REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE PROS AND CONS OF IMMUNIZATION—I

BY

ROBERT CRUICKSHANK, M.D., F.R.C.P., D.P.H.

Professor of Bacteriology, St. Mary's Hospital Medical School, London, W.2

The articles that have hitherto appeared in this series have dealt almost exclusively with the diagnosis and treatment of established clinical diseases and infections. My task is to discuss the specific measures which the family doctor may use or recommend for the *prevention* of infection, in particular the use of vaccines and antisera to protect against the more common fevers of childhood and adult life—for example, diphtheria, scarlet fever, measles, whooping-cough, influenza, tuberculosis, typhoid fever, and smallpox. When we consider preventive measures against infection, the unit is usually the whole family rather than any individual member of it. A schoolchild has a sore throat which may be diphtheria or the early stages of scarlet fever and the doctor must decide what he can do to protect the other members of the family. Or mother has an attack of diarrhoea which may be food-poisoning or bacillary dysentery or the beginning of paratyphoid fever, and again measures must be taken to prevent spread of the infection to the rest of the family. Or, again, the doctor may be asked about the possibility and advisability of protecting a young family against whooping-cough or measles or smallpox before there has been any exposure to the risk of infection.

The control or prevention of infection in a family group may be considered under three main heads: elimination of the reservoir of infection, blocking the spread of the infecting organism, and raising the resistance of the susceptibles. One or all of these measures may be applied according to the circumstances of the case. The reservoir may be eliminated by early recognition and isolation of the primary case in the family, or by active antibiotic therapy which quickly rids the tissues of the infecting germs; spread of the organism may be prevented in the case of intestinal infection by instruction about personal hygiene and avoidance of food handling; and resistance may be raised by the use of specific vaccines and antisera to give "immunity" to the susceptibles.

What Is Immunity?

The medical student often seems to have difficulty in grasping the principles of immunity. The accompanying diagrammatic schema is often used to illustrate the different ways by which resistance to infection may be acquired, and an understanding of these principles is essential for a rational use of the artificial means of protection.

Naturally Acquired Immunity

Apart from an inherent immunity, which may be due to a genetic resistance to particular diseases or to the protection afforded by healthy and intact tissues, the individual may acquire by natural means an immunity of varying duration to specific infections. Thus the infant seems to be immune to such infections as measles, diphtheria, scarlet fever, and chicken-pox for the first few months of life. The explanation of this immunity is that antibodies to these various infections have been "manufactured" by the mother and passed, via the placenta, into the blood of the infant. So long as the specific antibodies persist in sufficient concentration the infant is protected against the corresponding infection, but these antibodies have not been produced by the child's tissues, so that they gradually disappear and are not replaced by fresh antibodies. This is called passive immunity and obviously gives protection for only a short period of time—usually for three to six months. The duration of this passive immunity will have a direct relation to the concentration of antibody in the mother's blood, and if the mother has no antibody to any particular pathogen, as often happens with whooping-cough and sometimes with diphtheria, the infant will be susceptible from birth to these infections.

When, on the other hand, a child develops an attack of measles at the age of 3 or 4 years he (or she) manufactures antibodies to the measles virus and is, as a result, resistant to further attack. This is an example of active immunity, which lasts for a much longer period than does passive immunity, although there are notable exceptions, like influenza and the common cold, pneumonia, and streptococcal infections. Here the lack of persistent immunity may be due to the superficial nature of the infection, as in the common cold and possibly influenza, so that the antibody factories throughout the body are not stimulated into activity; or it may be due, as in the case of pneumonia and streptococcal tonsillitis, to fresh attacks with new and different serological types of the pneumococcus or streptococcus against which the body has not acquired immunity. A further point about naturally acquired active immunity is that many of us become resistant to infections like scarlet fever and diphtheria as a result of repeated subclinical infection. Consequently the past history alone does not tell us whether an individual is or is not susceptible to these infectious diseases, but certain skin reactions, like the Dick and Schick tests, may give us the answer.

Artificial Immunization

If immunity is to be induced artificially the two main procedures are again passive protection and active immunization by agents deliberately introduced into the tissues; there is, in addition, the procedure of inducing a modified infection. Passive immunity is obtained by

the injection of either an antiserum prepared artificially in the horse or other animal against the infecting micro-organism or its active exotoxin, or the serum of a patient who has already had the disease. This antiserum confers an immediate specific resistance which lasts only until it is all excreted, usually in a matter of two to three weeks, depending on the dose of serum and the concentration of antibody. For example, tetanus antitoxin is given to an injured person to protect him against the risk of tetanus while his wound is being treated surgically, and if the injury is a severe one the dose of antitoxin may be repeated weekly for several weeks.

Active immunity is induced artificially by the injection of an antigen in the form of vaccine containing the intact micro-organism or virus in a modified form—for example, typhoid or yellow fever vaccine—or as toxoid, which is the exotoxin of the organism rendered non-poisonous by treatment with formalin—for example, diphtheria toxoid. Two or more injections of the antigen are usually needed to induce a sufficient degree of immunity, since the first injection (primary stimulus) does not evoke much antibody but prepares the antibody factories for a more active response to further injection (secondary stimulus). The immunity takes some weeks to develop, but persists for a much longer period—several months to several years—than that induced by the injection of an antiserum. As it wanes it can be quickly raised again by a small “booster” dose of the antigen. It is, however, important to warn the inoculated individual or his relatives that no form of artificial immunization, with the possible exception of yellow fever vaccine, will ensure complete protection against any particular infectious disease.

Active immunity may also be obtained by deliberately inducing a modified attack—for example, vaccination with vaccine lymph produces the disease vaccinia which gives protection against the more serious infection smallpox; or injection of convalescent measles serum in a child who has been exposed to infection may result in a mild attack of the disease which gives the child an active immunity without the upset associated with the unmodified attack.

The Risks of Reactions

Any form of immunization should, before it is recommended for general use, satisfy at least three criteria: it must be safe, it must be practicable, and it must be effective. Under the Therapeutic Substances Act all biological preparations issued for distribution must conform to certain requirements and must satisfy tests of sterility, potency, and absence of toxicity. These tests therefore ensure a high degree of safety in the use of sera and vaccines. However, reactions to the injection of these substances do sometimes occur and the practitioner must be aware of the risks.

The Syringe and Needle

It is, in the first place, essential that the syringe and needle used for giving an injection should be sterile, boiling for five minutes in a saucepan immediately before use is the safest procedure. Ideally, the syringe and needle should be boiled between each injection, but if the doctor is giving a number of injections of the same material in a household he may adopt the method recently recommended by Fleming and Ogilvie.* Just enough material for one injection is taken into the

syringe. After the injection, with the plunger kept firmly home against the end of the barrel, the needle is withdrawn and, while still attached to the nozzle of the syringe, is immersed in boiling water for 10 seconds. This procedure sterilizes the needle. The syringe has not been contaminated and the doctor can proceed with the next injection without further sterilization.

If rubber-capped bottles are being used the top should be cleaned with spirit, and then with tincture of iodine, or the bottle may be covered with a metal cap on the under surface of which is a pad soaked in disinfectant. For injection of vaccines and toxoids a hypodermic needle of size 12–16 with a long bevel point should be used. For antisera a serum needle size 1 is best. It is most important that the needle should be sharp, and before the injection the point should be inspected to see that it is not turned. Needles of too fine a bore should not be used, as they may bend or break during the injection.

Reactions to Vaccines

Injections of vaccines and toxoids are best given in the deep subcutaneous tissues—for example, in the upper arm near the insertion of the deltoid or in the middle of the outer aspect of the thigh. The skin is sterilized, preferably with 2% iodine or 70–75% alcohol, a fold of the skin is picked up between thumb and first finger, and the needle is then injected with a stabbing movement into the fold of the skin. Reactions of two kinds may occur—local or systemic. The local reaction, coming on in two to three hours, is due to the irritation produced by the foreign material, and is more often present after the injection of bacterial vaccine, particularly T.A.B. vaccine, than after toxoid. If the toxoid contains alum a fibrous nodule and occasionally a sterile abscess or cyst may form, and therefore the material should not be injected too superficially. Constitutional symptoms such as headache, malaise, nausea, and pyrexia are again more common after an injection of bacterial vaccine like T.A.B. and may last for one to two days. Prophylactics which may be expected to produce some constitutional upset should be given in the late afternoon, and the individual should be advised to take 5–10 gr. (0.32–0.65 g.) of aspirin before going to bed. Very rarely a condition of protein shock with rigor and high temperature may come on within half to one hour after an injection if some of the material has accidentally entered a vein.

A more serious complication of prophylactic injections has recently come to light in the form of post-inoculation poliomyelitis. Certain cases of poliomyelitis have developed within a month of the injection of prophylactics like A.P.T. (alum-precipitated toxoid), or combined diphtheria toxoid and pertussis vaccine, and the paralysis has usually been in the inoculated limb, mostly an arm. Statistical analyses have indicated that this association is more than a chance coincidence, and the most likely explanation is that the injection has activated a pre-existing latent infection with the poliomyelitis virus and localized it, perhaps because of the tissue trauma, in the motor nerve cells associated with the affected muscles. This complication may best be avoided by giving the injection subcutaneously rather than intramuscularly, by using prophylactics that are least likely to produce local tissue damage—for example, formol toxoid rather than A.P.T.—and by suspending inoculation of children in the susceptible age group—that is, over 1 year of age—in an area where poliomyelitis is known to be occurring at the time.

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Reactions to Antisera

The injection of antiserum derived from horse or other animal may cause either a sudden anaphylactic shock or a delayed serum sickness. Anaphylaxis is extremely rare in the human subject, and in its fatal form is most likely to occur in persons who have some inborn or acquired predisposition to allergic disorders like asthma, eczema, or urticaria. Before giving an injection of antiserum, therefore, the doctor should inquire about a personal history of asthma or hay-fever, particularly from contact with horses, or any family or personal history of allergic disorders. If in doubt an intradermal injection of 0.1 ml. of the serum diluted 1 : 100 should be given; this will produce a local wheal and erythema reaction in a sensitized person, who may then be partially and temporarily desensitized by repeated small injections of the serum.

Serum sickness, developing seven to ten days after the injection of the antiserum, and characterized by an urticarial rash, joint pains, and fever, was common when crude unconcentrated antitoxin was used in large doses. The introduction of concentrated antisera, and later of enzyme-digested "refined" antitoxin given in small doses, has reduced the incidence of serum sickness to less than 3%, so that this complication is now a rare hazard. Antihistaminic preparations locally or systemically will usually give relief. The patient who has had an injection of foreign protein such as horse serum within the past three to six months may develop an acute anaphylactoid reaction, with dyspnoea, pains in the chest, and oedema of the face, within a few hours of receiving a second injection. This type of reaction, while alarming, can usually be prevented or controlled by an injection of 1 ml. of 1 : 1,000 adrenaline. With convalescent human serum, particularly if it is prepared from a pool of donors, there is the small risk of homologous serum jaundice coming on two to three months after the injection. This risk can be largely prevented by "sterilizing" the serum with ultra-violet light and is practically non-existent with concentrated gamma globulin. Injections of whole blood should not be given, because they may induce the formation of rhesus antibodies.

Prevention versus Cure

It is sometimes said in these chemotherapeutic days that there is no advantage in trying to prevent infections that can be easily cured with modern antibiotics. Why, for example, subject people to the inconvenience of T.A.B. inoculations when typhoid fever can be treated effectively with chloramphenicol? A similar argument was used many years ago for diphtheria, when it was hoped that the use of a specific antitoxin would bring this infection under control, but, in spite of all efforts at earlier diagnosis and better therapy, some 60,000 cases of diphtheria, and around 3,000 deaths, continued to occur every year in England and Wales until large-scale immunization was introduced in 1940. As a result there were 957 notified cases of diphtheria and only 49 deaths in 1950, while the saving in hospital beds and in expert medical and nursing care has greatly reduced the total expenditure on this once dreaded infection. Thus it has been calculated that the dramatic reduction in the incidence of diphtheria has meant a saving to Scotland of something over £300,000 a year, while reduction from nearly 10,000 to a few hundred cases annually represents a saving of about 750 hospital beds on every day of the year and an annual saving of some 250 full-time

nurses and a proportionate number of doctors, hospital domestics, etc.

Furthermore, in diseases with insidious onset, such as typhoid fever and whooping-cough, the damage to the patient and his contacts has already occurred before effective treatment can be given. There is little doubt, therefore, that where specific prophylaxis is safe, practicable, and effective prevention is always better than cure. On the other hand, certain infectious diseases, such as lobar pneumonia, cerebrospinal meningitis, and typhoid fever, tend to occur rather sporadically in civilian practice and to affect only a small proportion of the population at risk, so that even if effective prophylactics were available large-scale indiscriminate immunization would not be thought profitable. Where, in special circumstances, the risk is considerable and the prophylactic effective, as happens with typhoid fever among troops on active or foreign service, then obviously prophylaxis is again better than cure.

The specific measures that may be used to protect against particular diseases, and the indications for their use, will be discussed in the next article in this series.

THE INCIDENCE AND PROGNOSIS OF CEREBRAL PALSY

AN INTERIM REPORT

BY

IRENE M. HOLORAN, M.B., Ch.B., D.C.H.*Assistant School Medical Officer, Leeds*

In Leeds County Borough a special day school with 140 places caters for all types of physical handicaps other than defects of sight and hearing. The more severely handicapped from cerebral palsy attend here, and in addition it is expected that a residential school for the younger cerebral palsy children will be opened in 1952.

Incidence

The survey of cerebral palsy occurring between the ages of 3 and 16 in Leeds was begun in 1947. During that year an assessment was made of all the children on the school roll known to be suffering from cerebral palsy, including those attending ordinary schools as well as special schools. It did not include children already notified to the mental health authority as ineducable and many children under 5. All the children have been examined by Mr. J. M. P. Clark, orthopaedic consultant to the local authority, and by me. Those attending the day school for the physically handicapped have also been examined by Dr. J. D. Pickup, late lecturer in paediatrics, Leeds University.

The first survey in Leeds as published in the Annual Report of the School Medical Officer for 1947 mentioned 97 children, and the annual report for 1949 shows 136. The present figure is 141. The reasons for the rise in figures for Leeds appear to be as follows:

1. The knowledge that some plans were in preparation for the young cerebral-palsied resulted in more young children being referred from the paediatric and orthopaedic departments of the local hospitals. The latest ascertainment figure includes 19 children between 3 and 5 years of age and five not included in the survey who are under 3 years old. Since the school population includes very few children under 5 at the present time, a more