PET briefing

Positron emission tomography (PET) is an imaging technique which utilizes small amounts of radiation to study the structure and function of organs. It is therefore used in the diagnosis of disease.

Positron emission tomography (PET) is based upon the behaviour of certain rare isotopes – variants of elements which behave identically but differ slightly at the atomic level. These isotopes are radioactive, emitting particles called positrons, and can be incorporated into naturally occurring substances, such as glucose, and their movement followed around the body. Tiny amounts of these isotopes are used, and their radioactivity is very short-lived, making PET a relatively safe technique.

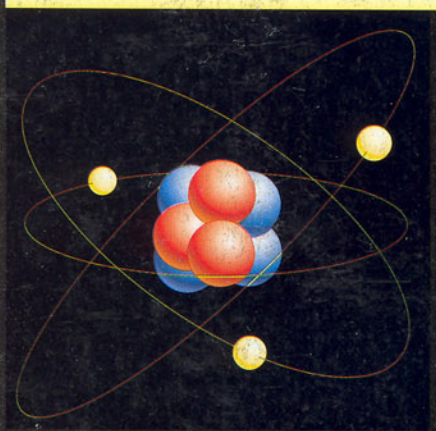
PERFORMING A PET SCAN

As these isotopes naturally occur in tiny quantities, it is necessary to produce them in the laboratory in order to yield sufficient amounts to use clinically. This is done using a machine called a cyclotron, a type of particle accelerator. Atomic particles are accelerated in a powerful magnetic field, where they collide with other particles, producing these novel atoms.

A PET scan usually takes one to two hours to perform, and requires the patient to lie completely still. If a brain scan is undertaken, the head is placed in a head-rest. A needle is placed in the patient's arm, enabling the tracer to be injected and blood samples to be taken.

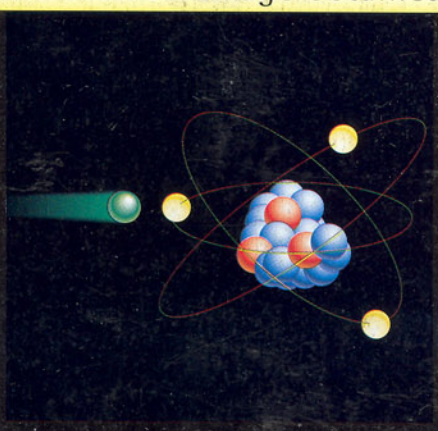
Like many modern imaging techniques, PET takes place in an enclosed chamber. This patient is undergoing a brain scan, facilitated by radioactive glucose.

How is a PET image obtained?



Structure of an atom

An atom is made up of a nucleus, consisting of protons (red) and neutrons (blue), which is orbited by electrons (yellow). In a stable atom the number of negatively charged electrons equals the number of positively charged protons. As neutrons carry no charge, the atom is electrically neutral.



Positron emission

Some isotopes have an excess of protons, and therefore carry a positive charge. The atom can become neutral by converting a proton into a neutron, which is achieved by throwing off a particle called a positron (green), which travels a short distance until it meets a nearby atom in the body.

Annihilation

Positrons are a type of matter called antimatter – a positron is actually an anti-electron. When it meets an electron, they annihilate each other. Though both particles disappear, they are converted into energy – in this case a gamma ray. This is detected by the PET scanner and converted into an image.

Applications of PET

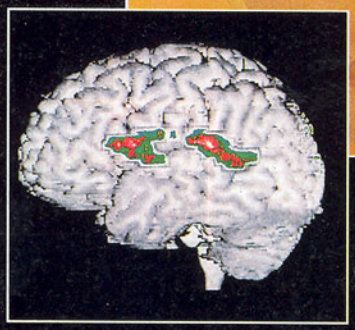
As it is such a new technique, new applications are continually being found. However PET is increasingly becoming a routine task, especially in imaging the heart and brain.

It is important to appreciate that radioactivity takes many forms. Radioactivity is referred to using a measure called 'half-life' – this is a measure of how quickly a radioactive isotope decays to half of any given quantity. The carbon isotope ^{11}C, often used in PET, has a half-life of around 20 minutes, whereas the half-life of the uranium used in nuclear reactors (^{238}U), is 4.5 billion years. The products of positron decay are not radioactive and the sensitivity of the technique means that the quantities used are very small.

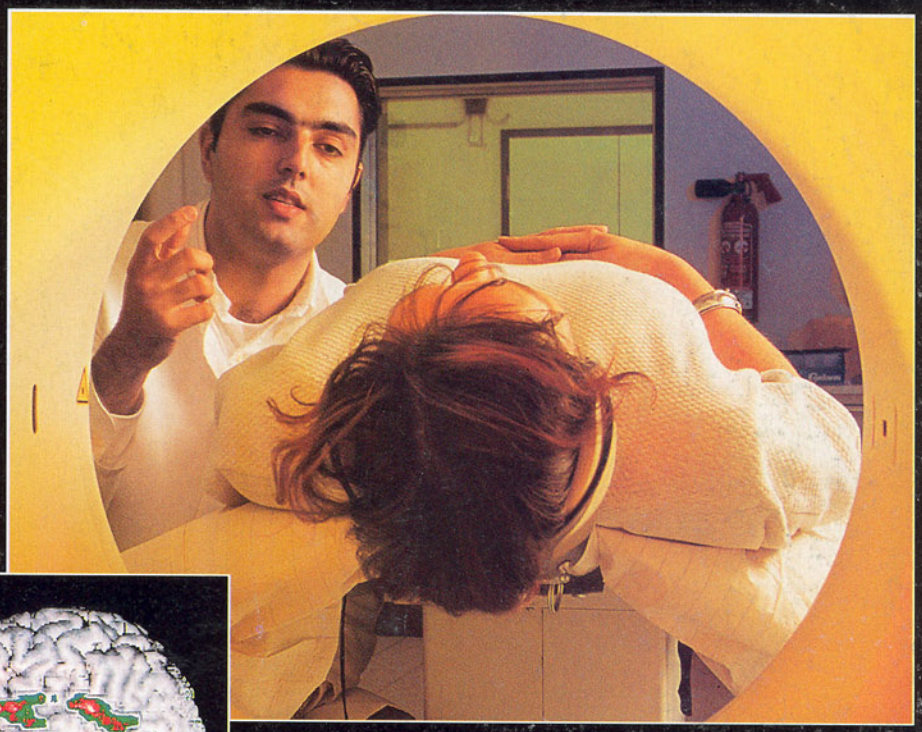
APPLICATIONS

New applications of PET are constantly being discovered, and the technique has already greatly increased understanding in a number of areas.

The great advantage of PET is that the isotopes can be easily incorporated into naturally occurring molecules. The molecules behave in an identical way to their normal counterparts, and their quantity, position and movement can be accurately monitored. For example radiolabelled water and carbon dioxide have been used to study local blood flow in the brain, labelled oxygen has been used to measure the activity of tumours and labelled ammonia has been used to study circulation.



This PET scan shows the parts of the brain involved in verbal short-term memory. The two red-green areas were activated by asking the patient to think of a string of letters.

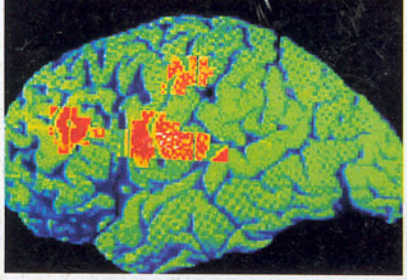


Patients enter the PET scanner lying on a platform, which slides into the receptacle. As it is vital that the patient's head remains still, it is supported in a headrest.

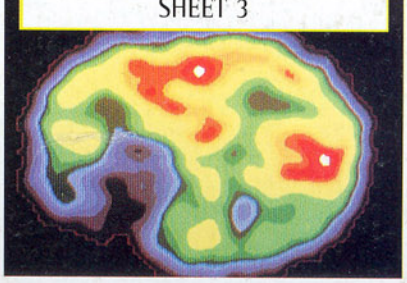
Future PET features in 'Inside the Human Body'

PET scanning is beginning to increase our understanding of brain function and the flow of blood within it. It is now possible to identify which specific regions of the brain are associated with particular functions, such as speech production and memory.

BRAIN IMAGING: SHEET 2



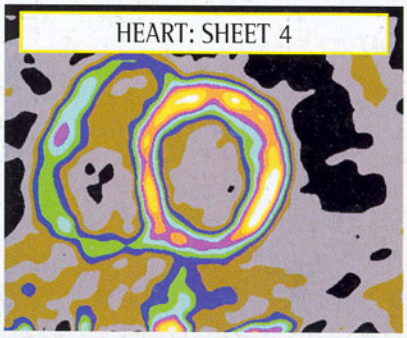
NEUROLOGICAL DISORDERS: SHEET 3



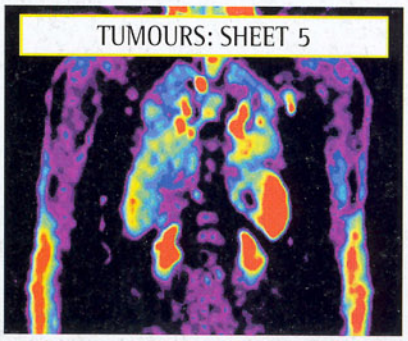
PET scanning is playing an increasingly important role in neurological disorders, such as epilepsy and Alzheimer's disease, and in stroke. Using PET, affected and damaged regions of the brain can be easily and accurately visualized.

Using different radioactive tracers, many different aspects of cardiac function can now be ascertained using PET. These include the flow of blood to and from the heart, the condition of heart muscle and the metabolism of the heart.

HEART: SHEET 4



TUMOURS: SHEET 5



Cancers and tumours show slight differences in their uptake and breakdown of metabolic chemicals. This can be used selectively to view the dimensions and location of malignancies, and whether they are localized or have migrated to other sites (metastasized).

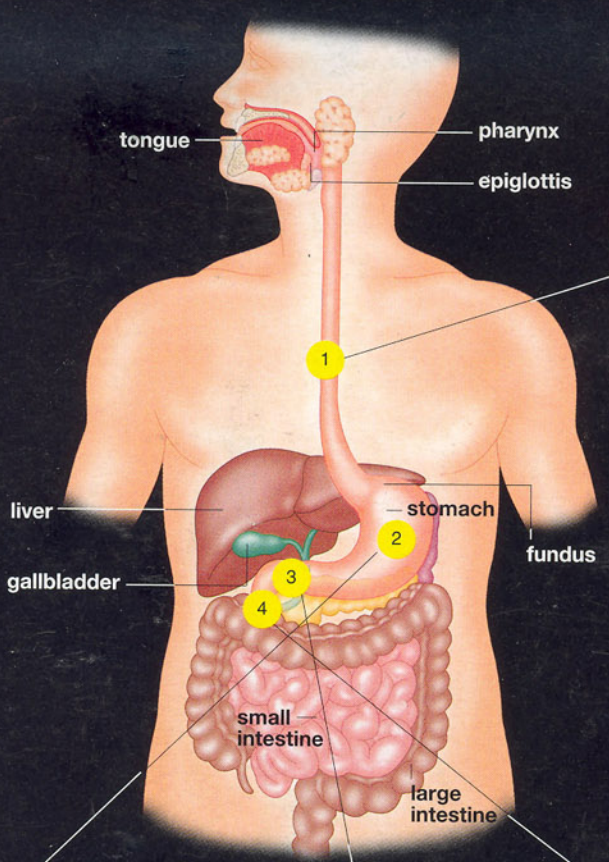
Looking down the throat

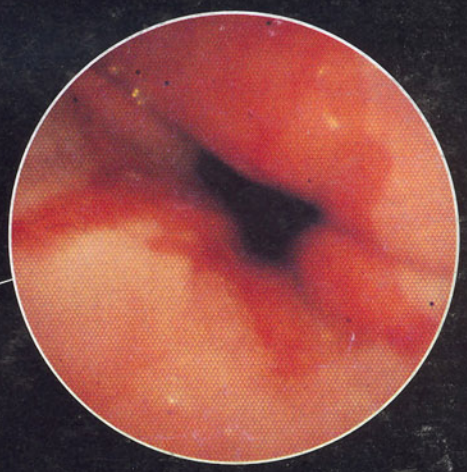
Endoscopy of the upper digestive tract entails close investigation of the oesophagus, stomach and duodenum. It is most frequently performed in order to diagnose ulcers, tumours and inflammation within the stomach.

As well as functioning as a diagnostic tool, endoscopy technology also allows procedures such as laser therapy, biopsy collection, removal of pre-cancerous growths and the widening of strictures (narrowings) in the oesophagus.

Endoscopies of the upper gastrointestinal tract are carried out via the mouth. The patient, lying on their back, is administered a local anaesthetic. Once the drug has taken effect, the endoscope tube is passed into the mouth, over the tongue. At the rear of the mouth, the tube is pushed past the epiglottis, the flap covering the larynx (vocal cords), and down the pharynx into the oesophagus.

At the end of the oesophagus is a muscle known as the lower oesophageal sphincter. Once past this opening, the endoscope enters the sac of the stomach. The doctor guides the tube through a right-angled turn in the stomach to reach the pylorus, another sphincter, which leads this time to the duodenum.

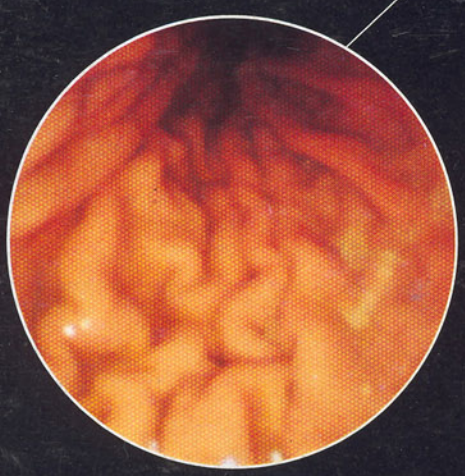




▲ *As the endoscope travels down the oesophagus, it reveals the narrow opening of the cardia – the orifice between the gullet and the stomach.*

1 Oesophagus

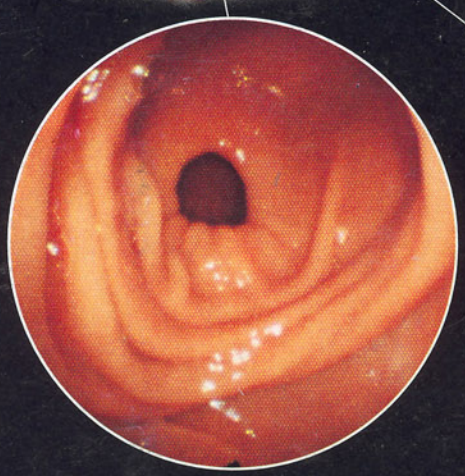
The oesophagus is a muscular tube that connects the pharynx to the stomach. In a fully grown adult, it is about 23 cm long. Also known as the gullet, it lubricates and propels food as it moves to the stomach. In the gullet, the endoscope can be used for, among other things, the diagnosis and treatment of ruptured veins.



▲ *Once the endoscope enters the stomach, it reveals the rugae (folds of lining that give the stomach its elasticity). This is where food is stored and partially digested.*

2 Rugae of stomach

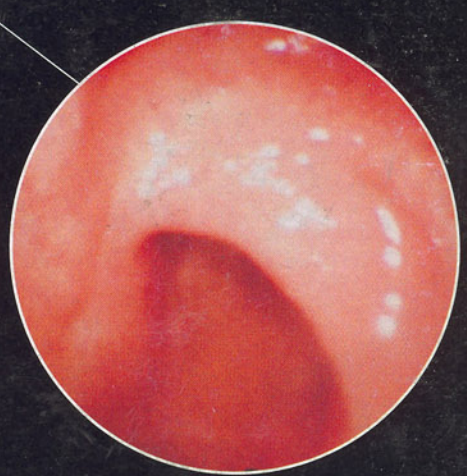
The majority of the stomach (the fundic and gastric zones) is formed from folds called rugae, which give the stomach elasticity and increase its surface area. This area acts as a reservoir for ingested food – there is no peristalsis here, but it is under the control of the nervous system.



▲ *At the base of stomach is a ring of muscle known as the pylorus sphincter. This is the gateway controlling the movement of partially digested food to the duodenum.*

3 Pylorus

Just before the endoscope leaves the stomach, it enters the pyloric zone, an area which does not possess rugae. At the end of the pyloric zone is a muscular sphincter which opens and closes, allowing controlled emptying of the stomach contents into the duodenum.



▲ *The next step on the endoscope's journey is the duodenum, the uppermost section of the small bowel. This part of the body stores bile and juices secreted by the pancreas.*

4 Duodenum

Breakdown of food into soluble matter begins in the duodenum, a 25-cm-long tube which forms the first part of the small intestine. Duodenal endoscopy is used to diagnose peptic ulcers, tumours and vascular abnormalities, all of which are common to the duodenum.

In search of ulcers

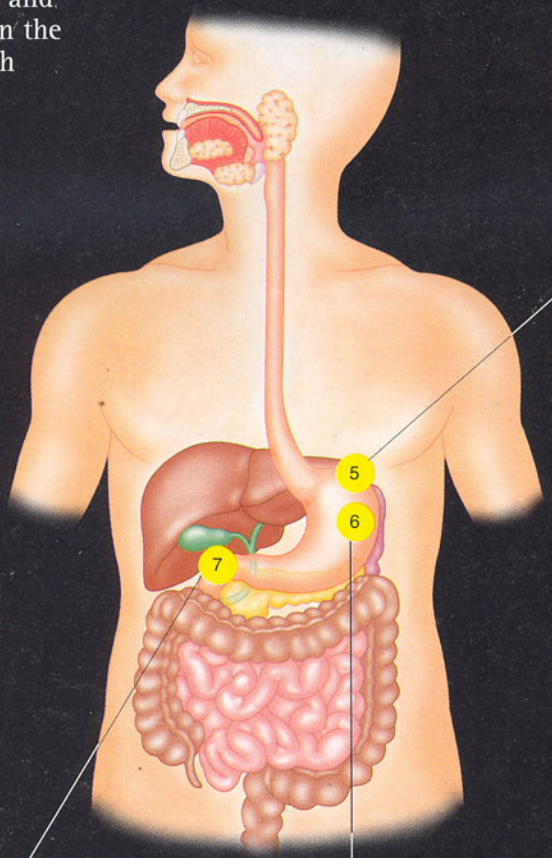
One of the more common uses of endoscopy is in the diagnosis and treatment of ulcers – breaks in the mucous linings of the stomach caused by an acid imbalance.

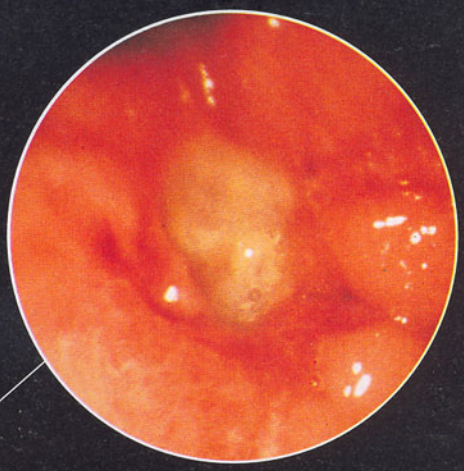
Gastric (also known as peptic) or duodenal ulcers are responsible for at least 5,000 deaths each year in the UK. The causes of gastric ulcers are not fully understood, but traditional theories imply an imbalance between acid secretion and the resistance of the gastrointestinal lining to acid.

The following factors are likely to prompt investigation:

- Age over 45 years
- Previous history of peptic ulcers
- Weight loss
- Use of anti-inflammatory drugs
- Nocturnal pain relieved by antacids
- Vomiting

Genetic susceptibility to ulcers has been noted, and smoking is known to delay healing and increase the rate of relapse. Stress and diet have also been implicated, but the evidence is less conclusive.



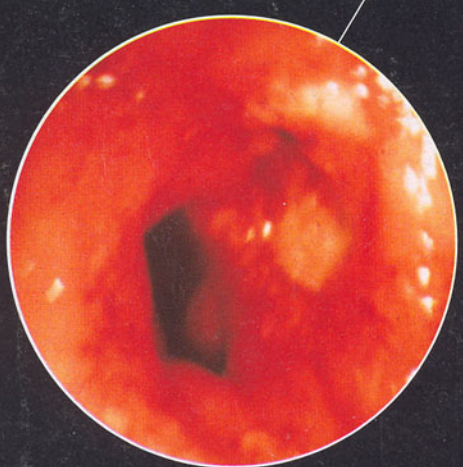


▲ *This gastric ulcer has been caused by disruption of the stomach lining. It shows the typical appearance of a benign stomach ulcer – a yellow-based crater with even, raised margins.*

5 Gastric ulcer

Pain is the most common symptom in ulcer sufferers – however, not all abdominal pains are due to ulcers. Ulcer pain tends to be present for only a few hours at a time, unless the ulcer has perforated. Most people complain of pain a few hours after a meal; pain is not usually present in the morning as there will not be any stimulation of the stomach to induce acid secretions. Possible complications of an ulcer include:

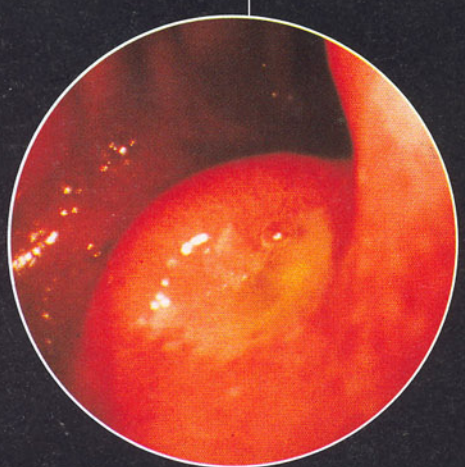
- Bleeding
- Perforation (creation of a hole)
- Pyloric stenosis – repeated scarring causes narrowing, leading to obstruction of the pylorus



▲ *The endoscope reveals an ulcer in the wall of the duodenal bulb, the upper part of the duodenum. This is the most likely site for a duodenal ulcer to occur (95 per cent of duodenal ulcers are located here).*

7 Duodenal ulcer

The majority (95 per cent) of duodenal ulcers occur in the duodenal bulb. Haemorrhage and perforation are the most common complications of this type of ulcer, and are treated by antacids or – in extreme cases – endoscopic removal (although surgery is now rarely required).



▲ *Deeper into the stomach, the endoscope picks up another gastric ulcer. Again, this benign ulcer typically appears with a pale, yellow-white base and a regular, slightly raised border.*

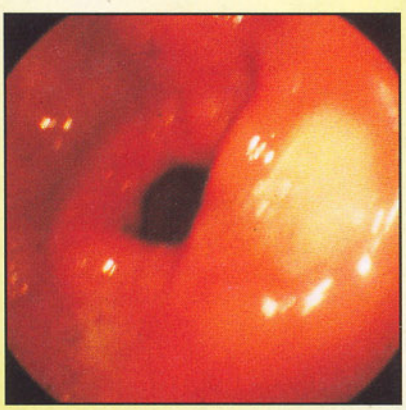
6 Gastric ulcer

There are a number of criteria for visually determining whether a stomach ulcer is benign. Indicators of a benign ulcer are:

- Simultaneous presence of a duodenal ulcer
- Being deeper than it is wide
- Projecting beyond the contour of the surrounding wall

Bleeding ulcer

Bleeding is a relatively rare complication, although some bleeding will always occur from an ulcerous tissue. A particularly deep ulcer may erode into an adjoining artery in the wall of the stomach or duodenum. This will be seen in vomit and will later appear in the faeces. In this case, immediate medical attention is required.

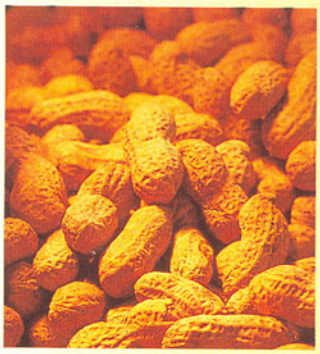


This gastric ulcer is bleeding; fresh, red blood is visible around the ulcer crater. The yellow base of the ulcer is obscured by black blood clots.

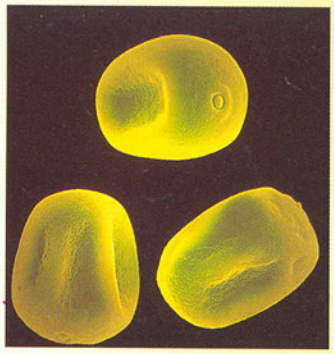
Common allergies

Allergies can be caused by anything from peanuts and bee stings, to penicillin and jewellery. Immunologists have divided these allergic, or hypersensitive, responses into four types.

Type I – Immediate, allergic responses

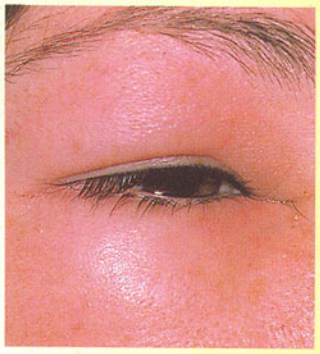


Allergy to peanuts is an increasingly recognised problem, that can lead to life-threatening anaphylactic shock.



Hay fever, an allergic reaction to pollen grains, is the most common example of a Type I, atopic allergy.

The faeces of the house-dust mite, which lives in bedding, carpets and furniture, are a common allergen.



This young boy has had a severe anaphylactic reaction to a bee sting, causing oedema – fluid accumulation around the eye.

Type I hypersensitivity is an immediate response, beginning within seconds of exposure.

The commonest examples are hay fever, childhood eczema and extrinsic asthma. About 10 per cent of the population have a tendency to develop such a reaction, called atopy.

Upon encountering an allergen, instead of making a normal immune response, the body produces a class of antibody molecule called IgE. These bind to mast cells, which are especially prevalent in the skin, respiratory passages and gastrointestinal tract, and cause the release of a number of inflammatory chemicals, including histamine.

Histamine causes blood vessels to dilate and become 'leaky', and is the main cause of typical allergic reactions - runny nose, watery eyes and itchy, red skin. Symptoms also depend upon where the allergen enters the body. An inhaled allergen causes the airways to constrict, causing asthma symptoms; if ingested, symptoms include cramp, vomiting and diarrhoea.

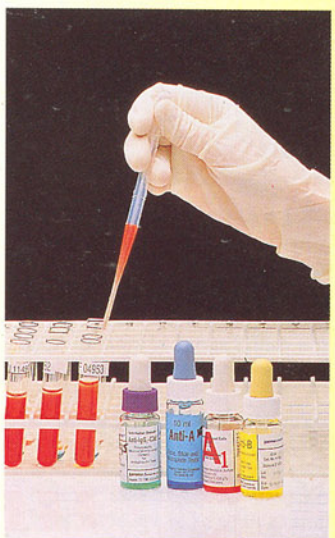
A second, more dramatic, reaction can occur if an allergen enters the bloodstream. This is called anaphylactic shock. The airways constrict (and the tongue may swell) making breathing difficult, and the sudden dilation of blood vessels and loss of fluid may cause circulatory collapse. This is typically triggered in susceptible individuals by bee stings and spider bites, injection of a foreign substance (for example penicillin, or other drugs) or certain foods, such as peanuts. Susceptible individuals may have to carry syringes of adrenaline (epinephrine) to administer in an emergency. Fortunately, reactions such as these are rare.

Type II – Reactions against 'foreign' cells

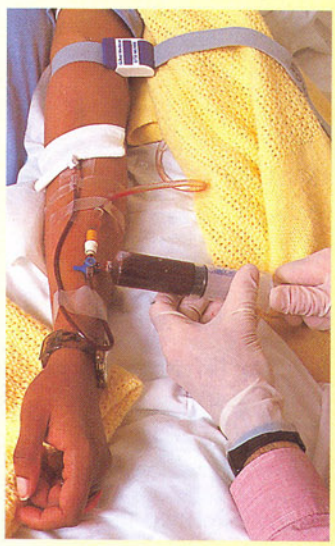
Type II hypersensitivity is caused by the binding of antibodies to 'self' molecules on the surface of cells. This does not generally cause damage, but may trigger a number of further responses.

One example of this may occur in mismatched blood transfusions. Another involves incompatibility between blood groups. All blood is either rhesus positive (Rh^+) or negative (Rh^-), depending on whether a certain protein is present on the surface of a person's blood cells. If a Rh^- woman is pregnant with a Rh^+ fetus, it is possible for fetal blood to enter the mother's bloodstream during delivery, or following abortion.

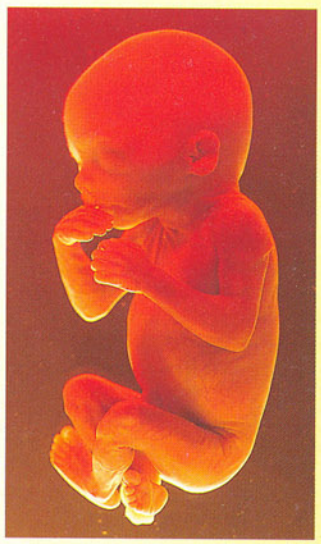
Upon a subsequent pregnancy with a Rh^+ fetus, antibodies may cross the placenta, enter the fetal bloodstream and cause a number of detrimental effects. Injection of antibodies shortly after birth of an incompatible child will destroy fetal red cells in the mother's circulation.



Accurate blood typing is crucial in preventing serious immune reactions in transplants. This occurs in both of the two blood matching systems.



If a mismatch occurs in a blood transfusion (such as a Rh+ patient receiving Rh-), host defences cause destruction of the 'foreign' blood.



A mother may form antibodies to her own fetus's blood, if she comes into contact with it. This can lead to immune reactions in subsequent pregnancies.

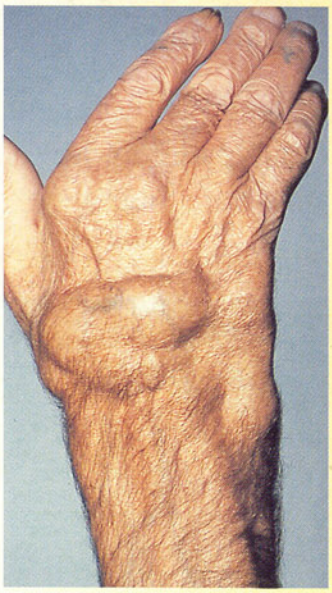
Type III – Reactions against antibody-antigen complexes

Type III hypersensitivity results when allergens are distributed throughout the body. The body produces antibodies, which form insoluble antibody-antigen complexes. The body is unable to clear these, and a large inflammatory response develops.

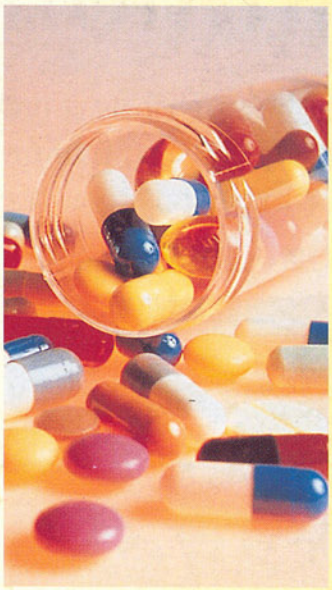
Examples of such allergies include farmer's lung, which is caused by the inhalation of mould growing on hay, and mushroom grower's lung, caused by inhaling the spores produced by mushrooms.

A number of microorganisms can trigger immune complexes. Streptococcal throat infection may be exacerbated by the formation of these immune complexes, as can the organisms that cause malaria, syphilis and leprosy. Drugs can also have the same effect.

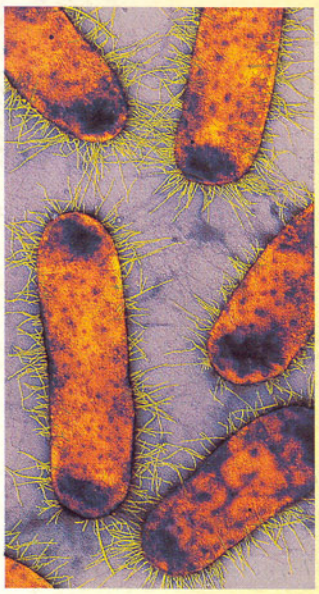
These responses are also involved in autoimmune disorders, when the body's defences attack host tissue. Examples are systemic lupus erythematosus (SLE) and rheumatoid arthritis.



Rheumatoid arthritis is an autoimmune disorder, in which the body's defences attack host tissues. In this case, it is the lining of the joints that are affected, causing erosion and damage, leading to deformity.

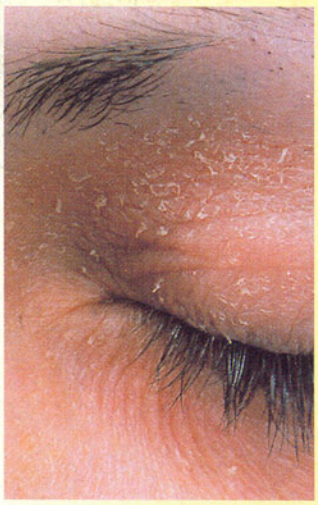


A number of drugs are known to cause allergic responses. For instance, penicillin in the body can bind to the protein albumin (the protein also present in egg white) and provoke a significant immune reaction.

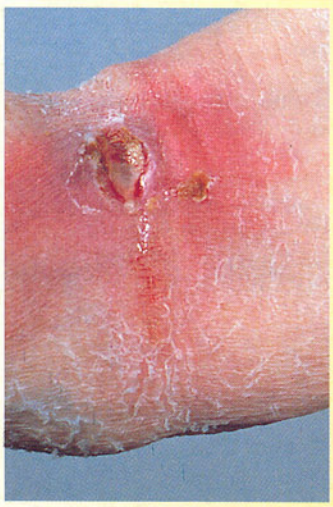


In microbial infections causing malaria, syphilis and leprosy, amongst others, the surface of the microorganism can trigger a Type III response. The complex of antibodies and bacteria can be harmful.

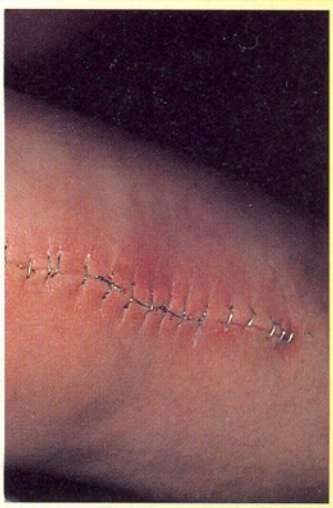
Type IV – Delayed reactions



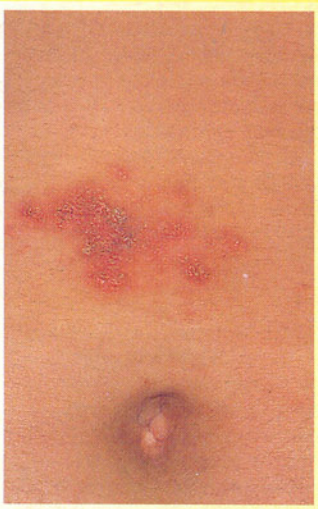
This type IV reaction is actually a reaction to nail varnish. These allergic reactions can occur some distance from the site of the original allergen – in this example, dermatitis has occurred on the eyelid.



This sore has been caused by an allergic response to sticking plaster on the skin, used to cover a wound. Such reactions are caused by the release of chemicals called lymphokines from T-cell white blood cells.



Here a patient has suffered a large wound, running across his knee. The red allergic patches which surround the trauma result from a hypersensitivity to the metal surgical sutures used to close up the wound.



Contact dermatitis in an 18-year-old woman, caused by a reaction to nickel in jewellery. The nickel is absorbed into the skin, where it binds to body proteins and becomes 'foreign' to the immune system.

Type IV reactions are known as delayed hypersensitivities. They appear much more slowly and are caused by the actions of a number of white blood cells. The main effects are caused by a class of immune cell called T-cells. Inflammatory responses are caused by the release of chemicals from T-cells called lymphokines. Therefore antihistamines are not effective against these allergies.

A well-known manifestation of a Type IV reaction is allergic contact dermatitis. This results from skin contact with, for example, nettles, poison ivy, heavy metals (such as lead and mercury), cosmetics and deodorants. These substances are often too small to evoke an immune response, but upon absorption through the skin, they bind to body proteins and become recognized as 'foreign' (this is utilized in the Heaf test for tuberculosis, in which the bacterial proteins are 'punched' beneath the skin surface).

Nickel and copper in jewellery may cause contact dermatitis, and in these cases, the cause is obvious. A wide number of potential allergens exist, and careful questioning of the patient's circumstances and relevant patch tests can establish the cause. Rashes can be chronic (long-term), patchy and some distance from the allergen. For example, allergy to nail varnish may manifest itself as a rash on the face or neck.

Understanding allergies

Sneezing, wheezing, watering eyes and itching are all common symptoms of an allergic reaction. This hypersensitivity results from a battle between antigens and antibodies, and affects up to 15 per cent of the population.

Allergy is a condition in which the body over-reacts to the presence of foreign bodies (known as allergens) such as pollen and dust. Instead of producing ordinary protective antibodies, the immune system starts making a special type called immunoglobulin E (IgE).

Once formed, the IgE antibody circulates in the blood until it specifically binds to surface proteins on cells in the skin, eyes, nose and lungs. These cells – known as mast cells – are covered in granules containing certain chemicals. The next time the foreign protein is encountered, for example, by breathing in a cloud of dust or pollen, the protein connects to receptors on mast cells and causes the cells to 'degranulate' – that is, to release the chemicals contained within them.

ALLERGIC REACTIONS

These chemicals – including histamine – cause a number of changes in the body, including widening blood vessels, inflammation of the mucous membrane of the nose (rhinitis), leaking of fluid in tissues, muscle spasms, sneezing and itching.

This hypersensitivity is specific for a particular protein, such as grass pollen protein. As a result, the symptoms (called hay fever when pollen is involved) only arise when the specific pollen particles are being shed. Such cases are known as 'seasonal allergic rhinitis'.

If symptoms occur throughout the year, this is more likely to be due to proteins shed by pets or house dust mites. This is known as 'perennial rhinitis'. In both types of allergy, hereditary cases are referred to as 'atopic'.

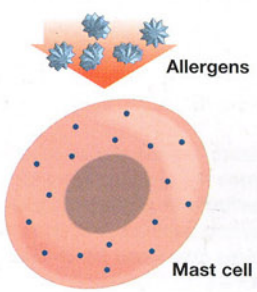
Hay fever is an allergic reaction resulting in inflammation of the eyes and the mucous membrane in the nose. It is triggered by airborne pollen grains.

When pollen particles are inhaled, they attach to certain cells, triggering a release of chemicals, including histamine. These in turn produce symptoms such as sneezing and runny nose.

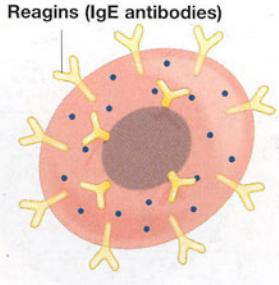
Pollen (orange) and dust (brown) become trapped in the hair-like lining of the trachea, as seen in this electron micrograph. This can trigger an allergic reaction in hypersensitive people.

The progress of an allergic reaction

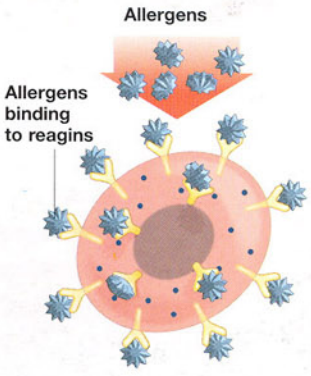
1 Allergens enter the body
Allergens are otherwise unreactive substances that cause a reaction in hypersensitive (or 'allergic') patients. Allergens, such as pollen and dust, enter the body by being swallowed or inhaled, or by coming in contact with the eyes or skin. At this point, mast cells – which can release allergy-causing chemicals – are not yet sensitized.



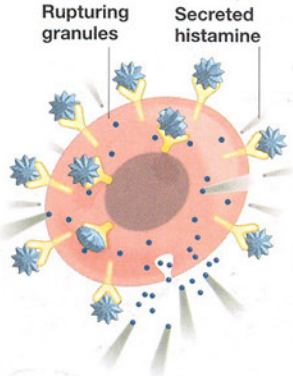
2 Antigens are produced
The presence of an allergen in an allergic person triggers the production of immunoglobulin E (IgE) antibodies. These Y-shaped proteins – known as 'reagins' – cluster around mast cells. Mast cells are found in connective tissue and mucous membrane. Up to half a million molecules of IgE can bind to a single mast cell, making it hypersensitive.



3 Allergen exposure
The next time allergens enter the body, an 'allergen-reagin' reaction takes place, otherwise known as an allergic reaction. The allergen binds to the antigen on the mast cells, resulting in a change in the cell.

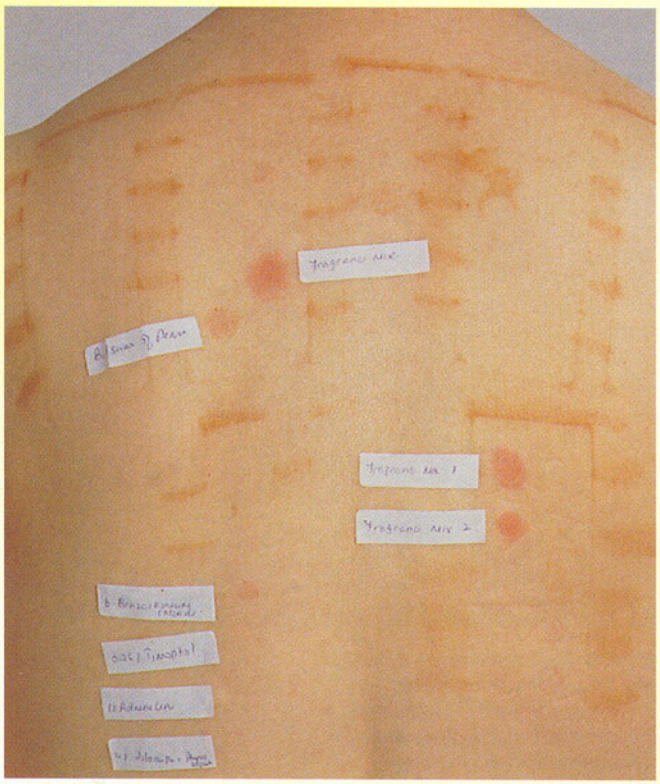


4 Degranulation
The allergen-reagin reaction causes some of the granules on the mast cells to rupture. These rupturing granules release chemicals, such as histamine, that cause breathing problems, excessive production of mucus and other allergy symptoms.



The skin prick test

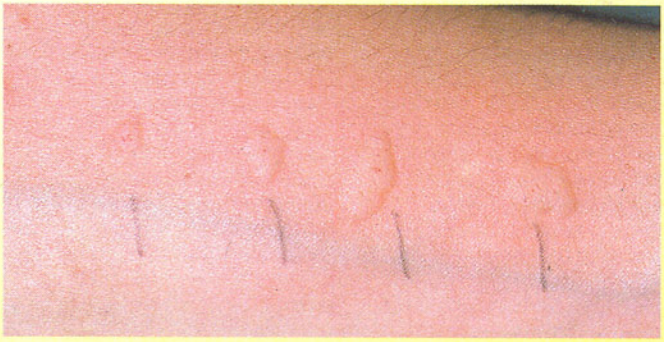
The procedure on the right refers to the skin-prick test, which is used to measure allergic responses. The immunologist limits allergic reactions to local areas of the skin, by pricking the skin with a small drop of allergen. A 'weal' indicates an allergic response – this is verified by pricking samples of saline and histamine as controls (these should give negative and positive results respectively). On discovering an allergy, the patient can then take steps to avoid the allergen or, in some cases, undergo desensitizing injections, which exposes the patient to increasing concentrations of allergen.



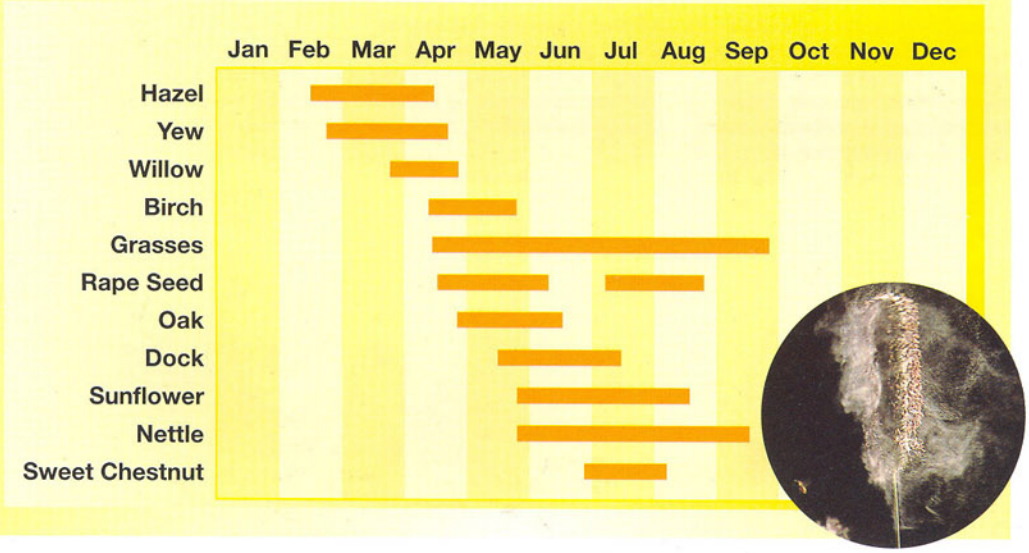
Skin prick tests may be carried out on the patient's arm or back. Drops of soluble substances, containing common allergens, are placed on the skin. The drop is then pricked into the skin, without drawing blood.

The extent of the allergic response can be quantified by measuring the weal, where local inflammation has occurred. With the information gained, the patient can then take steps to avoid the allergen or possibly undergo desensitizing injections.

1. The patient is questioned to identify the likely protein allergens.
2. These proteins are selected from a choice of purified solutions.
3. An area of rash-free forearm, or back, skin is labelled.
4. A drop of each chosen solution is placed on the skin.
5. Drops of histamine (positive) and saline (negative) controls are added.
6. Each solution is 'pricked' into the skin, with a needle or lancet This is almost painless, should not draw blood, and does not make the subject allergic.
7. Wait 15 minutes. Scratching is not allowed, although it may itch.
8. Measure the 'weal' (raised bump in the skin) – the 'flare' (reddening around the weal) is not measured.
9. Record the positive results. If the histamine (positive) control has no weal, this usually indicates that the subject has been taking antihistamine treatment; the tests are invalid and should be repeated. All anti-histamines should be stopped for a week before the test. If the saline (negative) control has a weal, this indicates that the subject may have 'dermographism', with very sensitive mast cells that degranulate on pressure; any positive test result measurements must be greater than this.
10. The delayed reaction: about 4–6 hours later, skin-prick test spots that were positive and have subsided may swell again and become mildly inflamed. This is due to mast cell granule substances that have recruited inflammatory cells to the site. This is not harmful. It indicates what happens in the chronic inflammation in the lungs in asthma.



The pollen calendar



Hay fever, one of the most common allergies, is caused by hypersensitivity to pollen grains.

Pollen is produced seasonally by plants and trees, and is the male sex cell, which fertilizes the female organs of another plant. Wind-pollinated species are responsible for causing hay fever. The plant produces a large number of pollen grains to improve the chances of encountering a plant of the same species. This is, however, bad news for the hay fever sufferer.

Plants release pollen at different times throughout the year. Sufferers may be sensitive to certain species, and knowing these times can be beneficial in managing hay fever.