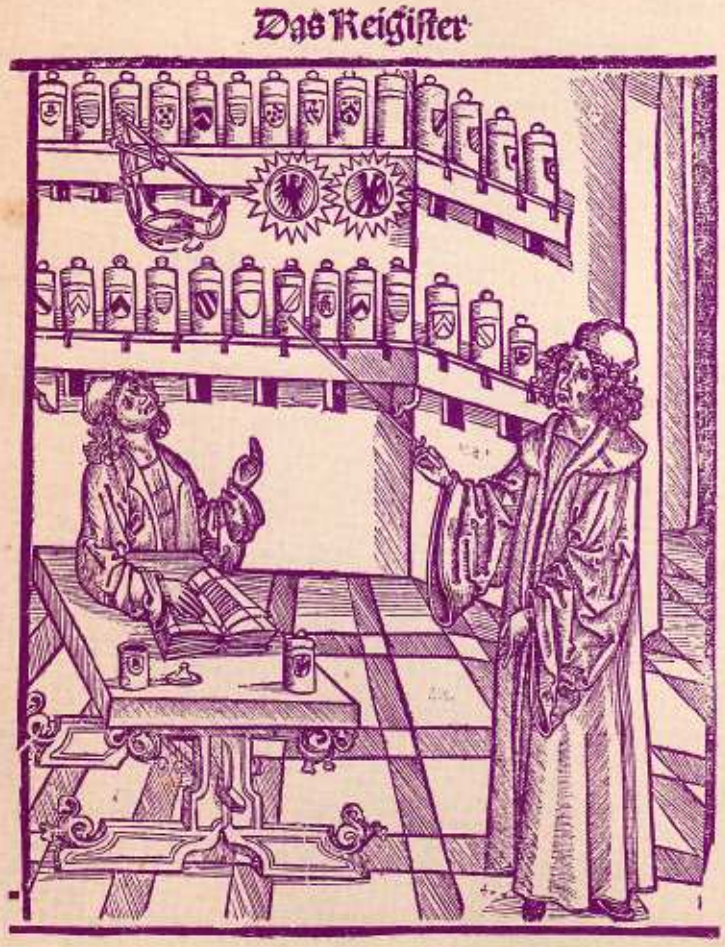
Chemistry Background Book

Drugs and Medicines

Drugs and Medicines

Apothecary's shop (1508). The physician is pointing out to the dispenser the jars from which he is to prepare medicines. The jars are labelled with mysterious symbols of the apothecary's trade.
By courtesy of the Wellcome Foundation



Hippocrates (*c.* 460–377 B.C.) and Galen (*c.* A.D. 130–200), two famous Greeks whose ideas about medicine formed the basis of treatment of disease for well over a thousand years.
By courtesy of the Wellcome Foundation

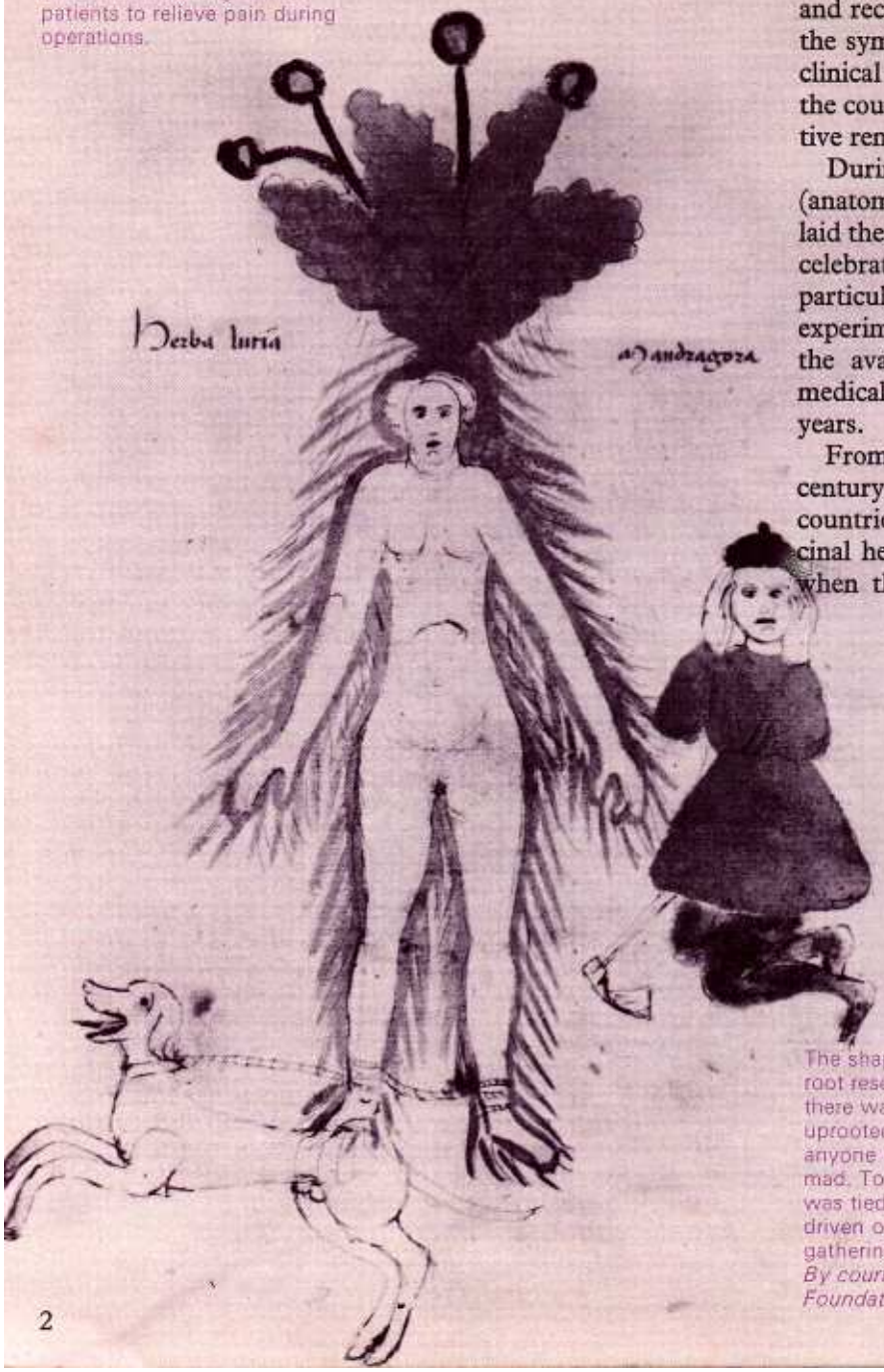
Because of modern medicine, you have a good chance of living to be seventy. A century ago, your expectation of life would have been less than fifty years; but since then much has been learnt about disease – about its nature, its prevention, and its cure. The chemicals called drugs have come to play a crucial part in the treatment of disease.

At first the administering of drugs was a haphazard and even an accidental business. Men have used medicinal plants from the earliest times, but only recently have the active principles of some of them been isolated as drugs. *Ephedra*, a coniferous plant containing the drug ephedrine, which is now used to relieve asthma, was one of several medicinal plants known to the Chinese five thousand years ago. The Jesuits brought cinchona bark from Peru to Europe three hundred years ago without knowing that the active principle is the drug now called quinine, long used in the treatment of fevers.

We do not know much about the treatment of disease before the time of Hippocrates, who was born on the Greek island of Cos in 460 B.C., and who is most often remembered because he drew up the ethical code still followed by practising doctors.

A chemist's shop – woodcut by Cruikshank published in 1845. It would seem that the medicine was not effective.
By courtesy of the Wellcome Foundation

Gathering mandrake which, before the discovery of gaseous anaesthetics, was given to patients to relieve pain during operations.



Disregarding the superstitions and beliefs which then abounded, Hippocrates made careful observations of the sick and recognized that illnesses could be classified according to the symptoms they produced. Thus was founded the art of clinical diagnosis. Hippocrates was able not only to predict the course of some illnesses, but also to select the most effective remedies from the medicines he compounded.

During the next 500 years, studies of bodily structure (anatomy) and of the functioning of the organs (physiology), laid the foundations for another step forward: Galen, another celebrated Greek, linked the symptoms of some illnesses with particular diseased organs. His treatment of sick people, his experiments on animals, and his monumental analysis of all the available medical knowledge, became foundations of medical teaching and were not challenged for a thousand years.

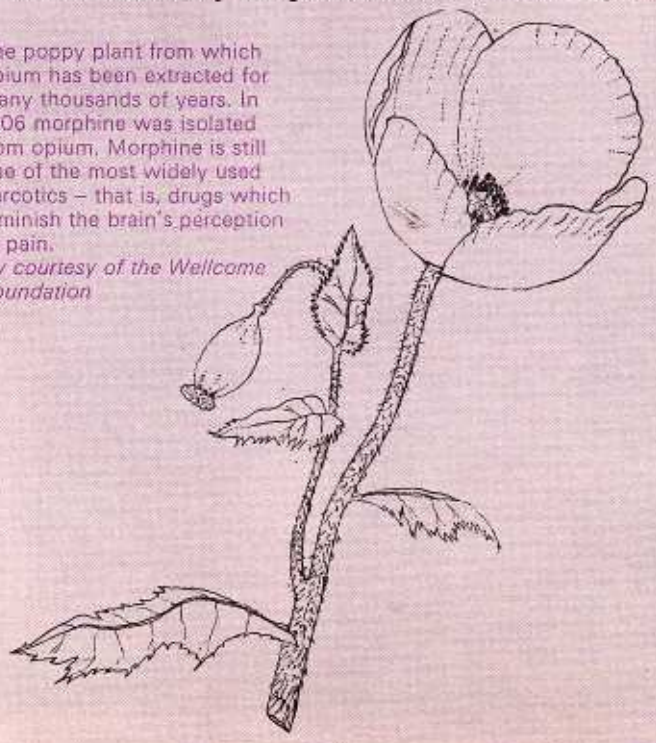
From the death of Galen (*c.* A.D. 200) until the fifteenth century, Europe depended to a large extent on the Arab countries for improvements in the practice of medicine. Medicinal herbs were cultivated in the monasteries of the West, when the word 'drug' made its appearance. Originally it

The shape of the mandrake root resembles a man, and there was a legend that, when uprooted, it shrieked and that anyone hearing it would go mad. To prevent this, the root was tied to a dog which was driven off while the man gathering it covered his ears. *By courtesy of the Wellcome Foundation*

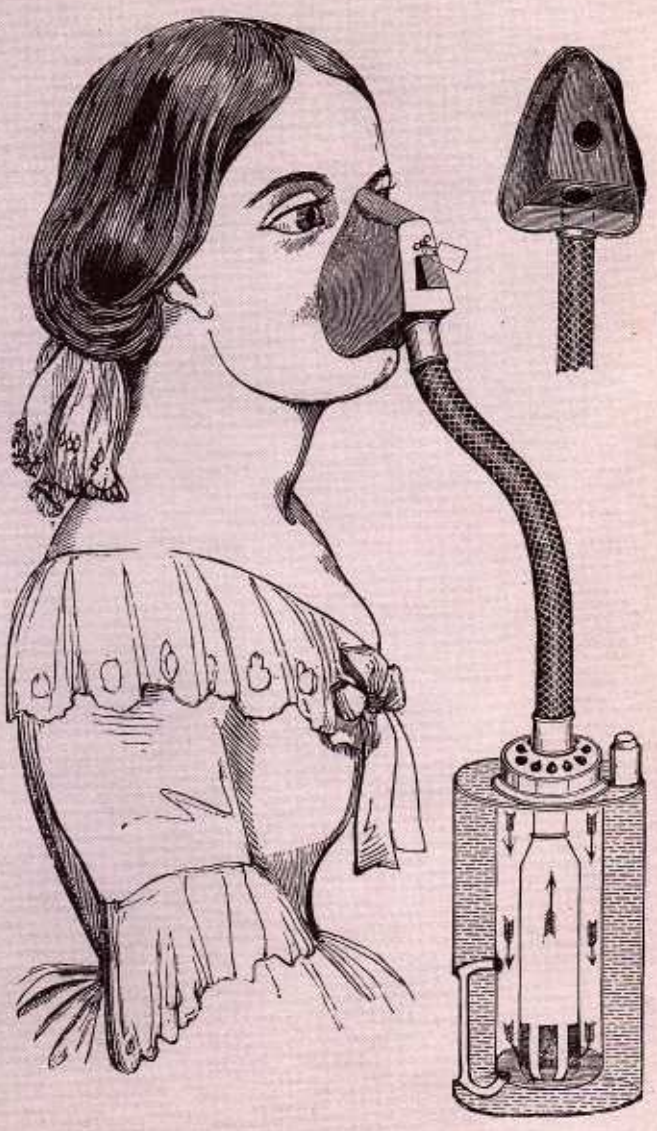
meant simply a dried herb. As the use of medicines increased, apothecaries' shops were opened, not only for making up prescriptions but for administering them as well.

Alchemy was meanwhile spreading from the East, but contributed little to medical practice. The alchemists were too intent on their search for an elixir of life and their attempts to change base metals into gold. At the end of the fifteenth century, however, Paracelsus, the Swiss physician, set himself more practical objectives. He believed that one of the objects of alchemy should be the preparation of drugs, and he began administering such simple chemicals as mercury, sulphur, iron, and copper sulphate. Later, other inorganic compounds were used as medicines – for example, Glauber's salt (sodium sulphate) and magnesia. But though many useful herbs were also introduced, the apothecaries continued to sell medicines which were revolting, or worthless, or both. He who could face 'Balsam of Bats' must have been ill indeed.

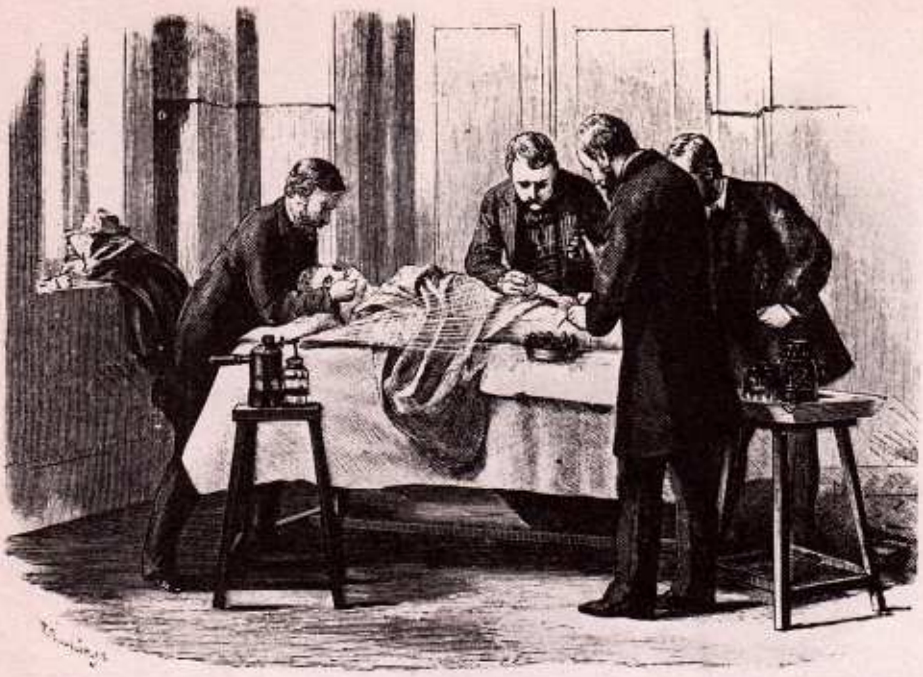
Systematic progress in the use of drugs came only with the rise of chemistry, and especially organic chemistry, in the last two hundred years. Lavoisier was probably the first to determine the elementary composition of animal and vegetable



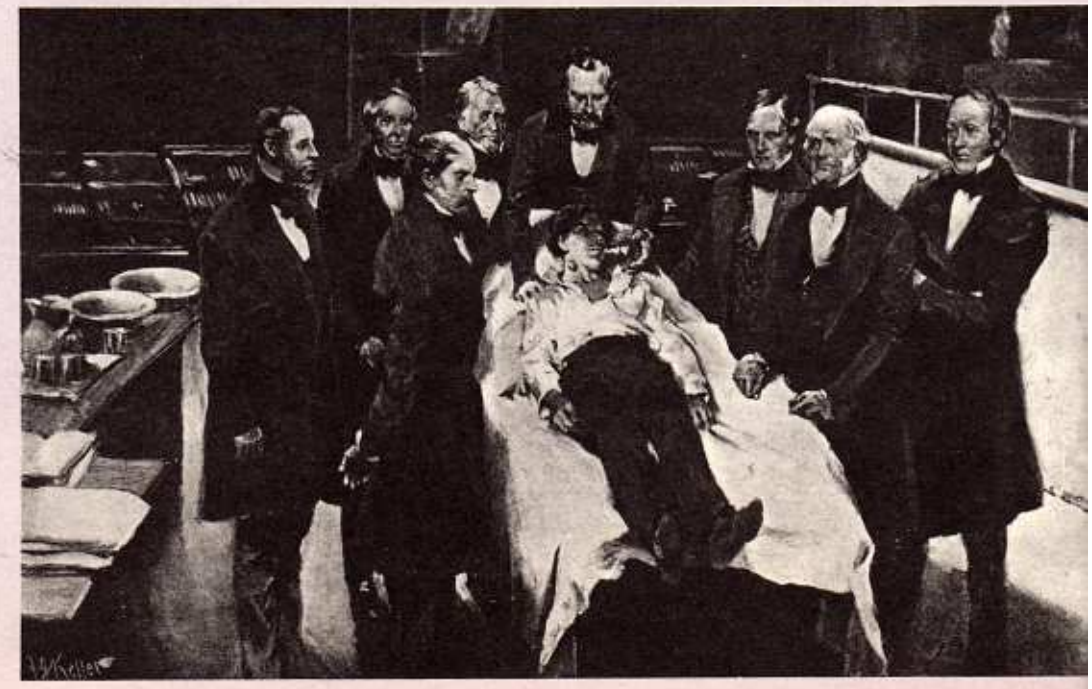
The poppy plant from which opium has been extracted for many thousands of years. In 1806 morphine was isolated from opium. Morphine is still one of the most widely used narcotics – that is, drugs which diminish the brain's perception of pain.
By courtesy of the Wellcome Foundation



A chloroform inhaler (1858).
By courtesy of the Wellcome Foundation

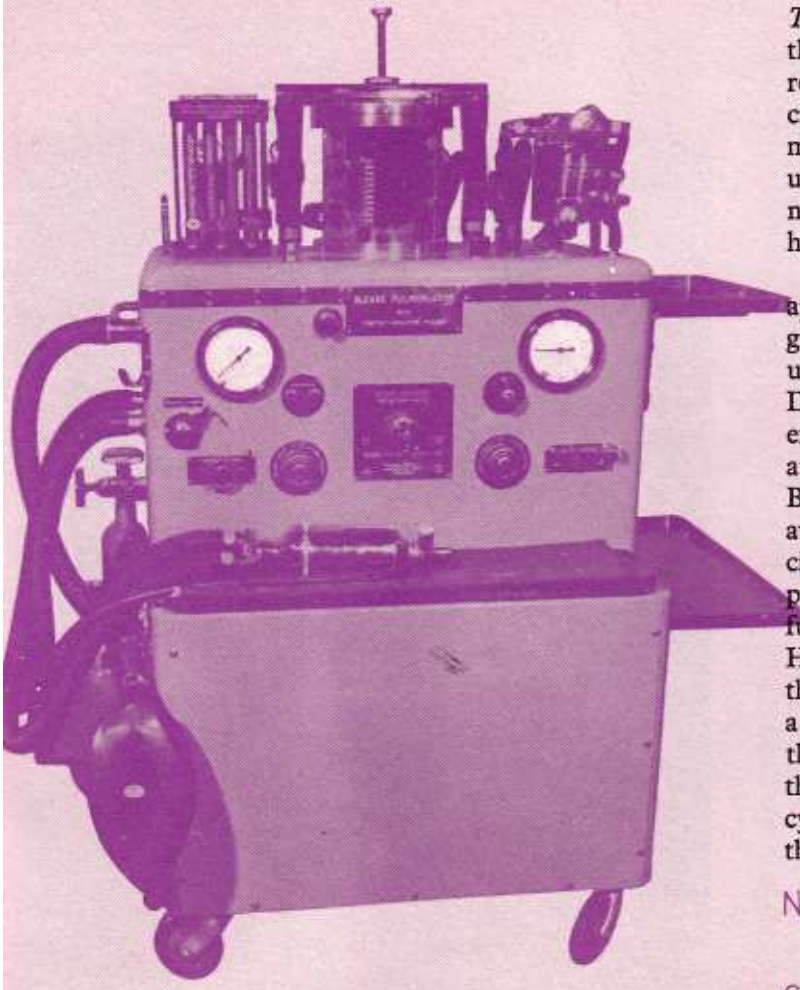


A surgical operation about 1870. By then Lister had begun using antiseptics to keep operating theatres and hospitals free from germs. Here a carbolic acid spray is on the stool beside the operating table.
Radio Times Hulton Picture Library



Dr Morton administering ether to a patient at Massachusetts General Hospital on 16 October 1846. This was the first time a gaseous anaesthetic had been successfully used during a surgical operation.
By courtesy of the Wellcome Foundation

Hospital apparatus for administering an anaesthetic.
St Mary's Hospital



substances, but it was Justus von Liebig, fifty years later, who differentiated carbohydrates and fats from proteins, and who first applied chemistry to physiological problems. From then onwards, organic chemistry advanced rapidly, stimulating a similar advance in pharmacy – the formulation and preparation of drugs.

The relief of pain – The discovery of anaesthetics was one of the first successes in modern medicine. Plant extracts to relieve pain were among the medicaments known to ancient civilizations. In the Middle Ages and before, the juices of mandrake and opium poppy, and even alcohol fumes, were used to produce some loss of sensation. But these reliefs were not sufficient. The surgeon still needed strong men to hold his patients down.

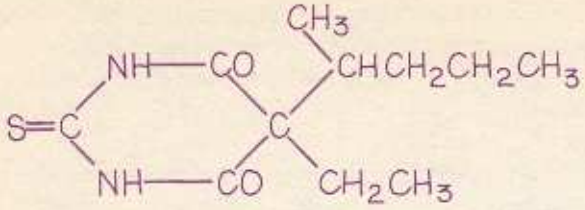
In 1799 Humphry Davy discovered that nitrous oxide appeared 'capable of destroying physical pain' (see the Background Book, *Humphry Davy*). He suggested that it might be useful in surgery, but forty years went by before an American, Dr Wells of Hartford, Connecticut, had one of his own teeth extracted without pain after inhaling the gas. (When Wells attempted to demonstrate the benefits of nitrous oxide at Boston, the gas bag was removed too soon and the patient awoke howling.) Shortly before this another American physician, Crawford Long, had discovered that ether had anaesthetic properties, and in 1846 Dr Morton, a pupil of Wells, successfully used it during an operation at the Massachusetts General Hospital. In Edinburgh Sir James Simpson was so intrigued that in 1847, with two friends at home, he set about inhaling a series of substances to see if any were anaesthetics. One of these was chloroform and they ended up unconscious beneath the table. Much later, other anaesthetics were discovered – cyclopropane (in 1929), trichloroethylene (in 1934), and halothane (in 1956).

N_2O nitrous oxide $C_2H_5OC_2H_5$ diethyl ether

$CHCl_3$ chloroform $CF_3CHClBr$ halothane

The way that anaesthetics work is still uncertain even though, chemically, they may be simple substances. Some of them are gases and must be administered as such. Other anaesthetics can be injected. One of these is thiopentone

(sodium pentothal), which is structurally related to the sedative barbiturates.



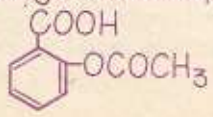
thiopentone

Compounds which relieve pain without making a patient lose consciousness are called *analgesics*. They include substances as mild as aspirin and as strong as morphine, together with local anaesthetics such as cocaine, which block either the brain's perception of pain or other sensations in the injected part of the body.

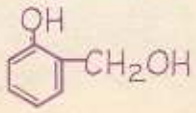
Aspirin is probably the most widely used of all drugs. Its history begins with 'An Account of the Success of the Bark of the Willow in the Cure of Agues' (fevers), which was read to the Royal Society of London in 1763 by Edward Stone, a clergyman of Chipping Norton in Oxfordshire. Stone thought of trying willow bark because it tasted bitter like cinchona (the quinine plant), and because it grew in marshy places where fevers were common. Stone, like his contemporaries, believed that a disease and its cure would be found together in the same environment. The argument was false, but the willow extract gave some small benefit.

Later it was shown to contain a derivative of salicyl alcohol, but there was little progress until 1852, when the related salicylic acid was synthesized and found to relieve pain as well as fever. Unfortunately the acid irritated the mouth and stomach, and the less damaging sodium salt had an unpleasant metallic taste. A more acceptable form of this drug was made in 1899 when Hofmann, a German chemist, found a simple way to make the acetyl derivative of salicylic acid. This compound, which became known as aspirin, retained the beneficial properties of the parent acid but was less irritating to the stomach.

acetylsalicylic acid (aspirin)



salicyl alcohol



Aspirin tablets being counted into bottles through an electronic counting machine. Aspirin, a mild pain reliever, is the most widely used of all drugs.
Boots Pure Drug Co.

Poliomyelitis has been virtually eliminated by the Salk vaccine developed in the early fifties in America. The vaccine is prepared from a culture grown on a suspension of animal kidney cells. Here a suspension of monkey kidneys is being prepared to grow the culture.
Pfizer Limited

The most powerful analgesics are the *narcotics*. Unlike aspirin, they act on the brain. Morphine is a well-known narcotic, obtained from the opium poppy. With drugs of this type there is a risk of addiction. Sometimes a small dose can set up a desire for more. The addict is soon caught in a vicious circle. He develops tolerance to the drug, which means that he is forced to take increasing amounts to produce the effect he seeks; to stop brings pain and sickness.

The attack on infection – The first important successes in the war against infectious disease came from improvements in hygiene. In Britain in the nineteenth century, for example, typhoid fever could be controlled once good public supplies of water became available. But the control of infection was enormously improved after Pasteur had shown in 1856 that putrefaction is caused by airborne micro-organisms. (See the Background Book, *Louis Pasteur*.) From this work grew the idea that many diseases are carried by germs or living organisms too small to be seen with the unaided eye. The micro-organisms are now known to include bacteria (size 0·5–15μ), larger organisms such as those responsible for malaria, and the much smaller viruses (size 0·01–0·2μ) which can only grow and multiply inside cells.

Joseph Lister, a young surgeon working in Glasgow, made good use of Pasteur's work. He reasoned that if putrefaction of wounds is caused by germs, a material that kills the germs will aid healing. Such substances are the *antiseptics*. Lister used carbolic acid (phenol) for sterilizing his hands and surgical instruments and also, in the form of a spray, to reduce the concentration of germs in hospital air. The death rate during and after surgery was markedly reduced. Even today, hospital practice still follows the principles laid down by Lister, though techniques for killing germs have been much improved.

If antiseptics fail to prevent infection, all is not lost. When a person catches a disease, the natural defences of the body are brought to bear against the invading germs. White blood cells may engulf them, or the body may produce 'antibodies' which prevent the invaders multiplying. This is why protection against some diseases can be given by encouraging the formation of these antibodies. This is how *vaccines* function.

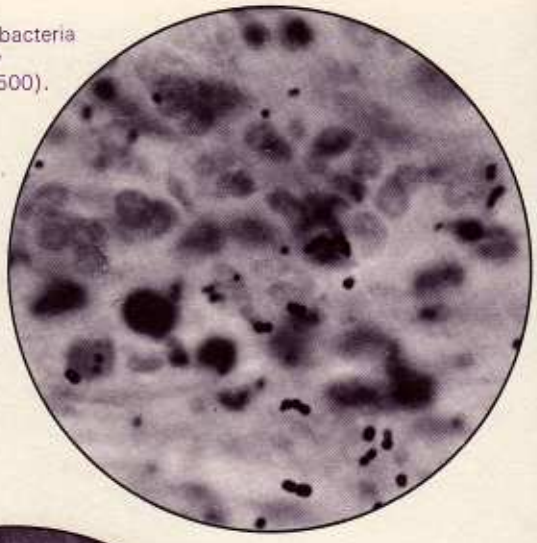
Vaccines are made from the germs which in their normal live state cause the disease. In some vaccines the germs are

dead; in others the germs are ineffectual versions of the harmful organisms. Vaccines of both types are now in use for preventing poliomyelitis. In each case a little of the vaccine will enable the body to deal with an attack of the infection itself. Vaccination has reduced the incidence of some of the most serious virus diseases. Smallpox, for example, has been virtually eliminated from Great Britain, and poliomyelitis has been much reduced.

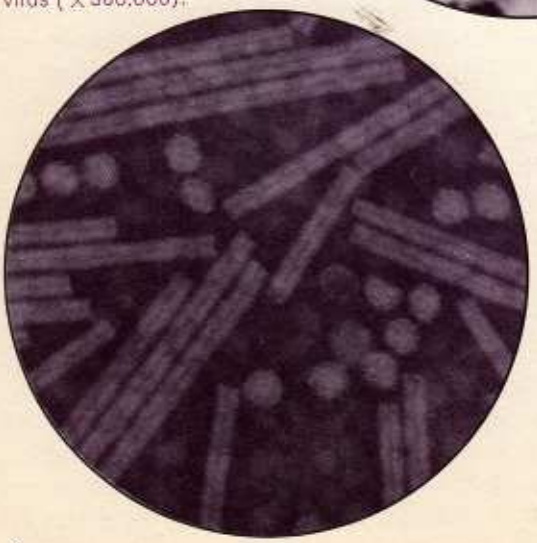
Developing new vaccines demands all the skill and insight of modern biology. If it is not possible to prevent a disease, curing it is the next best thing, and chemicals have a valuable part to play in this connection. It was the German scientist, Paul Ehrlich, who first introduced the idea of *chemotherapy*, the treatment of infections with drugs so as to destroy the germs without harming the body. One of his first successes was the discovery (in 1910) of salvarsan, an organic derivative of arsenic. This drug is used in the treatment of syphilis. Following Ehrlich's ideas, Domagk discovered that the dye prontosil will kill streptococci – a group of bacteria which includes those causing such illnesses as pneumonia (pneu-

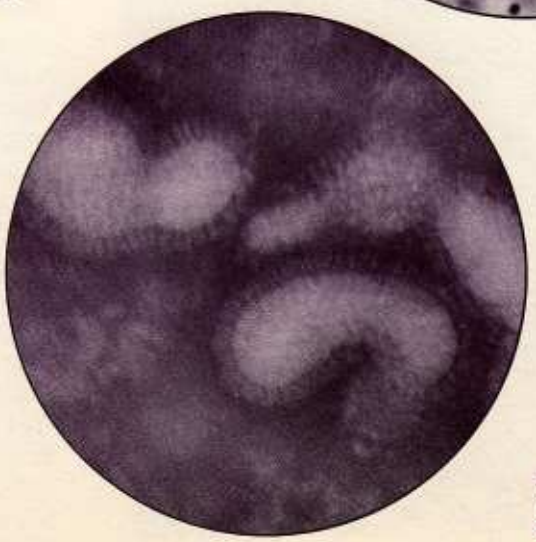
Chains of anthrax bacteria (×1500).

Streptococcal bacteria surrounded by pus cells (×1500).

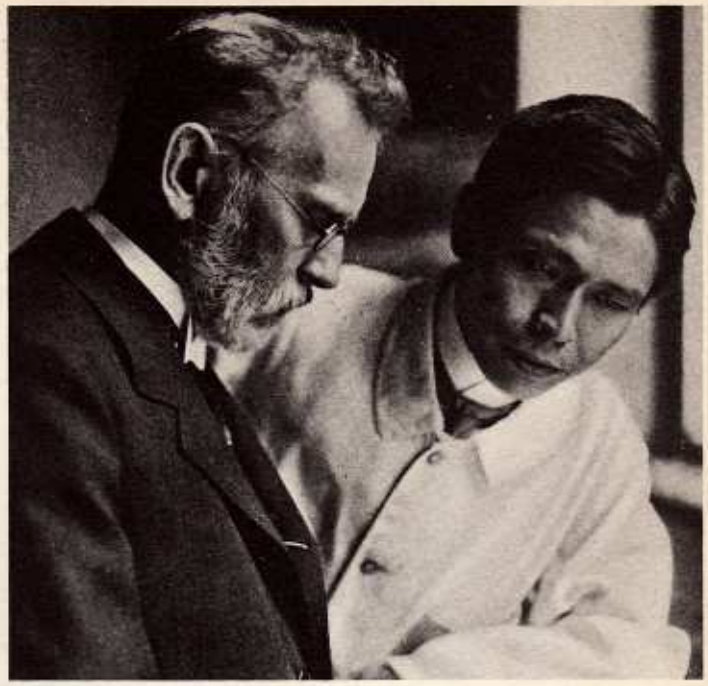


An electron micrograph of rods of tobacco mosaic virus and spheres of turnip yellow mosaic virus (×360,000).



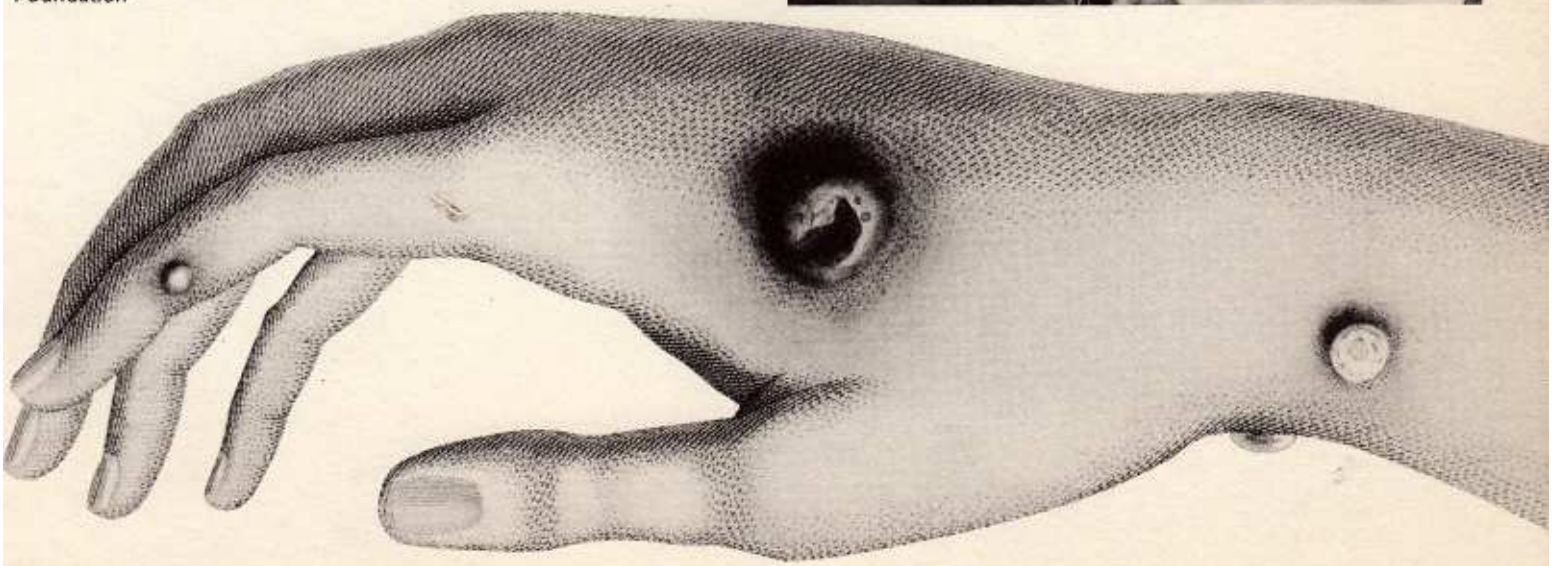


An electron micrograph of the influenza virus (×360,000). *St Mary's Hospital*



Paul Ehrlich (1854–1915) with his assistant Hata. Ehrlich was the first person to prepare in the laboratory a special drug for the treatment of a disease. The drug he prepared was called salvarsan or '606' (because it was the 606th compound he tried) and it was used to cure syphilis. From Ehrlich's work, the treatment of disease by synthetic drugs originates.
By courtesy of the Wellcome Foundation

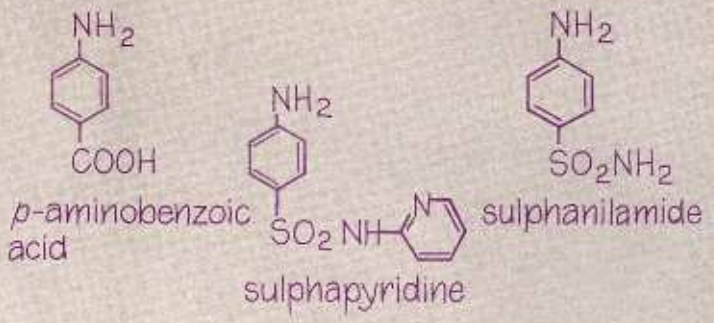
The hand of Sarah Nelmes who became infected with the relatively harmless disease 'cowpox' in 1796. Edward Jenner took lymph from the pustule on her hand to carry out his first vaccination against the dangerous disease smallpox.
By courtesy of the Wellcome Foundation



The original culture plate in which Alexander Fleming first noticed the antibiotic effect of penicillin. The penicillin mould shows as white patches on the germ culture.
St Mary's Hospital

A culture of the mould *Streptomyces rimosus* from which the antibiotic Terramycin is produced
Pfizer Limited

mococcus) and meningitis (meningococcus). Workers at the Pasteur Institute in Paris found that the part of the structure of the dye molecules containing a sulphonamide group ($-SO_2NH-$) was essential to kill germs. Many compounds containing this group were then synthesized, and a series of valuable chemotherapeutic agents was obtained. One of the earliest, sulphapyridine, became well known under the name M & B 693 after it had been used for the treatment of Sir Winston Churchill's pneumonia during the Second World War.

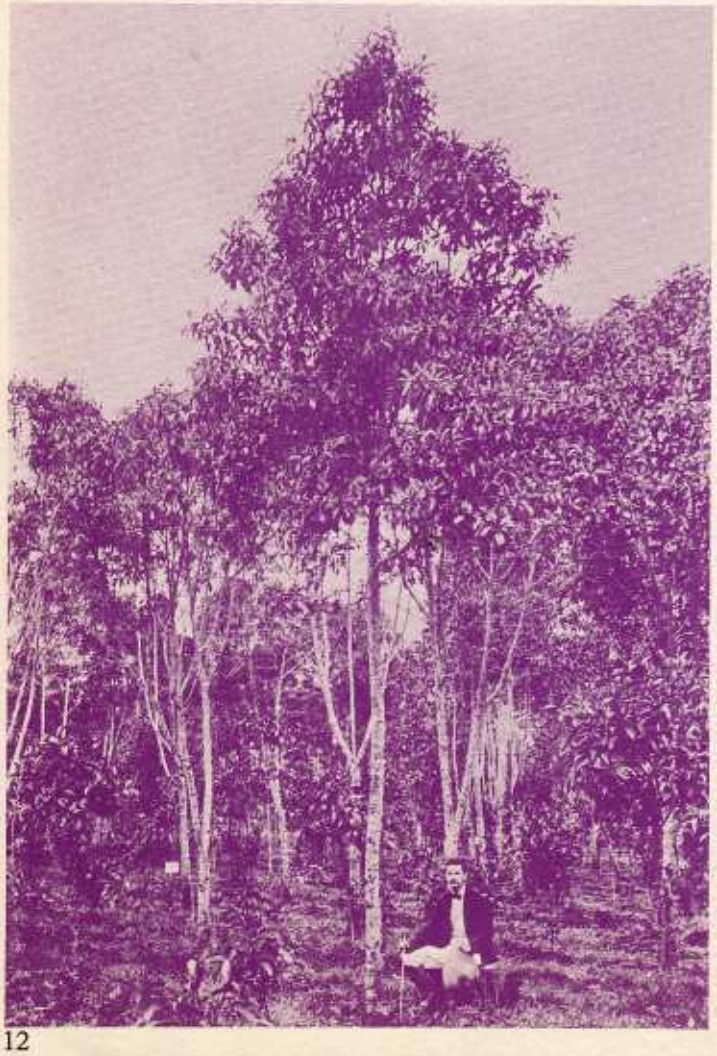


The sulphonamides are effective as drugs because some bacteria are unable to distinguish them from a chemical which is essential to their growth. The chemical is *p*-aminobenzoic acid and its structure is shown in the diagram. The drugs are derived from sulphanilamide – whose chemical structure is very similar. The bacteria die because they consume the drugs instead of their 'food'. Many drugs function in this way, which is known as competitive inhibition.

The sulphonamides were a notable advance in combating infection, but even more spectacular results have been achieved with a group of natural products called *antibiotics* which are obtained from the micro-organisms called moulds. The first antibiotic was discovered in 1928 by Alexander Fleming at St Mary's Hospital, London, though many years went by before it was applied in medicine. Fleming saw that a culture of spherical bacteria (staphylococci) had become contaminated by a mould and that the bacteria nearby had died. He identified the mould as *Penicillium notatum* and supposed that it must produce an active principle harmful to bacteria. In 1940 'penicillin', as the active principle was called, was isolated by a team of scientists working at Oxford under Professor Howard Florey and Dr E. Chain. Its value

Sir Alexander Fleming (1881–1955) who discovered the antibiotic effect of penicillin at St Mary's Hospital, London, in 1928. Penicillin was first used during the Second World War and saved many lives.
St Mary's Hospital

The cinchona plant from the bark of which quinine is extracted. Quinine has been used as a drug since the seventeenth century. Until recently it was used to cure malaria.



as a drug was quickly demonstrated. The *Penicillium* mould was grown on a large scale, and during the Second World War penicillin was extracted in bulk in factories in the United States. This was partly because the pharmaceutical industry in Britain was already too greatly involved in the war to produce it.

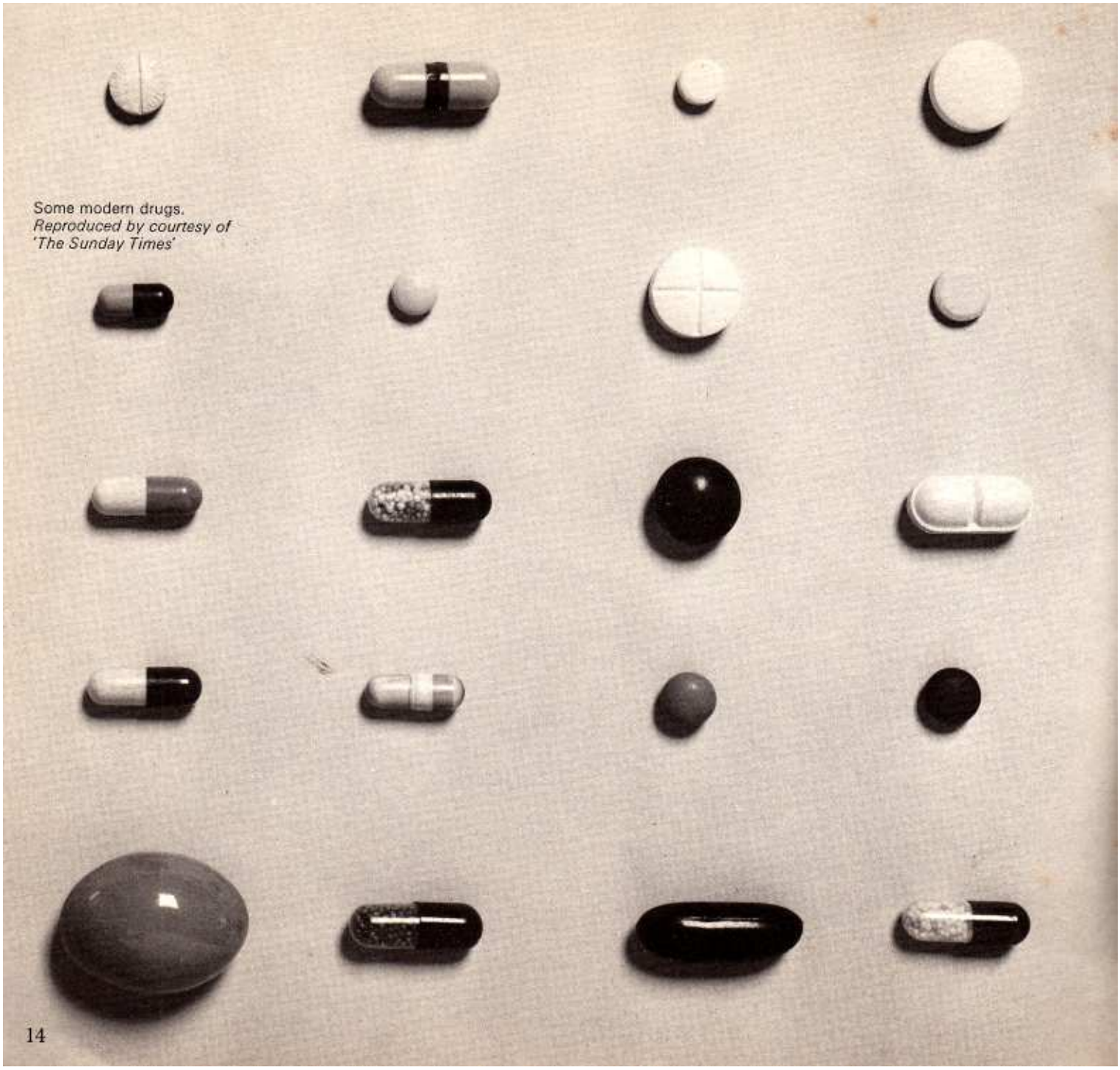
Since then a great many other antibiotics have been discovered among the chemicals formed by moulds of various kinds. Names such as streptomycin, chloramphenicol, the tetracyclines, and erythromycin have become commonplace. The moulds which produce them have been obtained from specimens of soil, from sewage works, and from tropical jungles. Some antibiotics can now be synthesized, and this makes it easier to modify them. For example, the structure of penicillin can be modified by chemical methods, and the result is a range of antibiotics with differing effectiveness against bacteria. Diversity is increasingly valuable, because the widespread use of such drugs carries with it the risk that germs will become resistant to particular antibiotics. If a patient suffering from tonsillitis does not respond to treatment with penicillin, it may well be that the bacteria belong to a strain which has developed resistance to the drug. But the same germs may be killed by some other antibiotic. Therefore the doctor tries another, often with better results.

The coming of the synthetic drugs and the antibiotics has done much to reduce infection. In western countries, for example, the death rate from tuberculosis has been sharply reduced by the introduction of streptomycin. Diphtheria, typhoid, and scarlet fever have also markedly diminished. In the tropics, where the improvement of hygiene and insecticides remains the most widespread need, drugs have been used successfully to treat leprosy, as well as diseases such as amoebic dysentery and malaria, which are caused not by bacteria but by larger micro-organisms.

Viruses still remain a great problem. Finding drugs to kill viruses without harming the body appears to be extremely difficult. Prevention by vaccination is still the chief defence.

The treatment of disorders – Disease can also be caused by disorders within the body. High blood pressure (hypertension), diabetes, cancer, and mental illness are examples of these. But even when the cause of a disease lies entirely within the body, modern drugs may bring relief and sometimes cure.

Leprosy, a common disease in the tropics. It used to be thought that leprosy was incurable but new drugs are proving that it can be cured. The pictures show a boy before and after treatment.
World Health Organization

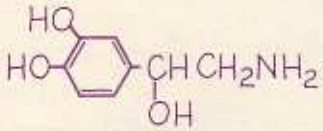


Some modern drugs.
Reproduced by courtesy of 'The Sunday Times'

The treatment of high blood pressure has been particularly successful in recent years, especially since 1946 when the first synthetic drugs for this illness were introduced. The condition of the blood vessels in the body is controlled by the nervous system. The nerve pulses leave the spinal cord and come to a break (synapse) at the nerve cells (ganglia). Here a chemical substance, acetylcholine, is released, stimulating the nerve cell to relay the impulse to the smooth muscle of the arteries and veins. At this point, another chemical, noradrenaline, causes the muscle to contract and so constrict the blood vessels. Errors in the functioning of the nervous system may cause over-constriction of the muscles in the blood vessels.

$CH_3COOCH_2CH_2N^+(CH_3)_3Cl^-$

acetylcholine chloride

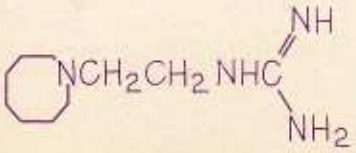


noradrenaline

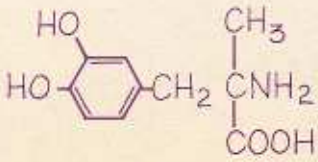
Most of the drugs for treating hypertension intervene in some way in this nervous mechanism. The first synthetic drugs to be used in cases of hypertension were simple ammonium derivatives (for example, hexamethonium) which interfere with the transmission of nervous impulses from the spinal cord to the blood vessels by blocking the action of acetylcholine at the ganglia. Other drugs (guanethidine, methyldopa, and reserpine) appear to act at the nerve ends by blocking the release or synthesis of noradrenaline. Reserpine is a powerful substance found in the shrub *Rauwolfia serpentina*, which has long been used in India as a medicinal herb.

$(CH_3)_3N^+CH_2CH_2CH_2CH_2CH_2CH_2N^+(CH_3)_32I^-$

hexamethonium iodide

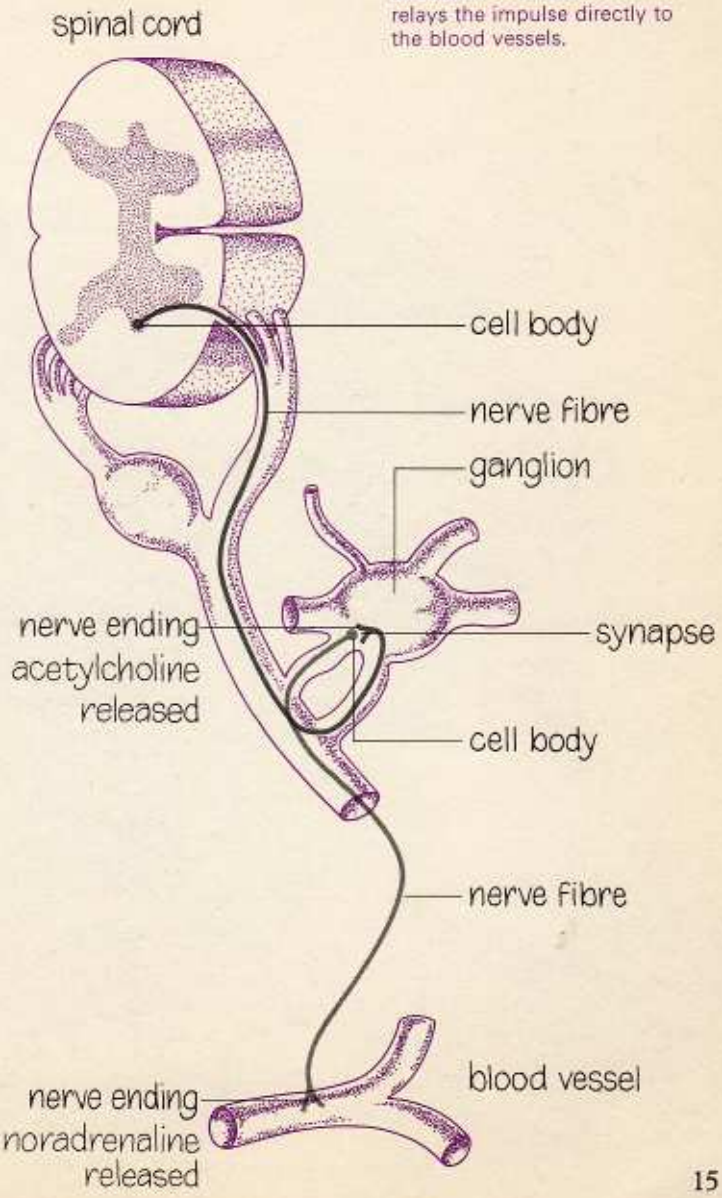


guanethidine



methyldopa

Diagram showing how blood vessels are constricted. Nervous impulses are carried from the cell body of the nerve to the end of the fibre where acetylcholine is released. This substance causes an electrical change in the cell body of another nerve fibre which then relays the impulse directly to the blood vessels.



Using X-rays to destroy a cancerous growth. It is important that the X-rays are concentrated on the growth or otherwise healthy tissue will be harmed.
Royal Marsden Hospital

A radioactive isotope of mercury is used to locate a cancerous growth in the brain – resulting from the uncontrolled multiplication of affected cells. Because little is understood about the causes of cancer, it has so far proved difficult to cure the disease with drugs.
National Hospital, Institute of Neurology

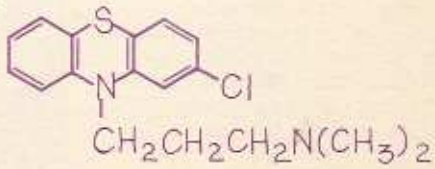
Yet another way of reducing the blood pressure is to reduce the total volume of the blood in circulation. Drugs known as diuretics can be used for this. They reduce the total amount of salt in the blood and therefore the total volume of water.

Most drugs are chemical compounds which differ from the substances normally present in the body. In the illnesses caused by the lack of some essential chemical, a patient can often be given the natural product itself or some related chemical. Diabetes is successfully treated in this way. The amount of sugar in the blood of diabetics is usually abnormally high, apparently because the body is less able to use up or store the sugar efficiently. There was no effective treatment of the disease until 1922, when Banting and Best in Toronto discovered a substance called insulin in the pancreas; insulin is the hormone which controls the amount of sugar in the body. Those who suffer from diabetes do not produce enough insulin, but it is possible to make good this deficiency by injection. Insulin from the pancreases of pigs and cattle appears to be a good substitute for the human variety.

The more that is known about the nature of a disease, the easier it is to produce a drug to cure it. Therefore with a disease like cancer, about which little is definitely known, drugs play only a small part in the treatment. In a healthy body, cells multiply in a controlled and orderly way; they stop growing, for example, when a wound is healed. Cancer cells, however, multiply in an uncontrolled way and although at first they may appear normal, they damage the surrounding tissues. There is probably some defect in the mechanism controlling the division of cells but the nature of this is still hidden despite a vast effort of research. The fact that the cancer cells are the patient's own may make it dangerous to use drugs for fear of harming the patient. But, because cancer cells multiply so fast, they can sometimes be checked by drugs which prevent cell division. These drugs are more effective in leukaemia and related diseases of the blood than in other forms of cancer where the growth is either cut out by surgery or destroyed by bombardment with X-rays.

Mental illnesses – The development and use of new drugs in the treatment of mental illnesses are handicapped by lack of knowledge. Although some drugs first used for treating other diseases have been found to help mental patients, the systematic development of drugs against mental disorders is quite recent. In the early 1950s there was introduced a chemical called chlorpromazine which had first been thought of as an anti-allergy drug. When taken by patients this was found to reduce the temperature of the body, and further tests showed that it affected the central nervous system. In small doses it produces a remarkable calming effect in agitated mental patients.

chlorpromazine

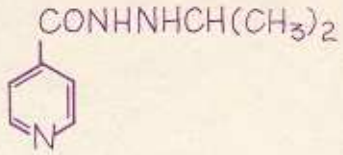


Other drugs in the same family of compounds known as the phenothiazines are now used in some hospitals for the treatment of schizophrenia – a category of mental disturbance. Still others, as for example iproniazid (originally introduced in the treatment of tuberculosis), have been claimed to have

A madman in chains at the Old Bethlehem Hospital in London. Often in the past, the insane were believed to be possessed by evil spirits. The moderately ill were ridiculed and the more severely afflicted were confined and sometimes, like this man, chained, in asylums. Towards the end of the eighteenth century an enlightened French physician called Philippe Pinel insisted that the chains be removed from the patients in his care at the Bicêtre and later at the Salpetrière asylums in Paris. Pinel was rightly convinced that sympathetic care and attention would help the mentally ill. Since then, the conditions in asylums, as in other hospitals, have steadily improved.
By courtesy of the Wellcome Foundation

an important role in the treatment of depression and anxiety.

New drugs have benefited not only patients in hospitals and surgeries but also animals and their owners. Diseases of animals at present cost £110m a year in Britain, which is by no means the most seriously affected country. Indeed, diseases are so widespread among domestic animals, especially in the tropics, that curing them could easily make some contribution to the feeding of the world's increasing population.



iproniazid

The way forward – Research to find new and better drugs begins with the study of biological mechanisms and the chemistry of body substances. The chemical struetures of these substances often provide a starting point for the synthesis of new drugs. So, too, do the structures of drugs which are known to be effective. The method is to modify the known chemical structure. Sometimes the modifications are simple, but where certain parts of drug molecules are more active than others these 'active centres' may be the only features of the parent drug that are retained.

When drugs are chemically modified, they often lose their activity. For this there are many possible reasons: sometimes they fail to react with the appropriate enzymes, sometimes they are not absorbed by the appropriate body cells. Even when compounds are highly active, very few reach clinical trial and fewer still reach the family doctor.

Watched by a male nurse, a patient in an up-to-date mental hospital paints a picture. The use of drugs is helping many mental patients to lead normal lives.
Linfield House, Photo: J. Brooke

Treatment with any drug carries the risk of undesirable side reactions. This risk must always be weighed against the advantages of the drug. Before any new compound is given to people, it is carefully tested in laboratory animals to find out how it affects them. If these tests suggest that the drug is safe to use, it is usually given to a small group of human subjects under close clinical supervision. The value of the drug in the treatment of a disease is then compared with an established treatment. If the results are favourable, large-scale trials are carried out before, finally, the drug is put on the doctor's prescription list.

Usually the harmful side effects are noticed in the laboratory but some, particularly those which are not readily observable in animals, may not appear until they are tried on people. The interaction of a new drug with other drugs and even with foodstuffs can produce surprising complications. Serious difficulties can also arise because some people are particularly sensitive to a drug. Even the most elaborate and lengthy experiments in animals cannot provide an absolute guarantee of safety in humans, particularly where individual sensitivity is concerned. Some people, for example, are unusually sensitive to penicillin, and come out in a rash when it is injected. The risks are highest in the very young and the old. The body mechanisms of young children may not have developed enough to break down the drug. Old people whose livers or kidneys do not function well may not be able to excrete it. One drug, thalidomide, had passed a variety of laboratory tests before it was found to damage unborn children when given to their mothers as a kind of sleeping pill. Public concern about the introduction of this drug was one of the causes of the setting up in 1963 in Britain of a committee (the Dunlop Committee) to regulate the introduction of new drugs.

As further advances are made in the discovery of drugs, so it may be possible to reduce even more the possibility of harmful side effects. The benefits the new drugs have brought already are enormous. One writer[1] 'well remembers the patients at Guy's Hospital in London in 1920 who were dying from Addison's disease or from pernicious anaemia; the small children with osteomyelitis or with a tuberculous ankle who

[1] Harold Burn, *Drugs, Medicines and Man*, Allen & Unwin, 1962.

were terrified when the time came to change the dressings, who cried and sometimes screamed; the patients who died in a week or two from pneumonia, and those diabetics who had only a year or two to live'. All these can now be cured or alleviated. Perhaps by the year 2000, an equal number of drugs will have been found to cure those diseases which at present defy medical skill. These diseases, some of which are fatal like certain forms of cancer, some of which are nuisances like the common cold, may then become diminishing scourges, as tuberculosis is today.

Questions

1. What drugs would you administer for the following complaints?
a. Pneumonia *b.* Hypertension *c.* Wound infection
d. Diabetes *e.* Schizophrenia *f.* Headache
g. Tuberculosis

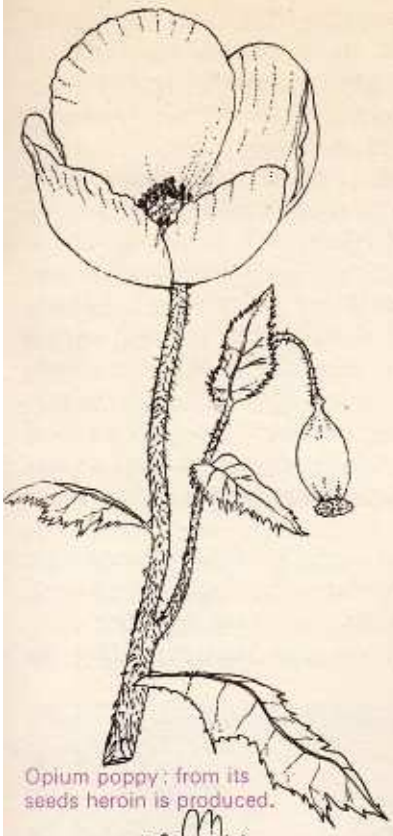
2. Do you think it is reasonable to test out new drugs on animals such as rats and monkeys before giving the drugs to human beings?

New drugs are often tested in volunteers among the scientists themselves. Work in preparing drugs is carried out at universities and government institutions, and in the research organizations of companies.
Beecham Research Laboratories

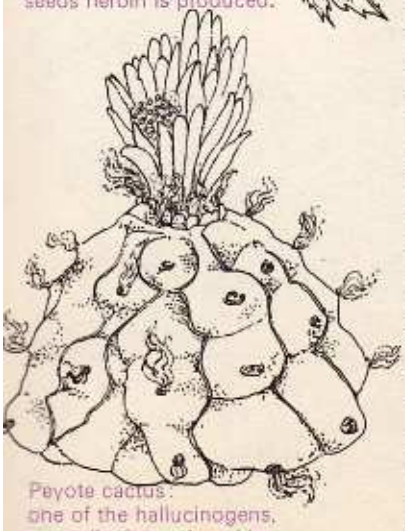
Studying the effect of a drug on an isolated organ.
Boots Pure Drug Co.

Drugs are taken in many ways – syrups, tablets, capsules, etc. Here tablets are being prepared. The active drug chemicals constitute only a small proportion of each tablet: the bulk is made up of binding materials which do not affect the action of the drug.
Boots Pure Drug Co.

Misuse of Drugs



Opium poppy: from its seeds heroin is produced.



Peyote cactus: one of the hallucinogens, mescalin, is produced by drying parts of this plant.

Misuse of drugs – The developments in medicine and medical technology which have been described have made life more pleasant for innumerable people throughout the world. Fewer children die at birth and the control of serious infectious disease ensures that most of us survive our prime. Drugs have been developed which suppress the normal mechanisms by which the body rejects foreign tissue, enabling diseased organs to be replaced. Skin, kidneys, lungs and even the heart can be transplanted with some success. People suffering from illnesses which used to be fatal can now be kept alive. Our parents and grandparents can look forward to their old age.

At the same time these developments have brought both medical and social problems. Some patients expect to be given something for every trifling ailment despite the unwanted side-effects possessed by most drugs. This can lead, for example, to the over-use of antibiotics and the appearance of resistant strains of micro-organisms. The indiscriminate mixing of antibiotics with the food of farm animals can have similar consequences. Traces may be passed on to human beings, so that the antibiotics are ineffective when they are most needed. Under what circumstances should powerful antibiotics be used? In what ways are drugs abused? The scientist, because of his specialized knowledge, bears much of the responsibility for his discoveries. The way in which these discoveries are applied, however, is for all of us to decide.

Old age – As a result of medical progress the average age of the population in this country is rising. We may look upon long life as a basic right, but for what purpose? To the intelligent, a healthy old age brings the opportunity to do those many things we had no time for in our working lives. Opportunities for developing new interests are now available for all, but some of us need educating for leisure. One hears of active men who decline and die shortly after they retire. The causes are varied but boredom, and a feeling of uselessness, play their part; it seems as if the will to live is vital for survival. People should be encouraged to divide their interests so that when work or sport are no longer physically possible a variety of diversions capture their attention. How can life in old age be made interesting and useful? Medicine and technology

The leaves of the coca plant (cocaine).

Cannabis indica: also known as hashish or marijuana.

have given a unique opportunity to develop to the full our true human potential, but unless social problems are treated with imagination and sensitivity many of the benefits of progress will be lost.

Alcoholism – The types of drug addiction we are going to consider have tended to overshadow the problem of alcoholism. However, because alcohol is so readily available, there are some who consider that alcoholism presents a more serious problem than all the other addictions combined. The moderate consumption of alcoholic drinks is to most of us a social benefit. 'Wine was created in the beginning to make men joyful', (Ecclesiasticus, v. 35). Unfortunately, alcohol brings to some individuals an uncontrollable craving for more, and an inevitable sequence of mental and physical degradation. The psychological factors which lead to this state of dependence are still unknown. Just as with the more notorious drugs of addiction, there is still much to be learned about the causes and treatment of alcohol dependence.

Drug addiction – Artificial stimulants or sedatives of some kind have been used in every society. In some parts of the world narcotics, such as hashish and opium, have been used for hundreds of years to produce relaxation and relief from emotional tension. In our own society, nicotine and drinks containing alcohol or caffeine are enjoyed for similar purposes. We know that smoking too many cigarettes increases the chances of developing cancer of the lungs. We know also that driving after too much alcohol can lead to injury or death in an accident. Why should the use of narcotics be so much more rigorously controlled than the use of cigarettes or alcohol? The answer lies in the inevitability with which narcotics, and certain other drugs, lead to a complete dependence. This results in mental and physical damage to the individual.

There may well be psychological links common to the compulsive takers of truly addictive and milder habit-forming drugs. The World Health Organization Expert Committee on Addiction-Producing Drugs, therefore, suggested that the general term 'drug dependence' was more suitable than 'addiction' or 'habit'. Drug dependence is first seen as an *emotional dependence* which results in mental anguish when the drug is withheld. *Tolerance* may then develop so that larger and larger doses are required to produce the same effect. Some drugs (colloquially, the 'hard' drugs), such as those derived from opium, also produce *physical dependence*. Severe physical pain and illness follows withdrawal of the drug (the withdrawal or abstinence syndrome).

One of the most dangerous drugs inducing dependence, morphine, is also one of the most powerful analgesics. It is, therefore, frequently used to relieve pain in chronic illness despite its capacity for producing a debilitating addiction. Heroin has similar properties. Many drugs have a destructive as well as a therapeutic effect and the line between use and misuse is a fine one. Cocaine, for example, was once widely used as a local anaesthetic; now it is only applied to the eye. Freud, the founder of psychoanalysis, discovered its local anaesthetic properties, but until he prescribed it for a close friend who became a confirmed addict, he had no idea of its sinister side effects.

The barbiturates are further examples of clinically valuable drugs which can, and do, produce emotional and physical dependence. The risk is less than with morphine-like compounds, but convulsions, delirium, and death can follow the

earlier stages of mental confusion, dizziness, tremor, vomiting, and disordered vision.

Stimulants too can readily induce dependence; amphetamine is an example. It is unlikely to lead to physical addiction but tolerance invariably develops, so that progressively larger amounts are needed to obtain the same effect. Severe damage to the brain may then be produced.

Lysergic acid diethylamide, or L.S.D., and mescaline, addictive drugs known as psychotomimetics (simulating madness) have little or no place in medicine. L.S.D. was tried in the treatment of mental illness but because of its dangers it has now been largely superseded. These extremely potent compounds may give hallucinations of creativity and power, or just visions of colour and sound; but often the hallucinations are horrifying and permanent mental derangement can result.

Possibly the oldest drug of addiction is the resin of *Cannabis indica* (hashish, marijuana, 'pot'). The effects are very variable and range from a state of near hysterical excitement to passiveness and disinterest in surroundings. There is no evidence of physical habituation, but because of the psychological deterioration produced by the drug, and the milieu in which it is sold, there is a strong risk that the subject will later turn to the lethal addictive drugs for more complete mental release.

A commonplace sight on modern farms. The widespread use of modern drugs on farm animals has led to an increase in the resistance that germs can build up to antibiotics in human beings.
Photo: John Topham

This child has no legs as a result of the drug thalidomide—used by pregnant women as a sleeping pill. A pitiful demonstration of the unforeseen consequences which attend the introduction of any new drug.
Photo by courtesy of TOPIX, Thomson Newspapers Ltd

The main social consequence of addiction is lack of drive and interest. This is often accompanied by a contempt for society and its institutions, but such an attitude may arise from the environment rather than as a direct result of the addiction itself. The habitual drug taker sees himself and his environment in an artificial light. Indeed, cocaine is notorious for the production of a psychotic state in which the addict imagines himself to be the victim of plots on his life and thinks that he can overcome any adversary. This sort of mental imbalance has been the main barrier to the acceptance of addiction as a medical rather than a criminal problem, particularly in the U.S.A. Although many addicts manage to lead outwardly normal lives, hepatitis, needle infection, and the general physical deterioration which accompanies drug taking often lead to premature death. Even more serious is the way in which the problem can spread. Because the minimum dose at any stage of addiction cannot be reliably determined, a registered addict may be able to accumulate a surplus which he is then able to sell. It is estimated that one registered addict may encourage up to three or four others to enter his degrading circle. In addition the addict may turn to crime to pay for a black market supply of drugs. Although the effect of narcotics is reputed to be pleasurable and calming at first, as tolerance grows the addict becomes less and less aware of a positive sensation and he comes to need the dose merely to prevent the unpleasant withdrawal symptoms. This pernicious physical dependence can only be cured by careful and gradual withdrawal from the drug. Even then deprivation is extremely unpleasant and painful.

It is the psychological motivation behind the first dose of addictive drugs that is most difficult to identify and eradicate. Permanent cures can be effected, but the rate of success is still only five per cent and there is a lack of proper after-care facilities. The addict is very likely to relapse into his old habits, for he is still left with the social and psychological situation from which he attempted to escape. Do you think dependence on cigarettes or alcohol is similar to dependence on drugs such as morphine? Can drug taking ever be an acceptable form of release from mental stress? Does drug addiction lead to crime?

The taking of L.S.D. is extremely hazardous. In this photograph the girl is probably suffering from a mixture of pain, muscle spasms, and sheer terror at the images the drug has conjured from her mind. Even in a medically supervised environment the result which L.S.D. may have on a patient cannot with certainty be predicted. *Photo: Lawrence Schiller, Camera Press, London*

Social tension has led to an increase in the amount of narcotic drugs used in Britain. Social disapproval and the law have forced the trade in them into furtive street-corner exchanges. *Photo: Syndication International*

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