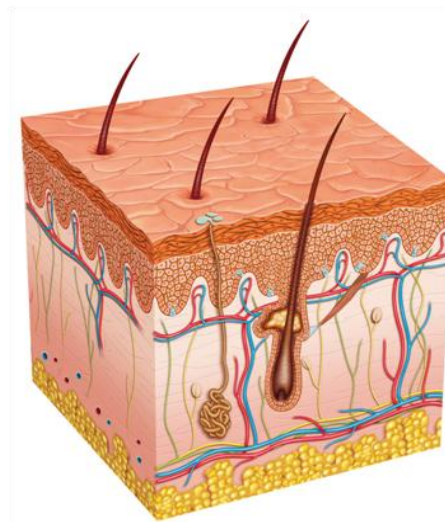


Figure 1 Beneath the skin.

Key mechanisms

Epidermis

The epidermis of the skin consists of many layers of cells. On the inside they are living and rapidly dividing. As cells are continually lost from the outer surface, new cells are formed below, pushing up new replacement layers.

The outer layers become progressively keratinised, dead and flattened. The keratin is progressively cross linked as the cells mature. When they die it forms a tough airtight and almost waterproof layer at the surface.

Dermis

The dermis is immediately below the epidermis. It is a connective tissue layer containing many elastin (stretch) and collagen (strength) fibres, together with a variety of sensors (specialised nerve endings) and numerous blood vessels. Sebum secreted by the sebaceous glands helps create a skin surface that is hostile to many pathogens. This encourages harmless bacteria, which compete with and displace pathogens, to grow. Also present are important components of the immune system, collectively called the skin-associated lymphoid tissue. If the skin barrier is breached by invading

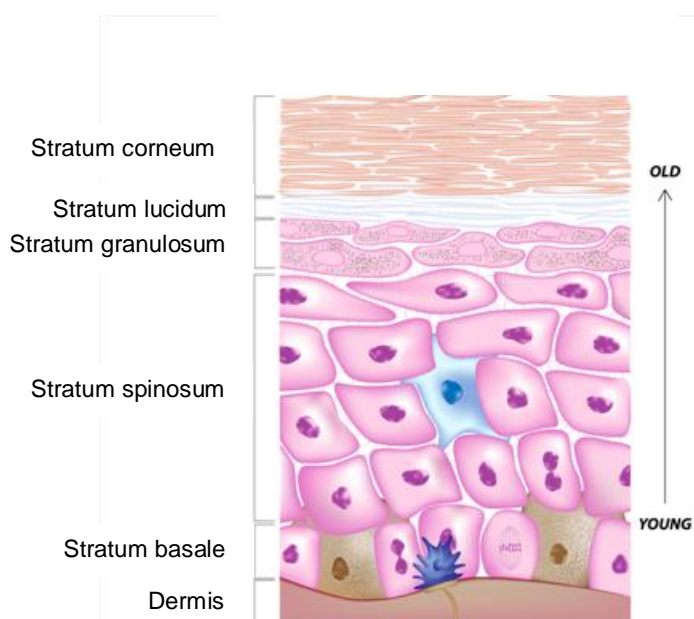


Figure 2 Structure of the epidermis.

micro-organisms, the immune system is alerted by Langerhan cells which detect and collect antigens¹.

Drug administration

While the skin barrier prevents or limits the entry of most materials, some (especially lipid-soluble substances) can pass through the lipid bilayers of the epidermal cell membranes. Drugs such as nicotine and oestrogen can be absorbed through the skin, so these may be delivered through a cutaneous patch. Some gels may be applied to the skin and are absorbed. The skin barrier is avoided when drugs are given orally or by inhalation, injection or drip. 'Hypodermic' refers to the layer below the dermis of the skin.

Body cavities

Some internal cavities are a continuation of the skin. The eyes, gut, urinary and reproductive systems are examples.

Defence mechanisms include:

- tears, saliva and urine contain a bactericidal enzyme lysozyme which hydrolyses components of the cell walls of many bacteria;
- vaginal secretions are converted to lactate by harmless bacteria, creating an acid environment which inhibits many pathogens;
- urine is acidic, inhibits bacterial growth and regularly 'flushes' through the urethra;
- mucus in the respiratory tract traps inhaled particles and micro-organisms, cilia sweep the mucus to the pharynx to be swallowed – in the stomach most pathogens are killed by the acid or proteolytic enzymes in gastric juice;
- bacteria in the gut ('gut flora') compete with and exclude pathogens;
- bacteria under the tongue convert nitrate in food to nitrite which converts to nitric oxide in the stomach and is toxic to various micro-organisms
- lymphoid tissue in the intestine contains lymphocytes which identify and destroy pathogens (part of immune system).

Platelet plugs and blood clotting

Damage to the skin and its blood vessels could cause severe fluid loss and allow the entry of pathogens. Minor damage causing leaks in arterioles, venules and capillaries is sealed before repair by the formation of platelet plugs.

- Damage to the smooth endothelial lining of blood vessels exposes collagen and activates platelets which release thromboxanes which stimulate platelet aggregation.
- Activated platelets adhere to the collagen and release adenosine diphosphate (ADP) causing nearby free platelets to become sticky.
- Sticky platelets adhere to the first layer of activated platelets and release more ADP.
- A platelet plug builds up to seal the defect, actin-myosin complexes in platelets contract to compact and harden the plug



Figure 3 Platelets (thrombocytes) are cell fragments 2 to 4 μm in diameter that circulate in the blood plasma.



Figure 4 A wound to the skin.

¹ See *Defences: the immune system*.

- ADP causes normal undamaged endothelial cells to release prostacyclin and nitric oxide which inhibit platelet aggregation – the plug only forms at the site of damaged tissue.

In more serious damage involving bleeding or skin damage, blood clots form to seal leakages and plug gaps in the skin. A cascade of responses involving twelve factors (I to XII) takes place, which lead to the formation of a clot when soluble fibrinogen is converted into fibrin fibres that trap blood cells to form a plug. Each step activates the next.

Role in homeostasis

The skin indirectly affects homeostasis by acting as a barrier. It helps to prevent harm to cells from pathogens or toxins that might enter the body. It makes the maintenance of a constant internal environment achievable by preventing the loss of body fluids. Other systems that are continuous with the external environment (such as the respiratory, digestive and urinogenital tracts) also have defence mechanisms against entry by harmful agents.

Skin has a direct effect on homeostasis by helping to regulate body temperature through evaporation of sweat from sweat glands and through controlling blood flow near the surface.

Examples of what can go wrong

Haemophilia

Haemophilia is a group of inherited disorders which interfere with blood clotting. Since it is a recessive X-chromosome defect, it occurs almost exclusively in males. As the genes involved are present on the X-chromosome, males with defective genes on their single X chromosome are certain to develop it. Females are extremely unlikely to have defective genes on both X chromosomes, but can be carriers passing it on, on average, to half their sons. Queen Victoria was a carrier for haemophilia.²

The most common forms are deficiency of clotting factor VIII (haemophilia A) and factor IX (haemophilia B). Because fibrin cannot form bleeding is prolonged. Prior to the 1960s, when effective treatment first became available, average life expectancy was only 11 years.

Mild haemophilia A can be treated with injections of desmopressin, a synthetic hormone which stimulates the production of factor VIII. In more severe cases, octocog alfa, a synthetic version of factor VIII is used. Haemophilia B is usually treated with injections of nonacog alfa, which is a genetically engineered version of factor IX.

Finding out

Recently, gene therapy has also been used to treat haemophilia B. In December 2011, a group of British and American scientists claimed the successful treatment of haemophilia B using gene therapy. The factor IX gene was inserted into an adenovirus which infects liver cells. The virus was infused intravenously into patients who were given immunosuppressants.³

- Why is haemophilia B a good candidate for the use of gene therapy?
- Why did the scientists use a virus that infects liver cells?
- Why were the patients given immunosuppressant drugs?
- Why would successful gene therapy be a better choice for treatment than the use of replacement factor IX?

² http://en.wikipedia.org/wiki/Haemophilia_in_European_royalty.

³ http://www.nytimes.com/2011/12/11/health/research/hemophilia-b-gene-therapy-breakthrough.html?_r=1.