response to stimulation soon returns, as the vessels quickly regenerate. If, however, a foreign body is inserted to prevent the vessels regenerating the system is put permanently out of order.

The control of the adenohypophysis is of special interest, because A.C.T.H. is liberated in response to the varied forms of stimulus known as stress. Whether stress causes secretion of adrenaline, which in turn stimulates the adenohypophysis, or whether it has a direct stimulating effect, or whether both occur, is not yet settled. Harris suggests that under normal conditions A.C.T.H. liberation is controlled via the hypothalamus and the hypophysial portal system by the level of circulating cortical hormones. Exactly how stress causes secretion of A.C.T.H. is not understood, but it seems likely that the impulses reach the adenohypophysis by the same neurovascular pathway. Some results are conflicting, and it is likely that different species of animal react in different ways. Moreover, the various theories put forward are not mutually exclusive, so that more than one mechanism may be called into play at one time. The subject of stress is now in fashion, and much research is being done on it. If all that research has the same qualities of patience and ingenuity that are apparent in the work of Harris and other authors he cites these problems will soon be solved.

VACCINATION AGAINST SMALLPOX

The Society of Medical Officers of Health have performed a useful service in publishing an authoritative statement on the policy, technique, and materials of smallpox vaccination, a subject on which there is, surprisingly, still much confusion. After reaffirming the society's complete confidence in vaccination as a means of protection of the individual and the community against smallpox if carried out properly and at appropriate intervals, the statement continues with recommendations that primary vaccination in the first six months of infancy should be encouraged to the widest extent; that in non-epidemic periods parents of children who have received primary vaccination in infancy should be urged to have these children vaccinated during school life; and that in non-epidemic periods parents of children who have not received primary vaccination in infancy should not be actively urged to have these children vaccinated for the first time at school entry or later, though vaccination should be carried out if the parents request it. The statement contains definite recommendations on such questions as, for example, the desirability of relying on selective vaccination of contacts in the presence of smallpox—a policy which helps the public to avoid the panic that may be induced by immediate resort to mass vaccination. Among the practical matters dealt with in the section on technique is included a recommendation that the site of vaccination should be covered only when the patient is engaged in some dirty occupation. There is no doubt that dressings tend to create a warm, damp atmosphere encouraging to secondary infection, and that free access to the air usually leads to the formation of a clean dry scab. Contraindications to vaccination are the presence of allergic eczema, septic skin conditions, or acute febrile conditions. "The danger of death following vaccination of those suffering from allergic eczema is so great that they should not be vaccinated."

It is perhaps a pity that some consideration of the duration of immunity after vaccination, the protection afforded by vaccination after contact with smallpox, and the methods of measuring individual immunity were not within the scope of the society's statement, since these are questions uppermost in the minds of many practitioners whenever an outbreak of smallpox occurs. In all immunological problems of this kind there are many individual exceptions to the general rule. Thus, if a group of men or of experimental animals are examined for their individual immunity after any form of preventive inoculation it will be found that there is wide variation in both the degree and duration of the resulting immunity. Although Jenner's original contention that vaccination conferred lifelong complete immunity cannot be maintained, it is probable that it does provide some permanent protection in that a person who has once been successfully vaccinated is less likely to die from smallpox than an unvaccinated person. General epidemiological experience, however, indicates that in order to maintain the immunity of the community at a sufficiently high level the frequency with which revaccination is desirable bears a direct relation to the existence of endemic smallpox in neighbouring countries, for on this is likely to depend the frequency with which infection is introduced. Thus revaccination is recommended at shorter intervals in Japan, Indonesia, and the U.S.S.R. than in most European countries. In 1896 a Royal Commission considered that, in general, immunity lasted for 10 years after successful vaccination, and 30 years later Leake recommended revaccination every 5 to 10 years. To-day it is thought that those who may come into contact with smallpox should be revaccinated after two years, since the immunity of an individual may be much less than that of the community as a whole.

1 Publ. Hith, Lond., 1951, 54, 214.
2 Publ. Hith Rep., Wash., 1927, 48, 221.
3 Docum. med. indones. eur. trop., 1951, 3, 163.
4 Lancet, 1944, 2, 697.
5 Mon. Bull. Minist. Hith, Lond., 1945, 4, 2.
There has been much discussion about the best way of assessing the duration of immunity. Three methods are available: epidemiological and clinical observation, the cutaneous reaction to revaccination, and the estimation of antibodies in the serum by measuring either its virus-neutralizing potency or its capacity to prevent the agglutination of red blood corpuscles by the virus. The first method has given much useful information about both herd immunity and the protection of the individual, though it has also brought to light startling exceptions to the general rule. The second method, which depends upon observation of the type of skin lesion that results from revaccination, has been generally accepted as a reasonably reliable guide to the immunity of the individual. The reactions are classified as primary non-immune, the "accelerated" (that is, vaccinoid or partially immune), and lastly the more debatable "immediate" reaction, which may or may not indicate a firm immunity. Recently some doubt has been thrown on the reliability of these skin reactions, and the measurement of circulating antibodies has been advocated. Collier\(^2\) in particular has recommended the measurement of the inhibition of virus haemagglutination by the serum, but it is uncertain whether this antibody bears a direct relation to the protection of the individual; if circulating antibodies are to be measured, the neutralization of virus growth either on the skin or in the chick embryo still seems to be preferable.

Despite individual anomalies, which Stevenson\(^1\) reviewed a few years ago, the reaction to revaccination is probably the more direct measure of capacity to react to infection. Although the titre of circulating antibodies may be low, the basic immunity to an antigen that has been encountered in the past enables the body to react rapidly, and this is indicated by the modification of the skin reaction. This is probably the reason why cutaneous immunity can be demonstrated for much longer periods than circulating antibodies. Stevenson concluded that herd immunity lasts for 10 years, but that individual protection is much more variable and may fall far short of this. He pointed out that protection was not dependent on the potency of the lymph, since it resulted equally from vaccination with undiluted lymph or lymph diluted ten-thousandfold. A vesicular "take" is sufficient, but the development of the vesicle may depend upon the idiosyncrasy of the host and not on the quality of the lymph; this variation exists in many species of animal as well as man. His conclusion that the immunity does not depend upon the dose of virus is relevant to the prolonged controversy over the desirability of multiple insertion of the virus and the relation of area of scarring to duration of immunity. It is not surprising that the immunity developing after the injection of a killed bacterial antigen or a toxoid should have some relation to the dose inoculated, but Jennerian vaccination depends upon the inoculation of a living virus which multiplies in the body of the host. The final concentration of virus bears little relation to the amount originally inserted, and this is why the development of a typical vaccinal vesicle is the all-important indication of successful vaccination.

If called upon to make a dogmatic statement about the protection afforded by vaccination after exposure to smallpox the practitioner can safely say that complete protection may be expected in most cases if vaccination takes place within 24 hours of exposure. Some modification of the disease may be expected if the patient is vaccinated within three days of exposure. Beyond that interval vaccination exerts little or no influence on the infection. The protection conferred by vaccination in the early stages of smallpox depends upon the more rapid evolution of the vaccinal infection, but the response of the individual and probably the degree of infection with variola must also have some effect. Thus the protection of vaccination cannot always be absolute.

**MUCINOUS SUBSTANCES**

In recent years emphasis has been laid upon the importance of localized disturbances in the connective tissues as manifestations of rheumatic and other conditions. Important among the components of these tissues are the mucinous ground substances containing mucopolysaccharides such as hyaluronic acid and chondroitin sulphate. These substances, like the more familiar starch and glycogen, are members of that larger group known as polysaccharides, being polymers of sugar derivatives. Mucopolysaccharides are distinguished from other polysaccharides by containing amines of either glucose or galactose or of both sugars. Hyaluronic acid and chondroitin sulphate also contain an acid derivative of glucose known as glucuronic acid. Other mucinous substances have in their structure a variety of sugars or sugar derivatives as well as the amines of these substances. In some the polysaccharide is closely associated chemically with protein, and it has been claimed that this is true of all mucopolysaccharides.

The history of the study of connective tissues is to some extent being reflected in that of the mucins. Hyaluronic acid and chondroitin sulphate occur in normal tissues as very large molecules and were seen