March of Medicine®

A. New Commercial Bank

What is claimed to be the world’s first tissue typed corneal bank has been opened at Queen Victoria Hospital, East Grinstead, England. Behind the announcement of the opening lies one of the most interesting and practical results of developments in the field of transplantation.

The cornea is the clear membrane in the centre of the eye through which light passes to the interior of the eye. If it is damaged and becomes opaque—for example, as the result of infection or an accident—the individual is unable to see. The remedy is to remove the damaged and replace it with a healthy one.

It was for this reason that a quarter of a century ago corneal banks were set up in Britain and people were to donate their eyes after death to these banks. If the eye, or cornea, is removed within ten hours of death, it can be kept in a “bank” for up to three weeks before being used.

This scheme has been a boon to many—restoring sight to people who would otherwise be blind for life. Originally it was thought that a cornea would not be rejected by the recipient’s body, as can happen with other transplanted organs, because the cornea is not normally in contact with the blood system and therefore with the white cells responsible for recognition and rejection.

But experience has shown that in certain cases the cornea is rejected—cases in which the damage to the cornea has been caused by a blow on the eye or by corrosive chemicals in industrial accidents. As these may constitute up to half of the cases needing a new cornea that is a very definite handicap. A follow up of 250 corneal transplants has shown that as many as nine out of ten corneas transplanted is such cases may be rejected.

* The three items in this feature are from the LONDON PRESS SERVICE.*

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So Professor Richard Batchelor, Professor of Transplant Research at the College of Surgeons of England, and director of the Mc Indoe Memorial Research at the Queen Victoria Hospital, investigated the problem of how this rejection could be prevented.

Four factors—technically known as antigens—are between them largely responsible for the rejection of a transplanted organ. These antigens are present in both the recipient body and the donor organ. If they match then the transplanted organ will “take”. If they do not match the organ will be rejected.

Professor Batchelor tested all corneas for these antigens and has shown that only two of them match each other in donor and recipient the chances of the cornea being accepted are increased by about 20%, while if three, or all four, match each other the success rate is about 95%.

So now all corneas received at the Queen Victoria Hospital are fully tested for four antigens and then deep frozen in the corneal bank for use on suitable recipients of these carefully-typed corneas have already been transplanted and another 20 are awaiting transplantation.

This is perhaps one of the most important advances in transplant and eye surgery in recent years, and people should make all the difference between almost certain failure and likely success. And as quite a high proportion of the people involved are relatively young adults injured at work they are being saved from a lifetime of blindness or near blindness.

B. Better Control of Drugs

Once a drug has been let loose in the body it is difficult to keep it under control. In the case of insulin for the treatment of diabetes mellitus, for example, it may be destroyed in the stomach so that to be effective it must be given by injection. In other instances, as in the case of certain enzymes, such substances may evoke the production of antibodies when they are given into the body and are destroyed by them.

In yet other cases, as with certain drugs for the treatment of cancer, it is not possible to give a big enough dose to kill all the cancer cells in the body because doses of that size kill healthy non-cancerous cells. So all too often the biggest dose kills off some of the cancer cells but leaves the others to keep on multiplying—thus maintaining the cancer growth.
**Nature of liposomes:**

During the past ten years much work has been devoted to producing what are known as liposomes to overcome this difficulty. Much of the work has been done at the Medical Research Centre and at Charing Cross Hospital Medical School in London. The liposomes are submicroscopic particles in form of concentric spherules composed of lipids alternating with aqueous compartments which contain the drug.

Lipids are substances which are insoluble in water but soluble in fat solvents such as alcohol and ether. One group of lipids plays an important part in the functioning of the membranes, or envelopes, which surround all the cells of the body, making them more or less permeable to substances such as drugs.

These liposomes are “marked” in such a way that they will affect only certain cells—cancer cells, for instance—or will be broken down only by certain enzymes (or ferments) in the body. As they remain intact in the stomach and the bloodstream they reach the affected part of the body intact and with their full quota of drug, which can then take its full effect.

As the Medical Research Council team of investigators has put it: “The largely uncontrolled behaviour of administered therapeutic agents can be overcome by the design of a carrier which could contain agents in isolation from the biological environment and which upon injection would deliver its contents to site of action.”

While much of this work is based on theory or laboratory work in animals, Professor Brenda Ryman and her colleagues at Charing Cross Hospital Medical School have just reported its first practical application in patients. This took the form of successfully supplying in liposomes an essential enzyme to a boy who was suffering from a disease caused by lack of the enzyme.

Equally interesting, though not yet with an immediate practical outcome in patients, are the team’s findings in animals which suggest it may be possible for diabetics to take insulin by mouth in liposomes, thus eliminating the need for injections.

The Charing Cross team has also reported promising preliminary results in the use of methotrexate, one of the drugs most widely used in the treatment of cancer. These show—again in experiments with animals—that by the use of liposomes this potent anti-cancer can be concentrated fivefold in the liver and over 260-fold in the spleen without any corresponding concentration in other parts of the body, such as muscle and bones.

Although methods have not yet been evolved of giving such high concentrations of a
drug in other parts of the body where they are wanted, it looks as if this will be a matter of time.

Liposomes are easily made in the laboratory so presumably there would be no great difficulty in making them on a commercial scale. Pharmaceutical companies are already showing their interest by taking out patents for them. It certainly looks as if this is a field in which we can look forward to interesting and valuable developments.

**A new Penicillin**

Penicillin is still the premier antibiotic. None more generally effective has been discovered since it first hit the headlines 30 years ago. But although it can be synthesised in the laboratory this is such a complicated and expensive procedure that it has never proved a commercial proposition.

On the other hand, what is known as the semi-synthesis of penicillin from the semisynthetic nucleus (6-aminopenicillanic acid), discovered in Britain by the Beecham Research Laboratories, has proved a most fruitful line of research and has led to the production of a wide range of penicillin preparations.

Among the first of these was one known as ampicillin, which had two advantages: benzylpenicillin (as the original penicillin is now known) could be taken by mouth and therefore injections were avoided, and it was active against a wider range of micro-organisms including the one causing typhoid fever.

Unfortunately it was also more likely to cause side effects, many of which resulted from the action of the micro-organisms that are essential for the normal healthy action of the gut.

The Beecham Research Laboratories have now produced a new penicillin which overcomes this drawback of ampicillin. Known as talampicillin it is a derivative of ampicillin and it has no antibacterial action until it is converted back into ampicillin in the body. This conversion occurs in the wall of the gut, so when talampicillin is taken no ampicillin is found in the gut - but neither is any talampicillin found in the bloodstream.

In other words all the talampicillin has been converted into the active ampicillin at the passage of the drug from the gut to the bloodstream.

The significance of this is clear from the preliminary clinical reports. These show that talampicillin is just as effective an antibiotic as ampicillin but the number of side effects, particularly diarrhoea, is much decreased because it does not interfere with the normal micro-organisms essential for the healthy gut.

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Thank you.