THE STORY OF THE SALK ANTI-POLIOMYELITIS VACCINE

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PREFACE

The author has attempted in the following pages to put before the reader some of the main facts relevant to the recent development and launching of the Salk poliomyelitis vaccine. In order to view these events in their true perspective it is necessary to glance, however briefly, at the story of persistent research and experiment which led up to the present situation

In this recital of the historical and scientific facts reliance has been placed upon the statements of leading authorities on the subject to build up a true picture without the intrusion of any undue comment on the part of the author In this way. although the presentation may lose something in interest for those who look for pungent criticism

and comment in a pamphlet of this kind, it may be that it will commend itself to the thoughtful reader who prefers to judge for himself and reach his own conclusions without the distraction of the interpolated opinions and beliefs of the author

HISTORICAL SURVEY

Poliomyelitis was first transmitted to monkeys experimentally in 1908 by Landsteiner and Popper. Soon after this it was observed that monkeys which had survived one attack became resistant to subsequent infection. This suggested the use of serum from human beings who had had poliomyelitis for the treatment of those who had contracted it. A serum derived from convalescent children and adults was introduced for this purpose in 1911 and was extensively used and widely eulogised in the public press for some years. Eventually it was abandoned as useless. In 1917, Pettit advocated the preparation of a serum against poliomyelitis obtained by inoculating a horse with virulent nervous tissue from monkeys that had been experimentally infected with the virus: and in 1932 he obtained another serum by immunising a chimpanzee by the same method. But neither of these serums proved more effective than Netter's serum from convalescent humans.

After twenty years' trial with these various serums the situation was summed up by the Editor of the *British Medical Journal* (December 30, 1933, p. 1221) in the statement: "In the light of the most recent investigations it is difficult to refute Dr. Walshe's contention that serum treatment has proved a broken reed." Even the Editor of the *Journal of the American Medical Association* (July 28, 1934. p. 262) felt obliged to call attention to "the total failure of statistical presentations to make a case for serum therapy in this disease."

A few years ago what is called gamma-globulin was introduced as a prophylactic against poliomyelitis and is still used for this purpose among contacts of actual cases of the disease. It will be recalled that Her Majesty the Queen and the Duke of Edinburgh were given this preparation during their Australian tour, on account of an outbreak of poliomyelitis in that country. It should prove of interest to describe this preparation in a little more detail.

GAMMA-GLOBULIN

Gamma-Globulin is contained in the blood of a person who has had the disease. It takes about a pint of blood to produce one dose of gamma globulin. This is injected into people who may be liable to come into contact with the disease with the idea of protecting them front infection. Its value in this respect was investigated in America in 1952, 54.772 children being inoculated half of them with globulin, the other half with gelatin. It was found that after the eighth week there was no protective value which

could be ascribed to the globulin and that the injection of gelatin in the controls was itself associated with an increase of paralysis in the limb injected.

In the following year 235,000 children were inoculated. The National Advisory Committee conducting the inquiry were of the opinion that "it had no apparent effect on the incidence or severity of paralysis developing in subsequent cases." According to Dr. Geffen (Public Health March 1955) "it is expensive, uncertain, unreliable, and at the best the immunity it gives is shortlived." Probably, he says. 5.8 weeks. At any rate it was unsuccessful in protecting a laboratory technician who (in November 1954) accidentally sustained an abrasion of one linger with a hone spicule from the vertebral column of a monkey that had died after repeated intramuscular inoculation with type 2 virus. He was given gamma-globulin intramuscularly on the same day, but developed symptoms of polio eight days later. (*Lancet,* April 2. l955. p 702).

Nor did it prevent the occurrence of 40 cases of poliomyelitis among 6000 inoculated persons during an epidemic in Manitoba in 1953. In 36 cases the disease developed within 7 days of the inoculation. *The Times* (November 16. 1953) in reporting the incident stated that the Manitoba health authorities, while holding that gamma-globulin is useful, concluded that it is not a final answer in curbing outbreaks of polio. No one could call this an overstatement.

The more favourable results which had been reported in the first of the two trials referred to above were due, it was explained, to the fact that in this trial (1952) the controls were injected with gelatin, while in the second (1953) they were given no injections of any kind. Hammon and his colleagues who conducted the former, "appreciated the possibility that inoculation of gelatin, like that of many other substances, might provoke paralytic poliomyehitis in certain cases, and so give gamma—globulin a false reputation for protective action." *(Lancet.* March 13. 1954. p.558).

It may hardly he credited that, in spite of this scientific proof of the ineffectiveness of gamma-globulin the President of the National Foundation for Infantile Paralysis. Inc.. announced that they were making three million doses of the serum available in l954 compared with one million in I953.

It is the more extraordinary that in the August 1954 issue of their own bulletin, *Poliomyelitis Current Literature* (Quoted in Medical Officer Nov 19, 1954, p260) they actually published the information that ‘ Dr. Draber studied the possible effect of gamma-globbulin in a mass inoculation programme in Wisconsin. He comments that there is no evidence that gamma-globulin had any effect in altering the course of the poliomyelitis outbreak or preventing cases of the disease.’ They also

admitted that "following the failure of gamma-globulin in household contacts this substance is not being provided in Illinois for use in 1954."

It was not, however on account of its failure as a prophylactic that in 1953 the Glasgow Public Health Department declined the offer of a supply of the serum by the trustees of the United States Roosevelt Memmorial Fund. The reason given was interesting and, according to the *Weekly Scotsman* (January 22, 1953), was that with the comparatively small incidence of poliomyelitis in that city, it would have required the inoculation of 1,250,000 people to prevent an epidemic that might attack, at most, only 250.

This alleged prophylactic is one more pitiful example of the unreliability of animal experimentation, for Bodian had found in 1949 that gamma-globulin was highly successful in protecting monkeys against subsequent infection with all three types of virus.'

POLIOMYELITIS VIRUS

Flexner and Lewis established a filterable virus as the causal agent in 1909, but more detailed study of this organism was hampered by the fact that monkey's and chimpanzees were for a long time the only susceptible animals in which the disease could be experimentally induced. Later some strains of the virus were adapted to rodents, but this did not prove very helpful, apparently, and the great advances in our knowledge of poliomyelitis during the past few years began with the discovery by Enders, Weller, and Robbins in 1949 that poliomyelitis virus could readily be grown in tissue-cultures. a discovery which won for them the Nobel prize for physiology and medicine in 1954. A monograph published by the World Health Organisation (No. 26, Geneva 1955) gives a comprehensive description of all the work done in connection with this, and shows how the diagnosis of the various types of virus has been made possible by the examination of the tissue-cultures. It was by these methods, too, that Cox, Sabin and Koprowski were able to segregate low virulence viruses and even what is believed to be an avirulent (non-poisonous) variant.

This last has been prepared from all three types of polio virus and is the basis for the manufacture of vaccines. Both Sabin and Koprowski believe that the live but avirulent vaccine will prove best in the end. This is more fully discussed later in this pamphlet. Here it will be sufficient to call attention to the warning uttered by the late Professor James McIntosh, who was Professor of Pathology at London University, when addressing the Royal Society of Medicine on October 19, 1926:

"Scientifically it cannot be disputed that from every point of view the injection of a virus capable of multiplying in the body of the individual is bad. When multiplication

of the virus occurs, then there is no possibility of estimating the dose to which the patient has been subjected. Thus the effect cannot be controlled, and in susceptible individuals this may lead to unforeseen results."

Professor McIntosh emphasised the fact that no one knew how long an attenuated virus could lie dormant and then assume its former virulence. Dr. Albert Sabin himself found that when 26 volunteers between the ages of 26 and 30 were given a minute droplet of a single strain of polio virus in milk " some of the virus changed in the subjects' bodies to *a* somewhat virulent form". *(Time.* May 23, 1955).

Further details regarding attenuated and tissue-cultured viruses will be round on pages 18-20.

POLIOMYELITIS VACCINES

As it became more and more clearly realised that animal and human *sera* were quite ineffective and that little progress could be expected in this direction, attention was directed towards the production of a *vaccine* which might prove successful in preventing the disease. The chief difficulty was to find a culture-medium in which the virus would multiply. As is well known, unlike bacteria which will grow on a simple medium such as potato, blood or agar in a test-tube, viruses require a living tissue for their development. After many years of research involving the use of many thousands of monkeys, it was found possible to grow the virus in brain tissue derived from humans, monkeys and certain rodents: but the procedures, according to Lederle Laboratories,' were most cumbersome and expensive and unsuited to large-scale production.

Also, it was realised, a vaccine prepared from such material would hold the frightful danger of causing an allergic inflammation of the brain which might well he even worse than the disease it was designed to present. (*Time.* March 29, l954). It was in l949 that a team of Harvard research workers headed by Finders reported that they had succeeded in growing polio virus in the kidney tissue of rhesus monkeys. Then Dr. Jonas F. Salk, of Pittsburgh, adopted Finders tissue-culture technique and improved upon it by devising a special broth (No. 199) in which to grow the kidney cells.

It was already known that there were three main types of virus: (I) Brunhilde. (2) Lansing, and (3) Leon. but Dr. Salk and his associates isolated and typed 74 strains. By 1952, after he had made experimental vaccines and tested them on monkeys, he was satisfied he had produced one safe enough to be given to human beings.

THE SALK VACCINE

AN interesting account of how the Salk vaccine is made appeared in *Time* (March 29, l954). The story begins with the trapping of rhesus monkeys in large numbers in the N Indian State of Uttar Pradesh. They are stuffed into cages and carried on shoulder-poles to Lucknow. A train journey of 260 miles takes them to New Delhi whence a transport plane carries them the 4.000 miles to London Airport.

From London another plane transports them another 3,000 miles across the Atlantic to New York, whence they travel in trucks for a final 700 miles to Okatie Farms in South Carolina. There these rhesus monkeys from India are caged with other hordes of 'Java' (Cynomolgus) monkeys from the Philippines."

"Though Okatie Farms," the reports states, may receive 5,000 monkeys a month, the supply never catches up with the demand. After 21 days for rigorous health checks, they are on their way to laboratories in Toronto, Pittsburgh, Detroit and Berkeley, California."

It was at the University of Pittsburgh's Virus Research Lab' that the bulk of the work in research was carried out and the vaccine initially produced. Dr Salk, who pursues his investigations here, has behind him 81 million dimes, contributed by the National Foundation for Infantile Paralysis Inc, to spend on this enterprise. This is part of the three billion dimes subscribed by the public to the National Foundation.

But in order to vaccinate the million children as proposed in the 1954 tests it was necessary to hand over the manufacture of the Salk vaccine to five pharmaceutical firms, Parke. Davis & Co, in Detroit: Pitman-Moore and Eli Lilly & Co, in Indianapolis: Wyeth Inc, in Philadelphia: and the Cutter Laboratories in Berkeley, California. For all of them, we are told, " the indispensable material is the monkey, and the procedure much the same."

HOW THE VACCINE IS MANUFACTURED

Let us take, as an example, the University of Toronto Medical Research Laboratories. Some 50 to 65 monkeys will be used in a single morning. Under an anaesthetic a surgeon removes the kidneys, after which the monkey is killed by an overdose of ether. Then the kidneys are cut into tiny pieces and placed in glass bottles with a special nutrient solution (No 199) devised by Dr. Salk. These bottles are then rocked in a mechanical machine for six days in an incubator to stimulate the growth of the kidney cells.

At this stage fluid containing live polio virus is introduced and the bottles again rocked. After about four days the virus has multiplied a thousandfold in the kidney cells and is now chilled in 21 gallon bottles ready for transportation from Toronto to

Eli Lilly & Co, and Parke, Davis & Co. There the brew is filtered free from the kidney cells (which might cause nephritis if injected into a human being) and diluted with formaldehyde to kill the virus.

As we have already seen, there are three main strains of polio virus, against all of which there is need for protection. Consequently three tankfuls each containing one type of virus, cultivated and killed in the above manner, are mixed together. After neutralising the formaldehyde with sodium bisulphite there begins a month-long process of testing to see if the vaccine is safe for injection into human beings. This necessitates inoculations into live monkeys, rabbits, guinea-pigs and mice. These tests are carried out simultaneously, on each batch issued, by Dr. Salk's laboratories and by the National Institute of Health at Bethesda, Maryland. Having passed the final tests the vaccine is distributed in little glass bottles for inoculation into children.

Before this complicated procedure could he devisd, Dr. Salk and his staff engaged in a long investigation to discover which part of the anatomy of the monkey provided the most useful virus-growing cells. Like John H. Enders. of Harvard, they came to the conclusion that this was the kidney: but a leading article in the *Lancet* (April l8, 1953. p. 777) stated that the testicles as well as the kidneys are used as source of the cells which form the culture-medium. Monkey-tissue is apparently preferred to human tissue because, it has been pointed out, it is more readily available and also because human material might contain the virus of serum-hepatitis and thus prove dangerous and even fatal, as was the case with the earlier types of yellow-fever vaccine. Nevertheless we learn that one country, Sweden, is experimenting with the production of a vaccine derived from virus grown in human foetal material.

THE LAUNCHING OF THE SALK VACCINE

IT was on April 12th. 1955, the tenth anniversary of President Franklin Roosevelt's death, that the Foundation for Infantile Paralysis told the world, using every possible means of publicity, that the vaccine devised by Dr. Jonas E. Salk was "safe, potent, and efficient." For it was on this day that the eagerly awaited report on the 1954 tests of the vaccine was issued by Dr. Thomas Francis, of Michigan University. who had been entrusted with the task of evaluating the results. At a meeting of 500 doctors and scientists at Ann Arbor. Michigan, Dr. Salk and Dr. Francis made such sweeping claims for the vaccine that nearly every American newspaper declared that Dr. Salk had abolished poliomyelitis.

Already, in the past year, before any report as to the efficiency of the vaccine was available, six manufacturing firms had had orders from the Foundation for Infantile Paralysis to manufacture enough vaccine to inoculate 9 million children and pregnant women. Two hours after the announcement by Drs. Salk and Francis the Government

Department responsible licensed the vaccine and released it for distribution to all the States that had agreed to employ it.

The British newspapers and more especially the scientific journals were somewhat more guarded in their statements and their cautionary advice was well justified by subsequent events, as was also the attitude first adopted by our own Ministry of Health.

THE SALK VACCINE DISASTER

Only thirteen days after the vaccine had been acclaimed by the whole of the American Press and Radio as one of the greatest medical discoveries of the century, and two days after the English Minister of Health had announced he would go right ahead with the manufacture of the vaccine, came the first news of disaster. Children inoculated with one brand of vaccine had developed poliomyelitis. In the following days more and more cases were reported, some of then after inoculation with other brands of the vaccine. Then came another, and wholly unlooked-for complication. The Denver Medical Officer, Dr. Florio announced the development of what he called ‘satellite’ polio, that is, cases of the disease in the parents or other close contacts of children who had been inoculated and. alter a few days’ illness in hospital, had returned home: they communicated the disease to others, although not suffering from it themselves.

On June 23rd, 1955 the American Public Health Service announced that there had been 149 confirmed cases of poliomyelitis among the vaccinated, with six deaths, and 149 cases among the contacts of children given the Salk vaccine, with six deaths. Nor is this the end of the story; how many vaccinated children will eventually be reported as developing the disease is as yet unknown, but it is at any rate limited by the fact that the distribution of further batches of vaccine was suspended on May 6th, the actual manufacture of Cutter vaccine, which had been responsible for most of the polio cases, having been stopped altogether, pending a full inquiry, by the National Institute of Health on April 28th.

But with regard to the "satellite" cases the situation is far worse. According to Dr. Florio, children when inoculated with a faulty vaccine may become carriers of the virus. He estimated *(Daily Express.* May 16. 1955) that all of the 1,500 vaccinated Denver children had become carriers. "We have created a group of carriers", he said, "and then there will be another group and so the cycle will go on. It is very distressing." Some of the contacts acquired the disease in its deadliest form.

The interval between inoculation and the first sign of paralysis ranged from 5 to 20 days and in a large proportion of cases it started in the limb in which the injection had been given. Another feature of the tragedy was that the numbers developing polio

were far greater than would have been expected had no inoculations been carried out. In fact, in the state of Idaho. according to a statement by Dr. Curl Eklund, one of the Government's chief virus authorities, polio struck only vaccinated children in areas where there had been no cases since the preceding autumn: in 9 out of 10 cases the paralysis occurred in the arms in which the vaccine had been injected. *(News Chronicle.* May 6, 1955).

This experience led to Mr. Peterson, the Health Director for the State of Idaho, calling a halt to the mass inoculation programme. According to the *Daily Telegraph* (June 19. I955) he stated: " We have lost confidence in the Salk vaccine." The report continues: He said that he holds the vaccine, together with the instructions for its manufacture. directly responsible for the outbreak of polio in Idaho. This outbreak has resulted in 86 cases of the disease, including seven deaths, since the mass immunisation programme began in April. Mr. Peterson expressed disappointment that scientists and officials had not visited Idaho." He contended: "This was the H.Q. of the biggest outbreak there was. This was the place where they could study the facts."

An article in *Time* (May 30. 1955 commented: 'In retrospect, a good deal of the blame for the vaccine snafu also went to the National Foundation, which, with years of publicity, had built up the danger of polio out of all proportion to its actual incidence. and had rushed into vaccinations this year with patently insufficient preparation."

CUTTER VACCINE NOT SAFE

As mentioned, the majority of the cases followed inoculation with the Cutter brand of the Salk vaccine, but the subsequent reports of laboratory tests were at first conflicting: The Minister of Health declared, in answer to a question in the House of Commons (June 17. 1955). that "No explanation for the Cutter vaccine incident has yet been found, but it is possible that certain batches contained live virus."
The *Lancet* (June 11, 1955. p. 1207) stated in a leading article that "the most likely explanation is that some of the vaccine contained live poliomyelitis virus which had not been completely inactivated by the formaldehyde treatment." At any rate, in contrast to one report speaking of failure to isolate the virus from the Cutter vaccine- a purely negative laboratory result- --a more convincing report by Dr. Louis P. Gebhardt. Professor of bacteriology and Director of poliomyelitis Research Laboratory in the University of Utah, asserted that he had found live virus in samples of Cutter vaccine. This was confirmed by Dr. Scheele in a statement on television.

The report issued by the United States Public health Service *(Lancet,* June I8, 1955) contains the definite statement, amidst much that is rather wordy, vague and technical, that during manufacture the formalin used for inactivation often failed to reach minute particles of live virus. This, together with several other circumstances connected with

the development of the disease among the inoculated children, led them to conclude that the Cutter vaccine may have contained live virus. There can be little doubt that in fact it did.

It was also revealed in this report that several of the six manufacturers licensed to make the Salk vaccine had the daunting experience of finding active virus-—in one instance in four out of six batches tested-- --in the vaccine, when it should have been safe and ready for use.

In the course of the investigations into the manufacture of the Cutter vaccine, it transpired that instead of tests being made upon every batch of vaccine before its issue, only "spot " checks had been made. This would appear, face on the face of it, to be a most culpable omission amid one deserving the severest censure. At all events the experts of the United States Public Health Service, who carried out the inquiry into the manufacture, testing. and distribution of the cutter vaccine after this most humiliating fiasco that brought suffering and anxiety in millions of American homes insisted upon the application of most stringent safety measures before any more of this vaccine, and indeed of any of the various firms' vaccines, could be issued for general use. *Time* (June 6, 1955) pungently commented: "The more the authorities congratulated themselves on the new tests, the more (by implication at least) did they condemn the old."

It is by no means reassuring to learn that Dr. Scheele, the American Surgeon General is reported in the *New York Times* (June 8. 1955) as telling the American Medical Association, at a meeting at Atlantic City, that the Salk vaccine is difficult to make and that no batch can ever be proved safe before it is given to children.

The explanation of this somewhat startling pronouncement is to be found in a statement made by the city health commissioner of Milwaukee. Wisconsin, in May 1955, when referring to the safety tests made on monkeys. He said: " Monkey tissues are not necessarily comparable to human tissues in this respect. This is exemplified by the fact that the amount of inactivated virus necessary to produce a good polio anti-body response in humans is far less than that needed in monkeys." In other words the monkey is not so sensitive in the presence of virus as is the human being.

Dr. Scheele also announced *(Lancet.* June 4, 1955) and the reader must do his best to reconcile the two statements--the safety of all Salk vaccines produced by the other American firms, and it was expected that the mass immunisation of children would begin again shortly. It had been the intention of the Government to inoculate 57 million people before August 1955.

NOT THE FIRST FAULTY VACCINE

Few probably, will recollect that twenty years ago Dr. J. P. Leake, then Medical Director of the United States Public Health Service, reported a series of 12 cases of poliomyelitis in children who had been inoculated with a chemically treated anti-poliomyelitis vaccine. The onset of the disease occurred 6-14 days after the first or second injection. Five died and three were left with severe paralysis. Dr. Leake, who was writing in the *Journal of the American Medical Associwion* (1935. 105. 2. 152) added the comment:

"Many physicians will feel that these cases make undesirable the further use of poliomyelitis virus for human vaccination at present."

The vaccine then being used was one of two which were being tried out, the Kolmer vaccine inactivated with 1% sodium ricinoleate, and the other. Dr. Brodie's, with 0.1% formalin. Both, according to the *British Medical Journal* (March 13, 1954. p. 636) were abandoned.

Even the *British Medical Journal* (April 4. 1936) declared in a leading article that "it seems probable that these disasters will defer any further attempts of this kind for a considerable time. That such attempts should have been made at all is only to be explained by the enthusiasm of the transatlantic public for methods of specific immunisation." The editor concluded: "He will be a bold man. therefore, who proposes to renew the attack on this problem in the clinical field." He underestimated the short memory of the public, its "suggestibility by well planned press publicity, and the pertinacity of the research workers' one-track mind.

A SOBER SUMMING UP

FOR a concise and sober judgement on the catastrophe it would be difficult to better the statement which appeared in the *Medical World News Letter* (June 1955), an official publication of the Medical Practitioners' Union, which is sent to every general practitioner in the Health Service. Under the heading "What We Think" the editor wrote: "There is a useful lesson to be learned from the sorry story of the Salk polio vaccine in the U.S.A. It is that a new therapeutic measure of fundamental importance should not be launched until every possible medical and social implication has been considered.

"Three months ago newspapers throughout the U.S.A. were celebrating one of the greatest medical discoveries of our time and hailing the final conquest of poliomyelitis. Indeed the claims seemed reasonably well substantiated, although more cautious voices were heard over here. The United States Public Health Service authorised commercial production and relaxed standards of safety testing. In the meantime the tremmendous publicity had created a universal demand for the vaccine.

Large-scale inoculations were undertaken with results that were catastrophic for a far from negligible number of families. Over 100 cases of poliomyelitis occurred among the vaccinated and, what was more significant, 60 cases among their immediate contacts. There is no doubt that the disease has been propagated by the vaccine. American experts agree that the total elimination of live virus from the cultures may be very difficult to secure.

"These misfortunes would be almost endurable if a whole new generation were to be rendered permanently immune to the disease. In fact there is no evidence that any lasting immunity is achieved. There are theoretical reasons for thinking it is not."

THE FRANCIS REPORT

ON the other side of the picture. we have to take into consideration, though with critical appraisement, the Francis report. Dr. Thomas Francis. Jnr., was entrusted with the evaluation of the figures submitted by Dr. Salk as the result of his elaborate and widely planned experiment in inoculating children with his vaccine. He is director of the Poliomyelitis Evaluation Centre at the University of Michigan, and his report, which is very favourable to the vaccine, was given on April 12th at a meeting of 500 doctors and scientists at Ann Arbor, Michigan.

Only a statistical expert could evaluate the results of the tests which were made in 44 States and involved nearly 2 million children. As statisticians of the calibre of Bradford Hill and the late Major Greenwood have pointed out, there are many sources of fallacy to be avoided when making comparisons between inoculated and uninoculated groups of people. Only a close study of all the relevant factors would enable one to decide whether the groups in these tests are strictly comparable in all respects save that of the one to be evaluated.

STATISTICAL ERRORS

THE Francis Report reveals, at any rate, that in one large section of the trials the inoculated children were not of the same age-group as the uninoculated controls. The *British Medical Journal* (April 30. *1955)* called attention to this doubtful procedure, stigmatising it as "open to criticism ". To quote the writer's own words: "It may not be a fair assumption, for instance, that the experience of second grade children would be the average of that for the first and third grades in the absence of vaccination. A more serious bias lies in the selection of children in the second grade whose parents agreed to have them vaccinated ", it is recognised among statisticians engaged in similar assessments that the social position and the care lavished upon the children in families of volunteers for inoculation are likely to be superior to that of the controls generally, and that this would affect the validity of conclusions.

Another source of error which, if it did not escape the notice of Dr. Francis, at any rate escaped mention in his report, is the fact, recorded in *The Times* (April13. *1955),* that no case was considered as immunised unless it had received two shots of the vaccine. This means that a child developing poliomyelitis after the first inoculation and before the second would automatically be placed in the uninoculated class. If this is true, it is obvious that any conclusions drawn from his figures would be invalidated.

CLAIMS FOR THE SALK VACCINE

EVEN if we accept the Francis report and its conclusions as it stands, it seems clear that the protection afforded by the vaccine by no means bears out the sweeping claims presented in the headlines and front-page reports of the world's press. Dr. Salk himself, who made an independent report on his own discovery, said he was sure the vaccine was potentially almost 100 per cent, effective and could bring complete triumph over polio.

One of the most extravagantly adulatory articles was written by Alistair Cooke and published in the *Manchester Guardian* (April 16. *1955).* In it he told of "A Day of Rejoicing" following "the biggest news story of many a peace-time year" which broke on the tenth anniversary of Roosevelt's death and "engulfed every foreign and domestic concern from the new British Cabinet and the Formosa Strait to the Supreme Court's thoughts on segregation and the prospects of the summer grain crop . . . Nothing short of the overthrow of the Communist regime in the Soviet Union could bring such rejoicing to the hearths and homes in America as the historic announcement last Tuesday that the 166-year war against paralytic poliomyelitis is almost certainly at an end." He also revealed that "The announcement of the perfected Salk vaccine was made with the most careful and dramatic timing. The ceremony at Ann Arbor was staged before the country's leading public health doctors and poliomyelitis experts. But it was relayed by closed circuit television to scattered medical audiences in the United States and Canada comprising 54,000 doctors . . . What the learned audiences were waiting for was the following report of Dr. Thomas Francis, jun. who had supervised a secret check of the efficacy of a series of tests, applied to a comprehensive statistical sample, of the new triple anti-polio vaccine……Within two hours of Dr. Francis's declaration that the New Salk vaccine was 'safe, powerful, and effective', the National Health Institute, a branch of the United States Public Health Service, issued an official licence. Mrs. Oveta Culp Hobby, the Secretary of Welfare, flashed the green light for the six pharmaceutical houses that have been making it to distribute it, according to the international commerce laws, all across the country. 'It's a wonderful day,' she pardonably proclaimed, 'for the whole world '." He mentioned that the Government hoped to inoculate 57 million people between April and midsummer.

The fact is that, on the basis of the data provided by the Francis report, the most striking effectiveness afforded by the vaccine was against the bulbo-spinal form of the disease, and here it varied from 81 to 94 per cent. Against the spinal paralytic form protection was much less: 60 per cent with a lower limit of only 39 per cent. In respect of the non-paralytic form there was no significant difference between the vaccinated and the control groups and we must remember that even these milder cases may nevertheless become disseminators of the disease among contacts. These figures (quoted from the *Lancet,* April 23. *1955.* p.*851)* would hardly suggest that the "war against paralytic poliomyelitis is certainly at an end

SOBERING CRITICISMS

ACOMMENT by Dr. A. M. Payne. of the World Health Organisation was certainly justified and salutary. He was quoted in the *Manchester Guardian* (April 14. *1955)* as declaring: "Poliomeylitis is not beaten. We do not know how long the effect lasts; we do not know if it will work in infants; we do not know if it will be effective under other conditions than those in which it was used; we do not know how best to use it. We do know that there are many intricate problems in the manufacture of this vaccine." The unfortunate events of the past few months have proved how right he was in regard to this last statement.

An American Correspondent in the *Lance:* (May 14. *1955,* p. 1019) pertinently remarked: "There are many sobering facts; for example, quite apart from any question of infective batches of vaccine, many vaccinated children will get poliomyelitis, for the Francis report made no higher claim than that the vaccine was effective in 60-90% of those who received it."

DR. SALK'S TECHNIQUE

IT should be noted that the first injection of the Salk vaccine gives, he has stated, only a degree of immunisation. Full protection is not conferred until three injections have been given. Dr. Salk recommends that the interval between the first two doses should be from 2 to 3 weeks; the third dose should be given 7 months later. This procedure has been accepted, according to the *Lancet* (May 28. 1955) by the United States Public Health Service. The injections are given intramuscularly and are stated in the Francis report to be followed by few reactions: incidence of minor reactions is 0.4 per cent; of major reactions, 0.004 per cent.

The editor of the *Lancet* (April 23, *1955,* p. *851)* reminded us that "A disadvantage of this form of vaccination is that the immunity it confers may not last long. Data from the bleedings performed five months after inoculation indicate some persistence of antibodies but a decline in antibody titre, particularly in children vaccinated with

‘poor’ batches (- Presumably, any beech of vaccine which tails to do what it ii supposed to do will be termed ‘poor". An easy getaway but will any action lie against the manufacturing firms which issued it? It is extremely unlikely) of vaccine; and Salk is reported to have said that children vaccinated last year should be given a booster inoculation this year." He continued; "If it is found that. contrary to Salk’s hopes, antibody levels cannot be maintained without a succession of booster doses, then a serious problem will arise. Will it be necessary to give injections every year: and, if so, for how long should they be given? . . . If injections are given regularly for several years to millions of children the risk of allergic reactions to monkey kidney tissue will become increasingly grave. We do not yet see any reason to be less anxious on this account than we were six months ago."

POTENCY OF VACCINES

THE reader will have noted that in many reports on the Salk vaccine the word "potency" is frequently used and reference made to the *stimulation* of antibodies in the blood of the vaccinated child. It may be necessary to explain that when the vaccine is declared "potent " it means that examination of the blood subsequent to vaccination reveals the presence of these antibodies which are considered to be an indication of a degree of immunity in the person concerned.

In preliminary experiments on monkeys it was found that after vaccination their increased resistance to subsequent infection with the virus could be correlated with the level of antibodies present in the blood. It must be pointed out, however, that this would not justify the conclusion that the presence of a high antibody titre *in human b/cod or serum* indicates that protection against poliomyelitis infection has been established.

ANTIBODY FORMATION AND IMMUNITY

THE fallacy of the assumption that antibody formation is a measure of immunity was fully demonstrated in a Report issued by the Medical Research Council in May 1950, entitled "A Study of Diphtheria in Two Areas of Great Britain." in this report by nine doctors (Percival Hartley. W. J. Tulloeb, M.Anderson. W. A. Davidson, J. Grant, W. M. Jamieson, C. Kenbarrer. R. Morton, and G. H. Robertson) it was stated that the occurrence of diphtheria in the inoculated "led to the investigation into the immunity state and the behaviour of the immunity mechanism."

In view of the extreme importance of this question, and because so many tests with various vaccines are likely to be made, both in this country and in others, in which it is taken for granted that the antibody formation can be correlated with immunity, it seems desirable to give a brief resume of the Medical Research Council’s findings.

It appears that in the course of the study conducted by these time doctors, inquiry was made into "clinical diphtheria in 95 fully inoculated persons at Newcastle and Gateshead with special reference to the antitoxin concentration of the serum of these persons, and of hospital nurses, familial contacts, and carriers."

There had already, it is stated, been an investigation in 1939 and in 1940-42, of "The antitoxin concentration of the serum of 62 inoculated persons who contracteed diphtheria in different areas in England and Wales." but in the first period of the investigation:

"Some of the results obtained were so unusual and unexpected, so contradictory and indeed paradoxical, that the inquiry as originally envisaged and put into effect had to be brought to a close ".

"The paradox ", they say, "was this: on repeated occasions it was found that a sample of serum, taken from a patient with a clear history of inoculation who had yielded diphtheria bacilli from nose or throat swabs, and who according to the clinical history exhibited some or other of the classical symptoms of true diphtheria, was found to contain quite large quantities of diphtheria antitoxin. Now according to Schick, persons whose serum contains not less than *one-thirtieth* of a Unit of antitoxin per ml, or, according to workers in this and other countries, not less than *one-hundredth* of a unit of antitoxin per ml, should not contract diphtheria. Yet of 62 of the patients investigated prior to April 1942 no less than 25 (40 per cent) were found to contain *one tenth* of a unit, or more, of diphtheria antitoxin per nil. of serum, and of these, 5 contained 10 units or more, 7 contained 1—4 units and 13 contained 0.1—0.8 units per ml. of serum

In explanation of this it was suggested that a mistake had been made somewhere but "critical examination of the procedures used for the determination of the antitoxin content of samples of blood and serum failed to reveal sources of error which could account for the high litres ". They therefore decided to renew the investigation on Tyneside and to take the greatest possible care in the selection of patients and collection of pathological material and in its examination. But still they found as many as 40 persons with clinical diphtheria in whom the antitoxin content of the serum was one-twentieth of a unit, or more, per ml.

They encountered another paradox. "namely, the occurrence of several instances of non-inoculated persons, having no circulating antitoxin. harbouring virulent organisms, and yet remaining perfectly well, of nurses with little or no circulating antitoxin regularly employed in diphtheria wards and remaining free front diphtheria; of persons. previously inoculated or not, with little or no circulating antitoxin living in intimate contact with diphtheria in their homes and yet remaining perfectly well. It

was confidently expected that cases of diphtheria would arise, either among the nurses or among the near relations of patients and thus provide the material for this part of the inquiry, hut this expectation did not materialise."

Part III of the Report deals with the diphtheria outbreak in Dundee, 1941-2, and here there is also a reference to the occurrence of diphtheria in persons whose serum contained an appreciable amount of antitoxin.

The facts disclosed in this Report proved the fallacy of the theory that the presence of antibodies in the blood shows protection against a particular disease; but in all the reports recently published regarding the testing of immunity against poliomyelitis infection they appear to have been conveniently ignored and the assumption made that the theory is firmly established.

It will he apparent that the existence of this fallacy must he taken into account when critically examining any reports which include antibody estimations. The Medical Research Council in this country have announced that in the tests to be made this year "the response to the vaccine will he judged serologically and compared with other information obtained from laboratory tests." *(Lamet* April 23. l955. p. 857).

KILLED VIRUS v. ATTENUATED VIRUS

THere has been a long controversy over the question of whether a virus killed by formalin and given intramuscularly or a modified (attenuated live virus given by mouth is likely to he the most effective vaccine. According to the *Lancet* (May 14. 1955. p. l0l8) "Dr. Jonas Salk and Dr. Albert Sabin have long held opposing views about vaccination against poliomyelitis, but this year it looks as though Sabin may be right. He favours the use of attenuated-virus vaccine given by the natural route of infection (by mouth)."

"Sabin has contended that intramuscular injections of killed vaccine will not confer life-long immunity and that it would he impracticable to re-vaccinate each time the short-lived artificial immunity runs out. If children received such a short-term vaccine, he argues, there would soon be a population of young adults with no protection against poliomyelitis; and as the disease is more severe in adults than in children, a vaccine which confers only a short immunity might eventually result in many severe illnesses when the children grew up."

On the other hand, the whole of Dr. Sabin’s claims as to the effectiveness of his vaccine are based upon estimations of the antibodies present (as the result of vaccination) in the blood-serum of the chimpanzees and human "volunteers" taking part in the experiment. The fallacy underlying this method of assessing the degree of

immunity induced by vaccination has already been fully described, so that it may justly be argued that the efficiency of the attenuated live vaccine is so far entirely problematical.

It should be noted, in passing, that the ‘volunteers" referred to in Dr. Sabin’s first tests upon human beings with live virus vaccine in January 1955 were 25 initiates of the Federal Reformatory at Chillicothe, Ohio. A few months later, on May 3rd, 1955, the *Chicago Herald Tribune* reported that another living virus vaccine developed some years ago by Dr. Hilary Koprowski, who is Dr. Harold Cox’s assistant at the Lederle laboratories, "is being tested on children in a California institution for the feeble-minded after having undergone long trials on animals."

WHAT IS AN ATTENUATED VIRUS?

IT may be of interest to know what is meant by a modified or attenuated virus. Dr. Sabin found that by passing virulent strains of polio virus through monkey tissue in a rapid succession of cultures a vaccine could be produced which did not produce poliomyelitis when injected directly into the brains of cynomolgus monkeys. It was evident that some change had taken place in the virus which rendered it far less virulent; it is claimed that this modification is permanent and that there is no tendency for the virus to return to its former virulence. In point of fact, the vaccine now being used by Dr. Sabin is prepared by mixing together the modified viruses of all three types: type I having been attenuated by rapid culture in monkey-kidney tissue 33 times; type II. 5I times, and type III, 34 times.

Whether in the course of mass inoculations it will prove to he less liable to produce undesirable reactions than those which not infrequently follow B.C.G. vaccinations remains to be seen.

The main argument, of course, against the use of an attenuated or modified vaccine of any sort is that put forward by the late Professor McIntosh, who was Professor of Pathology at London University. He stated before the Royal Society of Medicine on October 19. 1926:

Scientifically, it cannot be disputed that from every point of view the injection of a virus capable of multiplying in the body of the individual is bad. When multiplication of the virus occurs, then there is no possibility of estimating the dose to which the patient has been subjected. Thus the effect cannot be controlled, and in susceptible individuals may lead to unforeseen results." Commenting upon this address, the editor of the *Lancet* (May 24. 1930, p. 1138) wrote:

The reintroduction of the use of an attenuated virus in tuberculosis was described by Professor McIntosh as a retrograde step. Who knows, he said. for how long an attenuated bacillus can lie dormant and then assume its former virulence."

These scientific criticisms apply equally to the inoculation or ingestion of any living virus, and are as valid to-day as when they were made.

In spite of repeated asseverations that it was quite impossible for the attenuated form of the polio virus to return to its original toxicity. Dr. Sabin himself found that when 26 volunteers, between the ages of 21 and 30, were given a minute droplet of a single strain of polio virus in a teaspoonful of milk "some of the virus changed in the subjects' bodies to a somewhat virulent form." *(Time.* May 23, 1955).

Further details concerning the development of an attenuated virus cultured in egg-embryos by Dr. Herald R. Cox at the Lederle Laboratories will he found under the heading *Research in the Immediate Future,* on page 29.

Another killed-virus vaccine is being produced at Chicago in the Michael Reese Hospital by Drs. Albert Milzer and Sidney Levinson. It is similar to Dr. Salk's vaccine except that the virus is "killed by exposure to ultrtaviolet radiation. This, they believe, does less harm to the virus particles than formaldehyde and therefore produces a more potent vaccine. An account of their work will he found in the *American Journal of Public Health* (1954, 44, 26).

THE POSITION IN GREAT BRITAIN

IN this country the whole output of two large well known firms, Glaxo Laboratories Ltd., and Burroughs Wellcome & Co. are to be sold to the Government. Already, by the end of April 1955 Glaxo Laboratories had produced a pilot batch of Salk vaccine for use in the coming tests by the Medical Research Council. According to the *Chemist & Druggist* (April 16. 1955): "Messrs Glaxo will he ready for full-scale manufacture on completion of the Council's field trials." It was also reported in this journal that "Glaxo Laboratories Ltd., Greenford. Middlesex, have been undertaking poliomyelitis research at a suite of laboratories specially built for the purpose within the past twelve months at a cost of over £100,000."

It is hoped, the Minister of Health said on June 17th in the House of Commons, to make enough vaccine not only for the mass vaccination of British children but for export.

It appears that the research work by the Wellcome Research Foundation, to which reference has already been made, has been brought almost to a standstill by the

insistence on the part of the Ministry of Health that they must concentrate on the production of the Salk vaccine. Their public relations officers Mr. Sidney Rogerson, is reported in the *Beckenham Journal* (June II, 1955) to have stated that they had neither the staff nor facilities to carry out their own ideas and fulfil Ministry of Health orders at the same time. For years Wellcome's had been working on a polio vaccine but now, because of the immense publicity that had surrounded American research, public opinion had virtually forced them to produce the Salk vaccine, although they did not believe it was the best one. He confirmed the report that Wellcome's had been preparing a vaccine that could be taken by mouth, probably from a virus cultivated in eggs and known as an "attenuated virus." Mr. Rogerson thought that if the Salk vaccine had not been launched with so much "ballyhoo" British firms could have continued their own research without having to give way to pressure for an immediate vaccine.

THE VACCINE IN OTHER COUNTRIES

AUSTRALIA
The Australian Government hope to produce a better vaccine than the Salk vaccine. This should be ready in a month or so *(Daily Telegraph,* April 29, 1955).

DENMARK
In Copenhagen it is proposed to inoculate everyone up to the age of 18 in June. All Danish children will receive a second injection after one month and a third in a year's time. Already 400,000 children have been inoculated, presumably with the Salk vaccine. *(News Chronicle.* May 6, 1955).

FRANCE
The Pasteur Institute stated that an anti-poliomyelitis vaccine, developed by Professor Pierre Lepine would soon be produced in large quantities. *(Times*, London, April 4, 1955).

INDIA
The first country to be chosen by President Eisenhower to receive the formula of the Salk vaccine was India, and the presentation was made on May 5th to the Indian Health Minister, Rajkumari Amrit Kaur, by the U.S. Ambassador, Mr. Sherman Cooper.

This was in recognition of the contribution made by India in evolving the vaccine. A polio research centre in Bombay, financed by the Indian Council of Medical Research had been working on the problem for several years and was said to have produced valuable data; also because Rhesus monkeys imported into America from India bad

played an important role by supplying the kidneys which until recently had been the only live tissue in which the virus would grow.

The Indian Health Minister said that the Government would immediately take up. the question of the manufacture of the vaccine in India. *(India News.* May 14, 1955). According to a report from New Delhi *(News Chronicle,* July 4. 1955) the government of India is willing to continue exporting monkeys subject to two guarantees:

(1) They must be transported under humane conditions, and
(2) They must only be used for poliomyelitis research.

SWEDEN

According to the *Lancet* (May 7. 1955) plans are well advanced in Sweden for the manufacture of a vaccine derived from a virus grown in human tissue. Prof. Gunnar Olin, of the Swedish State Bacteriological Laboratory, reports that the virus has been grown in human foetal tissue and then inactivated with formalin. Enough vaccine has already been prepared to "immunise" 120,000 children. Human tissue has been selected as the culture medium in the hope that it will be freer from undesirable side-effects than might be expected from the use of monkey tissue. Owing to shortage of human culture material, American supplies may also be used *(Lancet.* April 23, 1955, p. 858), and the Swedish board of medicine have ordered enough American vaccine for 100,000 people.

POLIO RISK IN THE UNITED STATES

THE risk of contracting poliomyelitis has increased fourfold in America since 1939. In 1953 approximately 35,000 cases were reported compared with 4,538 in England and Wales. One in every 100 Americans reaching the age of 20 has, it is said, developed some degree of paralysis. This, no doubt, accounts for some of the hysteria shown by the American public in its demands for the vaccine before tests of its efficacy had been completed. As the *Lancet* (April 23, 1955, p. 864) commented: "Even before details of the elaborate and, I believe, careful experimental work bad been presented to any competent scientific society, television. radio, banner press headlines, and 4 complete pages of the *New York Times* have informed the public of its wonders…….Already anxious parents are demanding the vaccine for their children and worried administrators are requesting Presidential action to ensure its fair distribution. It is difficult for laymen here to see the risks of poliomyelitis in their correct perspective…..The risk of a child being killed or maimed by car accidents is incomparably greater."

There is no doubt, however, that the risk has been, for some years, vastly exaggerated, seemingly to prepare the public mind to accept the new vaccine more readily; as an article in *Time* (May 30, 1955), in commenting upon the Cutter incident, stated: "In retrospect, a good deal of the blame for the vaccine snafu also went to the National Foundation, which, with years of publicity, had built up the danger of polio out of all proportion to its actual incidence."

POLIO RISK IN GREAT BRITAIN

ONE should bear in mind, as Dr. C. H. Andrewes, M.D., F.R.S., and Dr. W. L. M. Perry. M.D., have stated (*Picture Post*, May 7, 1955) "Polio is a rare disease. In most years, your chance, in Britain, of catching paralytic polio is less than one in twenty-five thousand…..Your children are much more likely to be killed or maimed on the roads than to be killed or paralysed by polio. If the money which will have to be spent on vaccinating the whole population were spent in improving road conditions instead, more lives would probably be suvcd~ and more crippling avoided."

The actual figures given by the Registrar General show that during the years 1943-1953 the average annual number of cases of poliomyelitis notified in England and Wales was 3,328, giving a monthly average of only 277 in a population of 42,290,000, or 6 per million.

According to Dr. Dennis H. Geffen, O.B.E.. M.D.. D.P.H., of every 100 people who become infected with the virus, 90 per cent, remain symptomless, 9 show some slight sign of disease, such as sore throat or stiffness of the neck, whilst only 1 develops definite paralysis. He is reported in *Public Health* (March 1955) to have told the Metropolitan Branch, Society of Medical Officers of Health that "we are apt to forget that poliomyelitis is the least serious of all infectious diseases with the exception of that one complication or extension of the disease which destroys motor cells in the brain and spinal cord and causes paralysis. Apart from this it appears to be a mild infection lasting a few days, the symptoms of which are probably less serious than a cold in the head, and from which recovery is complete and immunity lasting. If we could be sure that an individual contracting poliomyelitis would not become paralysed then there might be much to be said for spreading the disease in order that a community might develop natural immunity."

PREDISPOSING HOST-FACTORS

Dr. Geffen is Medical Officer of Health for St. Pancras, and in his address from which the foregoing has been quoted he had some very interesting things to say about the importance of predisposing factors in the host as compared with that of the infecting

virus. He gave a list of four main host factors which predispose a person to developing the disease:

(1) Operations for the removal of tonsils and adenoids.
(2) The condition of pregnancy.
(3) Undue exertion, fatigue and chill.
(4) Small injuries such as the inoculation of vaccines, injection of drugs like penicillin. In these cases paralysis is usually observed in the limb which has received the trauma.

A large amount of inquiry, he said, had convinced Gaylord Anderson, Professor of Public Health in Minnesota, U.S.A., of the following facts:

(a) Persons with bulbar type of polio give a history of removal of tonsils and adenoids more frequently than do persons with other forms of poliomyelitis.
(b) If a person who has had tonsillectomy develops poliomyelitis, the likelihood of bulbar involvement is 4 times as great as in one where the tonsils are *in situ*.
(C) The higher proportion of bulbar cases in tonsillectomised persons occurs at all ages and regardless of the time that has elapsed since operation.(Dr. R. V. Southcott *(Med. Jour. .Aust.* 1953. ii. 281) believes that a child whose tonsils were removed at the usual age of 5-7 yrs suffers trauma to the nerves of the pharynx which increases susceptibility to bulbar poliomyelitis for at least ten years. In an outbreak in South Australia in 1947-48 he found that in 35 out of 39 cases of bulbar poliomyelitis the patient had been tonsillectomised).
(d) The higher proportion of bulbar cases in older persons is due primarily to absence of tonsils rather than to age *per se*.

The theory is that any injury to the body causes changes in the nerve-cells supplying the part so that they are rendered less able to resist infection with the virus. Dr. Geffen has himself observed that persons contracting polio after appendicectomy develop paralysis of the abdominal muscles or even of the muscles of the intestine. He is convinced that the injection of diphtheria-pertussis vaccine not only localises the paralysis of persons infected with virus but also increases the attack-rate. There can be little doubt, therefore, that even the vaccination of children against poliomyelitis itself may provide the very conditions which favour an attack and so increase the incidence of the disease. And this risk is by no means confined to the first injection. As a correspondent in the *Lancet* (March 6, 1954. p. 516) pointed out: "A child who is injected three times is at risk three times; there is replication of exposure..."

CONFIRMATORY EXPERIMENTS

NEEDLESS to say Dr. Geffen is able to cite numerous experiments on animals, performed by various research workers, which lend support to his contentions, though

clinical experience had already provided all the evidence required by any truly scientific standard. We are told, for instance, that D. Bodian of Baltimore [Bodian D. (1934) .*Amer. Jour. Hygiene.* 60, 339.] had in 1954 performed some experiments in connection with poliomyelitis following injections. They consisted in injecting the virus directly into the hearts of cynomolgus monkeys. Paralysis occurred in 50 per cent. of monkeys so treated and in at least 20 per cent. the initial paralysis affected the facial muscles. If, however, the monkeys were first injected with various irritant substances, including gelatin, cortisone, penicillin, or diphtheria-pertussis-tetanus vaccine within one to three weeks prior to the intracardiac injection of the virus, not only was there an undue proportion of cases where paralysis affected the limb receiving the injection. but that instead of 50 per cent, of the monkeys developing poliomyclitis the proportion was increased to 80 per cent.

He also referred to experiments which showed that castration in monkeys induced a greater susceptibility to the intra-nasal inoculation of the virus. It also appears that in spite of the fact that it had been a matter of clinical observation that human beings suffering from a deficiency of Vitamin B6 have a lowered resistance to infection, a considerable number of monkeys were subjected by Bodiant [Bodian D. (1948) .*Amer. Jour. Hygiene.* 48, 87-93.] to an investigation in which they were deprived of this vitamin (pyridoxin) and then exposed to infection. The results seemed to confirm clinical experience.

It is interesting to note that another predisposing factor to severe paralysis which has come to light is lumbar puncture for the withdrawal of cerebro-spinal fluid. A correspondent in the *Lancet* (May 29, 1954, p:l133) called attention to the danger of spinal puncture in cases of frank or suspected cases of poliomyelitis.

A predisposing factor which, it was pointed out by another correspondent in the *Lancet* (May 29, 1954, p. 1133), may be of equal importance to tonsillectomy and other minor surgical operations is the extraction of teeth. He asks if it would not be wise to postpone extractions in children whenever possible during any period of poliomyelitis prevalence.

PRESENT RISKS ATTACHED TO SALK VACCINE

IT is now admitted (Editorial in *Lance:,* June II, 1955, p. 1207) that at the present time "there is unfortunately a very small but definite risk that the vaccine may produce paralytic poliomyelitis. This risk may be reduced to something extremely small by the improved tests of the vaccine in tissue-cultures and in monkeys, but there will still be a fear that the tests may not reveal the presence of every live virus particle and that the occasional highly susceptible child may be given the disease by a vaccine which has passed the most rigorous testing."

According to Dr. Geffen, "It is not easy to be sure that in all batches of vaccine produced on a commercial scale the virus will be dead, and in trials of a vaccine some years ago in America some 12 children did develop poliomyelitis after injection, paralysis affecting chiefly the limb of injection or the contralateral limb."

In this connection it is well to remember that the risk is by no means confined to the first inoculation of vaccine. As a correspondent in the *Lancet* (March 6, 1954, p. 516) categorically stated: "A child who is injected three times is at risk three times; there is replication of exposure . . ."

On June 22nd, 1955, Dr. Sabin, testifying before a sub-committee of the House of Representatives in Washington, declared the Salk vaccine to be "Dangerous". A view gaining acceptance in some medical quarters is that while the Salk vaccine may reduce the severity of polio so that paralysis is prevented in some cases, there is reason to believe that a vaccinated person is not immune from acting as a carrier and passing on the disease to another *(Daily Telegraph,* June 19. 1955). This view, as we know, was fully borne out by the occurrence of what was termed "satellite" poliomyelitis among contacts in Idaho.

Then there is the danger of induced sensitivity to monkey-kidney tissue. It was reported in the *Manchester Guardian* (April 15, 1955) that "One of Britain's greatest physiologists -said to-day that if it means that a child should be re-inoculated at frequent intervals with a preparation derived from monkey kidney 'it is terrifying in its possibilities'. Among them is the risk of the child's developing sensitivity to some of the ingredients of the vaccine." This was also emphasised by the editor of the *Lancet* (June 11, 1955. p. 1207) when he wrote that, in addition to the possibility of producing the very disease the vaccine is used to prevent. "there is a risk, of unknown dimensions, that repeated injection of a vaccine prepared from monkey kidney may eventually sensitise the child in some harmful way." Mr. Iain Macleod, the Minister of Health, mentioned this drawback in the House of Commons in April, 1955.

Another grave possibility derives from the very fact, if established, that the vaccine produces definite even it shortlived immunity. The *Irish Times* (April 14, 1955) quoted a doctor, whose work is concerned with the treatment of such notifiable diseases, as saying:

"We do not know how long immunity it confers or whether booster shots are required every year…….There was also the possibility that immunisation of young children might transfer the danger of polio infection to a later group, those, say, between 18 and 35 when the contraction of the disease is much more serious and far more difficult to cure."

This is a particularly serious problem and one that does not appear to have received the attention it deserves. Its importance is increased by the well-known fact that the incidence of poliomyelitis has shifted within recent years to older age-groups, so that the name by which it used to be most commonly known— infantile paralysis—is no longer applicable.

J. G. Humble, of the Westminster School of Medicine, raised a pertinent question in the *Lancet* (May 7, 1955) when, referring to the fact that the Salk vaccine is prepared from monkey-tissue cultures, he asked: "is it certain that injection of this preparation will not produce rhesus antibodies when injected into susceptible human subjects, most especially those already sensitised?" So far, no one appears to have ventured to commit himself on this point.

It was after the publication both of the Francis report on the value of the vaccine and of the tragic events which had followed the launching of the vaccine on the public in America that one of the greatest authorities on the subject in this country, W. Ritchie Russell, C.B.E.. M.D., F.R.C.P. of the Department of Neurology, Radcliffe Infirmary, Oxford, wrote in a letter to the *Lancet* (May 21, 1955, p. 1071):

"It may also be pointed out that, however dead the virus may be, the giving of any kind of inoculation is likely to precipitate paralytic poliomyelitis in a relatively small number of children who perhaps arc already harbouring the virus. One is led to believe that these dangers are less than the benefits of protection, but when the protection is by no means 100%, the merits of the method and its statistics become debatable."

Dr. Ritchie Russell favours the use of a live virus, for, he says: "It is certainly more effective than the Salk method, and may even involve less risk, for should an oral vaccine lead unexpectedly to a febrile illness, there are still many chances that no paralytic disease will develop . . . When, however, poliomyelitis is precipitated by an inoculation the *natural defences of the nervous system seem to be ineflective,* and nearly all such illnesses develop into a paralytic form of the disease affecting especially the limb used for the injection." (My italics, M.B.B.).

IS MASS VACCINATION WORTH WHILE?

DR. Howard J. Shaughnessy. a well-known bacteriologist in the States, speaking to 100 members of the Association of Commerce Illinois Committee on June 2nd. 1955, described the reports on tests as probably a little exaggerated. The vaccine, he said, only gave 62 to 68 per cent, protection against the most prevalent strain of virus. Even if this amount of success should be maintained, it did not follow that mass vaccination was the answer to the problem.

Dr. F. Kingsley Sanders, speaking in the overseas service of the B.B.C. *(London Calling*, June 16, 1955). said: "There is still some doubt whether universal vaccination—for that is what it would have to be—is the best way of preventing polio in the long run." Of course he assumed the efficacy of the vaccine, but went on to say: "To protect each individual who actually needs protection we must vaccinate a very large number who would never have become paralysed. In the American trial the figures show that it would be necessary to vaccinate nearly 4,000 individuals to protect each potential paralytic. And in a European country such as Britain, where the overall paralytic rate is lower than in the U.S.A., even larger numbers of vaccinations would be necessary to protect each vulnerable individual. Not only would the cost of such a programme be very great, but among the 4,000 vaccinated we might expect sixteen reactions to inoculation."

McHammon (BMJ March 13, 1954, p636) gives even more startling figures. He says that even in an epidemic area it would be necessary to inoculate 11,000 children to prevent one fatal or paralytic case, and in a non-epidemic area perhaps 50,000.

On a previous page it has already been mentioned that in 1953 the Glasgow Public Health Department declined a supply of gamma-globulin, offered by the United States Roosevelt Memorial Fund, on the ground that with such a small incidence of thc disease in the City they would have to inoculate 1,250,000 people in order to prevent an epidemic that might attack at most only 250.

C. G. Learoyd, M.R.C.S., L.R.C.P., who wrote a most interesting article in the *Medical World* (February 1954), made this thought-proving suggestion (p. 181):

"in the U.S.A. they have tried and are trying huge experiments with gamma-globulin and various vaccines. There are definite drawbacks to mass injections and there have been some nasty accidents; also there is something rather unconvincing about immunising a one in a thousand chance. For God's sake—and I say that reverently—let's try the simple things thoroughly first."

This is not the place to discuss Dr. Learoyd's proposals for attacking the problem. They are sound common sense and concern the adoption of more hygienic habits in order to avoid faecal contamination of hands, food, etc., since this is now considered to be the method of infection. It is of more than passing interest. however, to note that the polio virus is readily destroyed by hydrogen peroxide, potassium permanganate and ultra-violet rays.

In the light of the foregoing there would appear to be much to justify the opinion expressed by Dr. W. H. Bradley, a senior medical officer in the Ministry of Health, when he was addressing the Metropolitan branch of the Society of Medical Officers of

Health on November 13th. 1953. According to a report in the*Medical Officer* (November 21, 1953):

"Dr. Bradley concluded by saying that some people believed immunisation to be the final answer to all epidemiological problems. The more experienced epidemiologist knew that this was not true and that he must use other more precise and immediate measures to contain an outbreak. We should still have to do this with polio even when safe antigens and abundant gamma-globulin were available."

RESEARCH IN THE IMMEDIATE FUTURE

AT the present time a good deal of research is still being pursued in connection with the mass production of the Salk vaccine by commercial firms, in order to ensure that the tests applied shall be sufficiently stringent as to make a repetition of the Cutter disaster impossible. But at the same time research in several important laboratories is being conducted by some of the world's greatest experts who are largely concerned with two main problems:

(1) To develop a vaccine from a virus that can be grown successfully in egg-embryos, and
(2) To produce an attenuated virus that can be given orally and can be relied upon to maintain it's a virulence and at the same time produce lasting immunity.

CHICKEN-EMBRYO VIRUS

A PERSONAL communication (9th May 1955) from the Lederle Laboratories Division, London, revealed that their laboratories at Pearl River, New York, are at work cultivating a polio virus on a chicken-embryo medium. This work is also designed to produce an attenuated live vaccine and for this purpose monkeys and chimpanzees are also used chiefly in the process of testing for safety and for estimating the amount of antibodies present in the blood after vaccination (For the fallacy underlying this test see page 16-18 ante).

According to a Bulletin issued by Lederle. (September 1954) they have succeeded in growing a deadly Lansing type of virus in chick embryos. This particular research is being pursued by Dr. Herald R. Cox who was Principal Bacteriologist of the United States Public Health Service, and was the originator of the chick-embryo-produced vaccine for Rocky Mountain spotted fever and epidemic typhus fever. This latter vaccine was manufactured in hundreds of millions of doses during the last war for the immunisation of all American and Canadian as well as Allied troops and the civilian population in typhus-infected areas.

Dr. Cox, now Director of the Virus and Rickettsial Research Department of the Lederle Laboratories, states that, in his opinion, chick embryo " is the ideal tissue for mass producing virus vaccines. The chick embryo is always readily available, cheap and free from potentially dangerous micro-organisms." The method is now well standardised. A technician uses a dentist's drill to break a tiny hole through the egg-shell. Through this opening another technician injects a small amount of living modified virus with a hypodermic needle. The hole is sealed with collodion and the eggs are placed in an incubator for a certain number of days. Before hatching, the eggs are cracked and the living embryos which are now swarming with tremendous quantities of virus are removed and "processed" by methods necessary to produce either killed or living modified virus vaccines. Lederle, we are told, has used as many as 14 million eggs a year in the production of various vaccines.

In Great Britain. it appears, Burroughs Wellcome are also working on this project, as is also a small team at Queens University, Belfast, N. Ireland.

It was at the end of 1954 that the National Fund for Poliomyelitis Research established a Fellowship at Manchester University. Dr. P. B. Stones has been appointed as the first fellow and will take up his appointment in October 1955. During the past year "a start had been made in cultivating poliomyelitis viruses."*(Lancet* December 25, 1,954).

HUMAN-TISSUE VIRUS

WE have already seen that Sweden has well-advanced plans for the manufacture of vaccine derived from virus grown on human foetal tissue (p. 22 *ante).* it has now been reported *(Lancet* July 9.1955, p. 88) that at the University of California E. M. Zitcer, J. Fogh, and T. H. Dunnebacke have cultivated all three types of poliomyelitis virus on human placental amniotic tissue (membranes removed with the afterbirth). It is claimed that "a vaccine prepared in this way would be free from one of the possible disadvantages of the Salk vaccine—namely, the risk of sensitivity induced by monkey-kidney tissue."

MANY MONKEYS NEEDED IN VACCINE PRODUCTION

"FOR the manufacture and safety testing of polio vaccines thousands of monkeys are absolutely essential ". This is a statement made by Dr. C. H. Andrewes and Dr. W. L. M. Perry in *Picture Post* (May 7, 1955). They went on to explain: "It is necessary, every time a fresh batch of vaccine is made, to take elaborate precautions to ensure that all the virus is dead. This means, among other things, injecting a large number of monkeys with the vaccine, and examining them closely, both while they are alive and after they have been killed, for signs of polio infection. It is this which makes the

vaccine expensive, and which has made the transport of thousands of monkeys from India to the U.S.A. necessary."

According to David. R. Preston (personal communication June 13, 1955) Director of Scientific information at the National Foundation for Infantile Paralysis, Inc., New York, U.S.A., one monkey's kidneys provide enough vaccine for 6,000 injections, that is for 2,000 children, assuming 3 inoculations for each child. From the calculation that 30 million children are born each year, this means that 15,000 monkeys would be required per annum. In addition, many monkeys will be required for testing and for further research. However, it appears, he says, "that the supply is equal to the demand. My understanding is that many millions of rhesus monkeys are available in India, assuming Government approval, and some are to be had elsewhere."

It may be explained here that according to Parke Davis & Co., Ltd., the final vaccine test consists in inoculating healthy monkeys intracerebrally and intramuscularly with the vaccine. Following this, the monkeys are observed for 28 days for symptoms suggestive of poliomyelitis. The monkeys are then killed and the organs examined microscopically. But, as the *Lancet* (May 7, 1955, p. 956) asked in an Annotation:

"Is it wise to apply the results of tests with scores of monkeys to the vaccination of hundreds of thousands of children?"

The medical correspondent of the *Manchester Guardian* (April 27. 1955), in a letter complaining of the "serious shortage of monkeys" which was holding up research, concluded: "If mass inoculation is to become a fact the demand for more monkeys will be great. It is estimated that between Messrs. Glaxo and Burroughs Wellcome about eight thousand animals would be required in the first year, and then probably more later if the results were satisfactory."

In the opinion of Mr. Michael Perrin. Chairman of Wellcome Foundation, the successful vaccine may differ from that to which Dr. Salk has given his name; in other words it will be derived from a living attenuated virus. He is reported in the *Sunday Times* (June 5, 1955) as saying that if that is the case "the animal kingdom will benefit even more than man, for the Salk vaccine requires an almost limitless supply of Indian Rhesus monkeys. The Americans were using five thousand a month in their initial tests, and with general inoculation, the Rhesus monkey population would quickly be wiped out."

It should have become quite clear by now that even if not required for their kidneys a large number would still be necessary for tests for safety and for estimating the potency of vaccines by measuring the antibody response after inoculation. (See section on Antibodies, P 16-18 *ante.)*

Some idea of the quantities of monkeys that are required in polio research can be gained from the statement, made by Dr. Salk when addressing an International Conference in Rome on the subject of poliomyelitis in 1954, that he had already at that time made use of 15,000 of them.

BAN ON EXPORT BY INDIAN GOVERNMENT?

IT does not seem likely that there will be any opposition on the part of the Government of India to the export of monkeys for the purpose of research into poliomyelitis and the preparation of vaccines. A report from New Delhi in the *News Chronicle* (July 4, 1955) said that American representatives from the polio research foundation were awaiting the verdict of the Indian Government on this question. It mentioned, revealingly, that India cannot afford publicity as the monkey is sacred to Hindus. but is reluctant to stop exporting her most valuable dollar earners which destroy ten per cent of India's crops.

At first it was alleged that in March. on the insistence of Premier Nehru, the export of monkeys from India had been stopped; he had been deeply distressed by the account of the suffocation of over 390 monkeys at London Airport while in transit to New York by Air. Later reports said that, on urgent representations from American research workers and under pressure from the English Ministry of Commonwealth Relations, export had been resumed, but on a limited scale.

It seems not unreasonable to suggest that had the ban on export been effective it would have been reflected in a reduction in the number of monkeys passing through London Airport. But more than twice us many monkeys were flown in during March of this year as in 1954.

In point of fact, during the first 6 months of 1953. the figures were 10,169; in 1954, 15,557; and in 1955, 47,710 more than thrice as many as in the previous year. The monthly totals for time first eight months of this year were:

January - 9,156 May - 11,529
February 8,500 June - 9,875
March - 4,512 July - 9,868
April - 4.138 August - 12,175

India now seeks two guarantees as a condition of exporting monkeys: Monkeys must he transported under humane conditions and must be used only for polio research. Anyone who accepted such a guarantee would have to be extremely naïve. No one can ensure that accidents like the one that happened at London Airport, will not occur again, and in any case the transport of hordes of sensitive and timid creatures like the

rhesus monkey can never under any circumstances be made humane. As to the second requirement, it is difficult to see how it could possibly be enforced, or how breaches could be traced.

VALUE OF RESEARCH IN MONKEYS

NEEDLESS to say, Dr. Salk's investigator's and conclusions have been based on innumerable experiments on monkeys, and his fellow scientists have openly criticised him for not publishing his data. Dr. Geffen, in mentioning this. *(Public Health*, March, 1955) brings forward a few facts which he obtained in an interview with Dr. Salk. It appears that, in a series of experiments, 10 monkeys were first inoculated and then challenged with intravenous injections of living virus. Eight out of the ten survived, but of ten controls (unvaccinated) only six survived. This might suggest (if one admits the statistical value of such small numbers) that two monkeys out of the ten were protected. If this represents a typical sample of the results obtained by Dr. Salk in monkeys, it seems strange that he should have had the temerity to suggest applying them to human beings.

According to an article in the *Lance:* (April 18, 1953, p. 755). "most of the recent work on poliomyelitis has been done in chimpanzees, which *seem* to react to infection much as man does." I have italicized the word "seem" because, although the infected monkey may suffer from similar symptoms to those observed in human poliomyelitis, and no doubt the inflammation of the central nervous system is equally severe and painful, it is questionable if further comparisons are valid.

As the writer of the article just quoted. Patrick Meenan, M.D., N.U.I., D.C.P.. bacteriologist at St. Vincent's Hospital, Dublin, wrote (p. 757): "The fundamental difficulty is to know how far experimental findings can be applied to natural infection in man. What is the relation between the disease in animals produced by large doses of laboratory-adapted strains and that in man produced by small doses of naturally occurring virus? Is the pathogenesis of poliomyelitis in man the same as in the chimpanzee?"

Leading authorities on the subject of poliomyelitis have answered this question with a direct negative. For instance, Dr. Jean Macnamara was reported in the *British Medical Journal* (August 12, 1933, p. 311) to have "emphasised the danger of applying facts determined in experimental poliomyelitis in monkeys to the natural disease in man. . ." The speaker stressed "the marked clinical differences between the preparalytic stage of poliomyelitis in children and in monkeys." This same authority was reported in the *Lancet* (August 19,

1933. pp. 42 1-2) as saying: "To draw analogies between the pathogenesis of poliomyelitis in man and the experimental disease in monkeys might lead us far astray. We know from other diseases, such as yellow fever, that a virus might behave very differently in different hosts." One important difference that Dr. Geffen mentions *(Public Health* March 1955) is that the rhesus monkey on which so many thousands of experiments have been performed is ordinarily insusceptible to poliomyelitis as a result of oral feeding. Bodian (clinical Excerpts Vol xxix, Summer 1954, p23) goes so far as to state that the findings in experimental poliomyelitis should be disregarded unless virus feeding be the method of infection. This seems to rule out the rhesus monkey for research purposes.

Bearing all this in mind, one can have little difficulty in believing the statement iii a leading article in the *Lancet* (March 16, 1946) that " Information derived from experimental infection of apes with poliomyelitis has sometimes been misleading when applied to human infections."

In an Annotation in the *Lancet* (May 7. 1955, p. 956) dealing with the tragic development of poliomyelitis in children following vaccination and the question of the complete reliability of the tests made to exclude the presence of live virus in the Cutter vaccine, the pertinent question is asked: "Is it wise to apply the results of tests with scores of monkeys to the vaccination of hundreds of thousands of children?"

That is a question which should exercise the minds not only of the scientists concerned with the development of these vaccines but also of every individual faced with the problem of whether to submit his children to prophylactic inoculation:

The answer, as we have seen earlier, is to be found in the statement of Dr. E. R. Krumbiegel, the city health commissioner of Milwaukee, Wisconsin. He was reported in the *Sentinel* (May 24, 1955) as saying in regard to these tests that they "do not rule out the' possibility that small amounts of weakened polio virus, which will not infect monkey tissues, may still be able to multiply in human tissues. ., Monkey tissues are not necessarily comparable to human tissues in this respect. This is exemplified by the fact that the amount of inactivated virus necessary to produce a good polio antibody response in humans is far less than that needed in monkeys, and far less in monkeys than in mice."

Dr. Alfred Byrne, in the course of a masterly article in the *Spectator* (July 22, 1955), in which he had many scathing criticisms to make in regard to the introduction of the Salk vaccine, stated when referring to the tests for safety: "it is known that the monkey test for the virus is so crude as to constitute a source of danger as it will not always. by any means, differentiate between the presence of no live virus and live virus present ill small amounts."

Dr. Byrne, in fact, considered it remarkable that so few cases of paralysis followed the use of the Salk vaccine. "The number of casualties ", he wrote, "might have been multiplied ten- or a hundred-fold. if the British health authorities had been as impulsive as their American counterparts this recent American tragedy could have been reproduced here."

THE COMMERCIAL ELEMENT

THE commercial element in the manufacture of these vaccines is an interesting and, indeed, an astounding one. The *New York Tunes* (October 19, 1954) contained the statement that "In the United States the National Foundation for Infantile Paralysis has contracted to buy enough poliomyelitis vaccine to immunise 9 million children and pregnant women next year the Foundation is taking a calculated risk in purchasing vaccine before it has been found to be effective."

The manufacture of the vaccine was entrusted to five pharmaceutical Houses: Parke, Davis & Co. in Detroit. Pitman-Moore and Eli Lilly & Co. in Indianapolis. Wyeth Inc. in Philadelphia, and the Cutter Laboratories. The purchase of approximately 9 million dollars-worth of the product in advance has, we are told, enabled them "to retain specialised personnel and facilities and thus be prepared to produce promptly a substantial quantity of vaccine to be available through the usual commercial channels."

Later, it appears that a sixth firm was added to the list, for in the *Daily Telegraph* (May 3. 1955) we read:

"The Wall Street Brokerage firm of Carl Loeb, Rhodes & Co., recently reported to its clients that it estimated the six firms licensed to make Salk vaccine in the United States would make a joint profit of about £7 million less taxes from it this year."

Immediately the Salk vaccine disaster was made known the Cutter Laboratories of Berkeley. California, whose vaccine was chiefly implicated, recalled all unused stocks of its vaccine, amounting to 256,000 cc. The estimated loss entailed by the destruction of all this vaccine was one and a quarter million dollars. Under the deluge of unfavourable publicity, Cutter stock slumped from $15.50 to $8.75 per share, *(Time,* June 20, 1955).

Nevertheless, despite all this, a few weeks later the Cutter Laboratories announced they were doing business as usual and that sales were running slightly ahead of last year’s figures—$ 14,850,000. In fact, they had even added a new biological control building to the 37 others at this huge plant. Said Fred. Cutter, one of the Vice-Presidents of the firm: "We are completely confident about the future." Cutter

Laboratories, founded in 1897, is now the second oldest pharmaceutical house in the States, the oldest being Parke, Davis & Co. Early in June the American Pharmaceutical Manufacturers Association, at convention at White Sulphur Springs, publicly showed their confidence in their competitor firm by electing Dr. Robert Cutter (President of Cutter Laboratories) as their President. *(Time,* June 20, 1955).

it is also of interest to note that at a meeting of the American Medical Association at which Dr. Salk expressed his dissatisfaction with the Public Health Service report on his vaccine, he was presented with a cheque for ten thousand dollars by the Omaha Insurance Company in appreciation of his discovery of a polio vaccine. He had already received the Congressional Medal at the hands of the President of the United States immediately after the release of the Francis report.

Another commercial element also comes into the picture in regard to the export of monkeys from India.

To quote the medical correspondent of the *Manchester Guardian* (April 27, 1955): "It is thought that the rhesus monkey population of India is somewhere about half a million, so the export of these animals was a handsome source of income, especially of dollars. The monkey, which fetches about £1 in Delhi, costs more like £7 or £8 by the time it reaches this country. Most of the traders were fair in their dealings, sending here young adolescent animals. But the pickings were too good. The result was that less meticulous dealers bought up reject animals, such as those which were either very old or very young, ill or pregnant, amid packed them off without due care for the packing. There was a very high mortality amongst the animals reaching the United Kingdom."

STOP PRESS! — ANOTHER SALK-TYPE VACCINE

As this second impression of the booklet is in the printer’s hands the public has learnt from the Press and Radio of the large-scale vaccination experiment which the Ministry of Health proposes to promote during the coming year.

It is hoped *(News Chronicle,* January 20, *1956)* by June next to inoculate 500,000 children under nine with a new polio vaccine described by Mr. Robin Turton, the Minister of Health, as "the best in the world ". At the same time he confesses that "it will not guarantee that a vaccinated person will not under any circumstances catch polio." Neither is it known if it will prove effective against the type of virus active in this country, nor if it is effective in children under six, nor how long its protective power is likely to last. *(Lancet,* December 17. 1955, and January 14. 1956).

Although based upon the Salk vaccine, it is claimed to be "not quite the same ", the difference being that the strain of virus from which it is made is not so virulent as that used in the manufacture of the American vaccine. This immediately raises doubts as to whether this does not lessen the antigenic properties claimed for it. What the public expects is a vaccine that protects against the paralytic form of polio; the milder, commonly symptomless form, as our own scientists have pointed out, are not worth bothering about (see p.23 *ante).*

The editor of the *News Chronicle* (January 1, 1956) wisely headed his editorial column "A Case for Caution ", stating: "Parents have the assurance that this vaccine will be as safe as the scientists can make it." No doubt; but is this as safe as the public will demand? It is scarcely reassuring to learn from the Minister of Health that "the British vaccine will have been subject to stringent safety tests and will, I am advised, be as safe as any vaccine can be." One recalls the statement of Dr. Scheele, the American Surgeon General, in June *1955* that "no batch of the vaccine can be proved safe before it is given to children."

There is also the grave statement by the editor of the *Lancet* (June 11, 1955, p. 1207) that although the risk of the vaccine producing paralytic poliomyelitis "may be reduced to something extremely small by the improved tests of the vaccine in tissue-cultures and in monkeys, there will still be a fear that the tests may not reveal the presence of every live virus particle and that the occasional highly susceptible child may be given the disease by a vaccine which has passed the most rigorous tests."

This possibility was again stressed by the editor of the *Medical Officer* (August 3, 1955) when he wrote in regard to the Salk type of vaccine that "there is the perpetual danger that should a breakdown in the process of manufacture occur live virulent vaccine may be administered with disastrous results."

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