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## *Pointers*

**Vaccination against Measles:** Report to the Medical Research Council by its Measles Vaccine Committee concludes that live vaccine, whether alone or after killed vaccine, could reduce the incidence of measles substantially in Great Britain (p. 441). Leader on this page.

**Infection after Splenectomy:** Follow-up investigation in children throughout England and Wales by the late Professor A. G. R. Lowdon and his colleagues (p. 446).

**Urinary Stones:** Dr. B. E. C. Nordin and Dr. W. G. Robertson suggest measuring ion-products in the urine for assessing the medical treatment of kidney-stone disease (p. 450).

**Thrombolytic Therapy:** Standard dosage scheme with streptokinase described by Dr. M. Verstraete and his colleagues from Louvain in Belgium (p. 454).

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# Vaccination Against Measles

The Measles Vaccines Committee of the Medical Research Council is to be congratulated on the organization of the large-scale trial the preliminary results of which are published in the *B.M.J.* this week at page 441. It is an excellent example of the collaboration which can be achieved for work of this kind between the Medical Research Council, the Public Health Laboratory Service, medical officers of health, and general practitioners.

The possibility of immunizing against measles arose more than 10 years ago, when J. Enders and his colleagues isolated the virus in tissue culture and developed an attenuated strain.[1–4] From this strain, known as the Edmonston strain, a live vaccine was prepared which, when injected into non-immune children, produced both specific antibodies and immunity to the disease.[5 6] The Edmonston strain, although a highly effective immunizing agent, was unacceptable for large-scale immunization because of the severity of the febrile reactions it produced in a high proportion of children. Consequently work was started on developing a vaccine which would cause fewer reactions and still give adequate immunity.

One procedure widely used in the U.S.A. has been to give at the same time as the live vaccine a small dose of human gamma-globulin. Because of the measles antibodies it contains this substance suppresses the reactivity of the live vaccine without much reducing its immunogenic activity.[7] But this procedure is somewhat complicated for routine immunization because it may not always be possible to obtain the correct balance between gamma-globulin and vaccine to ensure the desired result, and, moreover, gamma-globulin is scarce in Great Britain. Another method is to use live vaccines prepared from the Edmonston strain after further attenuation by passage in tissue culture. The Schwarz[8–10] and the Wellcome[11 12] vaccines fall into this class and were shown in a small pilot trial in Britain to give promising results.[13]

Another approach has been the production of an inactivated (killed) vaccine[14] in the same way as Salk poliomyelitis vaccine is made. Killed measles vaccine causes few or no reactions in children, but its immunogenic activity is at present far from ideal, since even after three spaced injections the levels of antibody soon decline.[15] In future its antigenicity may perhaps be increased by purification and concentration, and work along these lines is being done in Sweden,[16] where success has clearly been achieved in eliminating poliomyelitis by the use of killed poliovirus vaccine. Yet another attempt to find an acceptable procedure has been to immunize first with killed vaccine and some weeks later to give a dose of live vaccine.[17 18] The low level of immunity produced by the killed vaccine has the effect of damping down, although not completely inhibiting, the reactivity of the live vaccine. When the Schwarz and Wellcome live vaccines were given in this way[13] the clinical disturbance to the children was exceedingly slight, while production of antibody appeared to be satisfactory.

In deciding on the most suitable method to use in immunizing against measles in Britain two main factors should be considered. First, any reactions must be of an acceptably low degree of severity. Measles in this country is in general a mild disease, and though complications often occur[19] many of them can be dealt with by antibiotic treatment. The disease cannot be regarded as serious enough to justify a vaccination procedure which causes untoward reactions in a high proportion of children. Secondly, vaccination should produce an adequate immunity of long duration. There is little point in replacing the life-long immunity which follows a natural attack of measles by an immunity which fades away after a few years. This might merely result in shifting the disease to later in life, when it is often more serious. It may be argued that, even though an immunity of long duration was not established, the disease could be adequately controlled by mass vaccination of a high proportion of children in the susceptible age groups, and that protection in later life would result from the virus having been eliminated from the community. But to depend on controlling measles in this way is taking a considerable risk. Measles is a highly infectious disease, and its introduction into a community whose members have been free of it for some time, and, though previously immunized, may have lost their immunity, could result in a large outbreak.

How do the immunization procedures used in the present Medical Research Council trial stand up to these needs? The trial has included two different schedules—the Schwarz attenuated live vaccine alone, and a single dose of killed vaccine followed one month later by live vaccine. Children in the highly susceptible age group of 10 months to 2 years took part and were followed up for six months through the measles epidemic of 1964–5. About 10,000 children were allocated to each schedule and about 16,000 remained unvaccinated, serving as controls. It was found that the live vaccine alone resulted in more illness during the three weeks after vaccination than when it was preceded by killed vaccine, but that on the whole the majority of children remained well or had only trivial complaints. But there were a few cases of febrile convulsions in both groups of vaccinated children and also in the unvaccinated group, and it appeared, from the time of their onset, that live vaccine was responsible for some of them when given alone but not when given after a dose of killed vaccine. However, the report considers that such febrile convulsions are not serious in children of this age and also points out that there is a much greater risk of convulsions from an attack of measles. In general it would appear from the results that both schedules are acceptable so far as vaccination reactions are concerned, though killed vaccine followed by live vaccine had a slight advantage over live vaccine given alone. As to immunizing activity, the trial showed that substantial protection (about 85%) was achieved by both schedules during the six months' follow-up. There was also evidence that measles when it occurred in vaccinated children was on the average of a milder form than in those who had not been vaccinated.

These results are encouraging, but the fact that only 85% of the children were protected must arouse some misgiving. Moreover, an attack of measles leaves behind it immunity for life, and unless this degree of immunity, or something closely approaching it, can be reproduced by artificial means vaccination against measles may merely have the effect of postponing the disease to adult life and doing more harm than good. More information will doubtless be available when the children in the present trial have been followed up through one or two further epidemics. But until we know what the potentialities of the vaccines are, and until we learn by further field trials how best to apply the vaccines in practice so as to obtain both a high individual and a high herd immunity, there seems every reason to postpone routine immunization of children in Britain on a national scale.


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# Wassermann

In general, medical students and doctors are ill-informed about the history of Medicine, but none of them can be ignorance of the name of August von Wassermann, who was born in Bamberg, Bavaria, 100 years ago on 21 February. When he died in 1925 the *B.M.J.*'s obituary notice[1] pointed out that, though he was best known as the originator of the test which bears his name, this was the outcome of only a small part of his investigations into immunity. It was his knowledge and experience in this field which enabled him to appreciate the potential importance of the complement-fixation reaction discovered by Bordet and Gengou and of the organism *Treponema pallidum* discovered by Schaudinn and Hoffmann. In 1906, with his collaborators Neisser and Bruck, Wassermann showed the value of this reaction in the diagnosis of syphilis and so achieved one of the most beneficial medical discoveries of the century. It threw an entirely new light on the natural history of the disease and initiated a revolution in its diagnosis and the control of treatment.

Wassermann's original antigen for use with the reaction was an aqueous extract of syphilitic foetal liver, which was known to be rich in treponemes. It soon became evident that an alcoholic extract of the tissue was more satisfactory. Moreover, extracts of tissues which did not contain the organism were equally effective. Satisfactory antigens were made from human heart, ox heart, and the hearts of guinea-pigs from which the major part of the fat had been removed. Such crude extracts were employed for many years, but differences in techniques of preparing the antigen made the test more complex and difficult to standardize. It was found that the sensitivity of the antigen could be increased by

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