

ADULT SERUM IN THE PROPHYLAXIS OF MEASLES

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T H E S I S

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for

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by

ROBERT NEIL WALKER M.B. Ch.B. (1925)

THE ISOLATION HOSPITAL

B R I G H T O N.

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INTRODUCTION.  
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The seriousness of measles in young children, especially in those who are debilitated and subject to unsatisfactory home conditions, has been frequently stressed already by members of our profession; facts and figures bearing on the subject therefore seem unnecessary here. But if our experience in Brighton is to be taken as a true index of the lay attitude towards the disease, the public still underestimate the gravity of measles and must be educated further on the subject.

Attempts to establish the etiology of measles have, so far, not been crowned with success; moreover measles does not occur naturally among the lower animals, and in one species of ape only has the illness been artificially induced. Consequently we have no means at our disposal of producing active immunity in the human subject nor can we readily confer passive immunity by the use of immune substance of animal origin. The efficacy in measles prophylaxis of the serum of individuals convalescent from an attack has been firmly established but the finding of a sufficient number of suitable convalescent donors has proved so difficult that prophylaxis on a large scale has not been possible.

In those infectious diseases where antibody in the blood can be measured by laboratory methods it is found that the

protective substances diminish very rapidly subsequent to attack becoming very small in amount a few months later. By analogy, therefore, we might expect the serum of adults who had suffered from measles many years previously to be so poor in antibody as to be valueless as a substitute for convalescent measles serum. Degkwitz, who first pointed out the possibilities of adult serum, abandoned it on theoretical grounds and since evidence on the value of adult serum still seemed lacking, it was decided to investigate the method as will be described in the following pages. The interest of the enquiry is twofold.....

- (1) It is of scientific interest that antibody in considerable quantity should persist in the blood for many years subsequent to an attack of measles.
- (2) It is of considerable practical importance that adult serum, in dosage not too great to be readily obtainable, should be a suitable substitute for convalescent measles serum.

In conclusion I wish to express my indebtedness to Dr. Duncan Forbes, Medical Officer of Health, Brighton, for his encouragement and for the facilities provided.

REVIEW OF LITERATURE  
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In the following review of the work which has been done on measles prophylaxis by means of adult blood or serum chronological order will be adopted. Many of the articles are extremely short and inconclusive and to such, only brief reference will be made.

1.

ABROAD

The credit of first suggesting the use of adult serum is due to Degkwitz who commented in 1920 on its possibilities although he did not try it till the following year. He was of the opinion that in adult serum there were probably few or no antibodies but that it possessed some character which caused antibody production when in contact with a further supply of virus. In 1921 he used adult serum in an attempt to protect seven children who had been exposed to measles. Three escaped, four being attacked by attenuated measles whose incubation period fell within normal limits. He concluded that adult serum in large doses up to the third day did not delay illness (if it did not prevent) but attenuated it; and that the method was a good one for infants except for the large doses required. Later he appears to have abandoned adult serum on purely theoretical grounds. In the same year Rietschel injected nine children with defibrinated adult blood with encouraging results.

In 1922 Schilling injected ten children with adult serum four of whom escaped, while one developed measles in four weeks and five were attacked by "light measles" in ten to fifteen days. The following year work was done separately by Rietschel, Solomon and Van Torday who reported good results but their articles are unconvincing. In 1924 Goebel used adult serum or blood in twenty two cases and reported "encouraging results" but gave no details and in the same year Gerlach used defibrinated blood in forty five cases, but his article is not detailed enough to be convincing.

In 1925 several articles appeared but only that by Hilsinger will be mentioned. He protected sixty children using 20 c.c. fresh adult blood there being forty unprotected controls. A high proportion of the injected developed measles but on the whole they were less severely attacked than those of the control group who suffered.

In 1927 Karelitz and Levin reported on fourteen cases and while admitting that modified measles might be so mild as to be almost unrecognisable they actually described prodromal rashes in some of the cases. The same year Lopffel reported on eighteen cases while Caronia summarising the results of various workers (including three hundred cases by Debré) stated that adult serum was weaker and not so sure as convalescent. Two years later Bader reported on thirty cases while Baar injected seventy three children with serum

from donors whom he had attempted to activate by injections of fresh measles blood. The following year Hottinger carried out attempts at prophylaxis after the method of Baar but the most interesting paper is that by Morales and Costa Mandry. These workers reported on cases, from six months to fifteen years, which were injected with serum from adults, the dose ranging from 10 to 40 c.c. Every third child was used as a control the cases under observation being visited at two to four day intervals for a period of eight weeks. Of the three hundred and ninety three who were given their adult serum two hundred and twenty seven (57.8 per cent) were not attacked while of the one hundred and eighty three controls only thirty four (18.6 per cent) escaped; they also give figures to show that both in the injected and the controls the escape rate was higher in the higher age groups. In further tables they point out that with smaller doses the proportion of complete protection is much less than with equal doses of convalescent serum; but 20 c.c. or more of adult serum will give results which compare very favourably with those obtained with convalescent serum. They give a clear definition of attenuated measles as something distinct from the natural form of the disease, stating that 41 per cent of the adult group who were attacked suffered from the attenuated type, having an incubation period up to thirty nine days. Unfortunately they say that none of their donors had measles less than one year previously or more



than ten so that one wonders how far the serum they used was strictly "adult serum": Adult donors recovered from measles one year only would be as hard to find in this country as convalescent donors.

In 1931 a number of articles appeared on the subject and a majority of the writers seem to be of the impression that adult blood or serum is of value in the prophylaxis of measles although the series of cases dealt with is small as a rule. Blauner and Goldstein however concluded from their series that there was no appreciable difference between measles incidence in the injected and the controls but the article is a very confused one. To my mind the best article is that by Bader. He had injected thirty cases in 1929 and obtained results which made him suspect the method was worth while. At the later date he injected eighty children aged seven to twelve months with whole blood the dose varying from 20 to 30 c.c.; the injections were given within the first seven days following exposure. Of the eighty, forty one escaped completely, thirty one had attenuated measles which is fairly well defined by him, while eight were attacked by ordinary measles with Koplik's Spots.

In conclusion he expresses his belief in the measure stating that the ideal dosage is probably a variable but suggesting 30 c.c. as an arbitrary dose. He unfortunately says his donors suffered from measles two to thirty years

before so that the same objection applies to his adult serum as to that of Morales and Mandry; moreover like many other workers he does not mention whether the date of injection is reckoned from the time of appearance of the rash or whether it is counted from the day of onset of catarrhal symptoms. Writing in 1932, Elterich discusses at some length the prophylaxis of measles by convalescent and adult serum but deals only with generalities and brings forward no proof of the efficacy of the latter. Early in 1933 Lewis and Barenberg, working in the New York Home for Hebrew Infants, injected 30 c.c. of parental blood into fiftysix infants who were exposed to continuous infection in an epidemic and reported that thirteen escaped entirely while the remainder suffered from measles of varying degree of severity: Twenty three controls were all attacked.

In the above summary an attempt has been made to show that, for a considerable number of years, work has been done in other countries on the prophylaxis of measles by adult blood or serum without the accumulation of any certain evidence of the value of the method. There are several defects in the articles the most outstanding of which are. ....

- (1) Conclusions drawn from insufficient data with much speculation as to whether the effect (unproved) of adult serum is specific or not.
- (2) Lack of clear definition of attenuated measles; there is much difference of opinion as to its incubation period.
- (3) Inexactness in stating how the date of injection is reckoned.
- (4) Talk of "sucklings" being injected without any information as to whether they are over the age of six months.

- (5) Use of serum from donors who are comparatively recently recovered from an attack of measles.

2.

THIS COUNTRY

The earliest record I have found of work on adult serum in this country is that by Burn of Birmingham. In 1931 the Health Department of that city took up the prophylaxis of measles using serum prepared from the blood of volunteer members of the health staff (clerks, health visitors etc.) On an average 300 c.c. were collected from each donor at one session, the blood being sent to the City Bacteriological Laboratory for separation and testing. By July 1932 Burn had injected some 300 children and claimed that the method was successful in 98 per cent of the cases. At that time 10 c.c. was his maximum dose and he appeared to be able to choose between abortion and attenuation of attack by fine adjustment of dosage.

PREPARATION AND SUPPLY OF SERUM  
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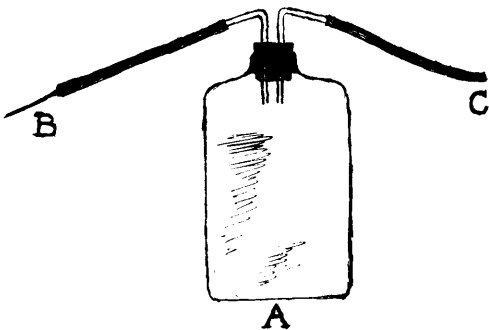
At the commencement of the campaign, a number of cases were given parental whole blood and, though the number was too small for conclusions to be drawn, the general impression was in favour of continuing attempts at prophylaxis by this method. Certain German workers have expressed the opinion that the withdrawal of blood from a parent, followed by immediate intramuscular injection into the child to be protected is a method which finds favour with the public. This was certainly not our experience in Brighton; the sight of blood is unpleasant to a considerable proportion of the laity and many parents seemed to regard the proceeding as unnatural and objectionable. It was therefore decided to continue prophylaxis using serum prepared from the blood of healthy adults who gave a clear history of an attack of measles many years previously.

Donors selected were six members of the medical and nursing staffs of the Isolation Hospital; they were very willingly volunteered to give blood and I feel much indebted to them. The hospital does not admit measles as a routine, only dealing with cases where there are special circumstances calling for admission and it may be taken that the donors, in the course of daily duty, were not more in contact with the disease than members of the public during the course of a measles epidemic.

Some details of the donors may be of interest. Their

ages ranged from twenty to twenty nine years, the average being 24.3. The shortest period between attack and giving of blood was twelve years while the longest was twenty two; this gives an average of 17.15 years. It was considered an advantage that the donors were members of the staff, both from the point of view of observing their general health and of easy access when venesection was required.

The methods of blood collection were extremely simple and satisfactory, requiring little or no special apparatus and giving rise to minimal discomfort in the donors; the technique employed will now be described briefly. Sterile glass bottles were used as illustrated below, and the volunteer was in a comfortable semi-recumbent position.



- A. Sterile Bottle, pint size. No citrate used. Stopper bears two bent glass tubes.
- B. Needle (14.B.W.G) connected to Bottle by stout rubber tubing
- C. Rubber connection to Potain aspirator.

The veins of the ante-cubital space were rendered prominent by the usual methods of muscular exercise of the limb after which a sphygmomanometer armlet was applied to the upper arm at a pressure of 80 to 100 m.m. Hg. A few drops of 2% novocain having been injected subcutaneously over the vessel to be punctured, the aspirator bottle was partially exhausted

and the needle then inserted into the vein. As a rule, blood flow was thus easily induced being maintained by continuous gentle use of the aspirator but in a few cases, where bleeding was not so satisfactory, hyperextension at the elbow was found useful in accelerating the stream. At one session some 300 c.c of blood was collected from each of the six donors and in all there were three such sessions,

Preparation of the serum as finally employed is a matter of considerable difficulty and responsibility and we were fortunate in having it done by Dr. R.A.O'Brien at The Wellcome Laboratories, Beckenham, Kent. The six blood bottles were dispatched immediately after collection to the laboratory from which supplies of serum in suitable ampoules were obtained as required. We were very grateful to Dr.O'Brien for his invaluable assistance.

The serum, which was prepared as described, will be referred to as "Adult Serum" throughout the rest of this work. At no time was serum employed more than two months old.

It was supplied by a fixed group of donors each contributing equally. We think it may be taken as a fair representative sample of adult measles serum in general and its quality was kept as constant as possible.

In the literature there are numerous references to the need for organised effort to make available a supply of serum for measles prophylaxis. The arrangements for serum supply which have been outlined could easily have been made to serve a demand many times greater than that made upon it. The bias of public opinion, not difficulty in finding serum,

12.

was the reason for the comparatively small number injected.

METHODS OF CAMPAIGN  
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Prophylactic injections of adult serum were given to young inmates of other institutions and also to children living at home. The parents of the latter were given the option of having the injections done in their own houses or bringing children for protection to the Isolation Hospital. A few were sent by practitioners but the majority of cases were referred from the Health Office. The home of each school child suffering from measles was visited from the Health Office and prophylactic injections offered to contacts of suitable age who had no history of having suffered from measles. A majority of the institution cases were healthy children living in Public Assistance Hospitals where results could be carefully watched.

In view of the well known fact that infants under six months hardly ever contract measles if the mother has suffered from the disease, there are no cases under six months in the series. Some of the cases are past the age at which the serious complications of measles are likely to arise but their inclusion was considered advisable since refusal to inject would have influenced the parents of others against having their children protected. The dose of Adult serum employed was a uniform intramuscular



one of 10 c.c. administered as soon as possible after the appearance of the rash of the primary case.

It is highly desirable in carrying out an investigation of the value of a method of treatment or prevention in medicine to have a series of controls: this has been done in some of the cases as will be seen in the section on selected groups but in the home cases there were no controls. At the outset one realised clearly that parents objected to anything in the way of experiment on their children, so that they would have been very unfavourably impressed by the use of control methods. In any case the attack rate of measles among the susceptible when an epidemic exists is sufficiently high to render the need for controls much less than in many other types of investigation.

Since no reliable test for susceptibility to measles exists, one had to rely solely on past medical history; in some of the children who had lived in an institution since birth, history was considered very reliable.

Subsequent to injection the children were kept under careful observation for a period of three and a half weeks; in institutions temperature charts and other hospital records were kept while home cases were visited every few days during the observation period.

GENERAL RESULTS.  
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Here results as a whole will be discussed, selected groups being considered later. Table "A" gives the total number while home cases are set out in Table "B"

TABLE "A"

TOTAL 138	NO ATTACK	MODIFIED ATTACK	UNMODIFIED ATTACK
Institution cases 81	74	5	2
Home cases 57	29	19	9

TABLE "B"

AGE	Days between rash of primary case and giving of serum to contact	Days between giving of serum and development of rash	Classifica- tion
1 yr.	4		NO ATTACK
1 yr.	3		
13 mth	5		
14 "	4		
18 "	5		
18 "	5		
23 "	3		
2 yrs	3		
2 "	3		
2 "	2		
2 "	1		
2 1/2 "	5		
2 1/2 "	5		
2 1/2 "	5		
2 1/2 "	5		
2 1/2 "	5		
2 1/2 "	5		
3 "	3		
3 "	3		
3 "	3		
3 "	6		

TABLE "B" continued

AGE	Days between rash of primary case and giving of serum to contact	Days between giving of serum and development of rash	Classification
3 yrs	2		NO ATTACK
3 " "	2		
3½ " "	2		
4 " "	3		
5 " "	3		
5 " "	1		
7 " "	3		
7 mths	4	8	MODIFIED ATTACK
10 " "	4	10	
1 yr	2	10	
1 yr	3	6	
1 yr	2	10	
18 mths	1	8	
18 " "	1	7	
2 yrs	2	14	
2½ " "	4	8	
2½ " "	4	8	
34 mts	3	9	
3 yrs	4	9	
4½ " "	3	10	
4½ " "	4	7	
5 " "	1	12	
8 " "	1	12	
8 " "	1	10	
8 " "	6	9	
10 " "	6	9	
1½ " "	4	4	UNMODIFIED ATTACK
2½ " "	5	4	
2½ " "	7	6	
2½ " "	8	3	
3 " "	4	4	
3 " "	6	2	
3 " "	6	3	
4 " "	6	5	
4½ " "	4	3	

It will be seen from the above tables that in one hundred and thirty eight injected children there were only thirty five

cases of measles three and a half weeks after the date of injection. Considering the high infectivity of measles during an epidemic in children who have not been previously attacked, the facts are suggestive that adult serum is of value in preventing measles but no conclusion is drawn from figures which are too small for statistical proof. However, among the one hundred and thirty eight were twenty four cases of modified measles which seems clear proof of the efficacy of the serum. It will be well to describe modified measles as it occurred in Brighton; many of the workers abroad make no effort to define modified illness, talking vaguely of "light measles" and since natural measles is met with in all degrees of "lightness" their results are not satisfying.

Twenty three of the modified cases were very similar and ran a course as follows. The illness was extremely slight in all, there being little or no constitutional upset. There were no catarrhal symptoms and Koplik's Spots were not observed. Discrete papules appeared on the face and trunk and occasionally on the limbs. These were often very sparse and lighter in colour than the rash of natural measles; they faded in one to three days. In some cases there was little temperature disturbance while <sup>in</sup> others there was a sharp elevation, but in all normal temperature was attained by the end of the third day. This form is referred to later as the "usual type"; there was one case different from the others

which is described in detail later.

As pointed out earlier, Burn is of opinion that it is frequently possible to choose between prevention and attenuation of attack but our impression is that such choice is not an easy matter.

SELECTED GROUPS OF CASES  
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In the previous section an account has been given of the results obtained in the whole series of injected cases: Here it is proposed to give details of selected groups considered to be of special interest. All the injections were given in institutions where results could be carefully watched and a "closed community" could be maintained.

(1) A severe case of measles occurred in one of the wards of the Brighton Hospital for Sick Children. The rash which was dusky appeared on 9.1.33, and on the same day, eight contacts who had no past history of measles were given 10 c.c adult serum. They were all under five except one child who was seven years of age. No case of measles developed in the ward which was released from quarantine at the end of three and a half weeks.

(2) This group of cases was collected in the Children's Homes of the Brighton Public Assistance Committee. On 18.3.33 two cases of measles occurred, infected from a common source. These children had been in contact with all the others in the institution including twelve children who were convalescent from various minor ailments and in the infirmary attached to the homes. Two days after the appearance of the rash of the primary cases, the twelve infirmary children who had not suffered from measles were given 10 c.c adult serum; their ages ranged from three to

fourteen years. The results were as follows: On 30.3.33 a boy of nine developed an attack of modified measles; on 31.3.33 a girl aged fourteen developed a similar attack, while on 31.4.33 a boy of fourteen also suffered from measles in modified form. None of the others suffered at any time during the epidemic in the homes, although they were exposed to measles throughout.

The eighteen institution children under five years of age are housed in a block apart from the "general population" and it was hoped to keep them free from measles by isolation methods only, but on 30.3.33 a maid who looked after them developed measles. On the same day as her rash appeared the eighteen children, amongst whom there was no past history of measles, were given 10 c.c. serum; None developed measles subsequently.

In addition they were kept isolated, from the day of injection.

As already stated the epidemic commenced on 18.3.33 and altogether fifty eight cases of measles occurred in the unprotected, the date of the last case being 17.4.33. Therefore three modified cases occurred in a protected group of thirty as compared with fifty eight in the uninjected population numbering two hundred. It is possible that the nine infirmary cases who were injected and exposed throughout, enjoyed immunity as a result of the effects of repeated doses of infection combined with temporary protection

conferred by the serum.

(3) the Third and last group to be described is of particular interest. It was collected at the Children's Homes of Southlands Public Assistance Hospital, situated some six miles from Brighton. On 19.4.33 a case of measles occurred in one section of the homes, and on the same day thirty contacts were given 10 c.c adult serum. Their ages ranged from four to seven years, the majority being five. The hospital matron, who had known the children since birth was confident that none had ever suffered from measles.

The results were as follows: On 4.5.33 there were two cases of modified measles. One was of the "usual type" (see page 17.) the other being the only <sup>one</sup> of its kind observed by the author. It had the following features. A rash in character typical of unmodified measles appeared on the face which looked slightly swollen, while the trunk and limbs were sparsely beset with the papules described in the "usual type". There were no Koplik's and no catarrhal symptoms and, though the temperature reached 102<sup>0</sup>F., the child did not appear ill. By the following day the temperature had subsided, the rash had faded and the patient was convalescent if one can use such a term in so mild an illness.

There were no further cases of measles till 16.5.33 when three cases of the unmodified form occurred. Subsequently there were ten cases of unmodified measles, occurring at the ordinary intervals the date of the last being 5.6.33.



To summarise therefore, thirteen unmodified cases occurred in individuals, some of whom had been temporarily protected by serum, the unmodified cases of 16.5.33 having been infected from the modified cases. The following points are of special interest:--

- (A) Modified measles can be infectious in the absence of catarrhal phenomena in spite of the traditional view that measles infection is largely disseminated by the expulsion of infected droplets
- (B) Apparently 10 c.c. of adult serum given on the first day can not be trusted to confer passive immunity longer than two weeks (approx).
- (C) Dosage of infection would seem to play a part in determining whether an injected case develops modified measles or escapes completely, because the cases of 16.5.33 were the same age and weight as the modified cases. This view has been advanced in an earlier part of the thesis.

SKIN TESTS IN MEASLES  
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In Scarlet Fever it is possible to produce blanching of the rash in suitable cases by intracutaneous injection of immune serum, but in the case of measles no such reaction is known. However, it is established that subcutaneous injection of convalescent measles serum during the invasion period will prevent the appearance of the measles rash round the site of injection; the phenomenon bears the name of Debré, and is specific in nature.

During the work on measles prophylaxis in Brighton it was decided to carry out skin tests on the lines of the Debré, using adult instead of convalescent serum. Only three patients were admitted to hospital at a suitable stage and the following is an account of those cases with the results of the tests carried out.

(1) J.R. aged seven was suspected of being in the catarrhal stage of measles on 4.4.33; on 5.4.33 Koplik's Spots had appeared and the child was admitted to the Isolation hospital. Shortly after admission the following injections of adult serum were given subcutaneously.

- (a) 2.5 c.c on the dorsal aspect of each wrist.
- (b) 5 c.c. into the right flank, an equal volume of Diphtheria Antitoxin being injected into the left flank, to act as a control.

The measles rash appeared on 8.4.33 and was of moderate intensity. All the injected areas were spared with the exception of the left flank; on the wrists the spared areas

were approximately one and a half inches in diameter whereas that in the right flank was three inches. On 9.4.33 the rash had faded slightly but the contrast remained quite distinct till 10.4.33

(2) D.W. aged three was admitted on 9.4.33 from the Children's Hospital: 10 c.c. of adult serum had been injected subcutaneously on the outer side of the right thigh on 5.4.33 in an attempt to prevent an attack. On admission the child was moderately ill and had a well marked measles rash which had appeared the same morning. On the outer side of the right thigh, a short distance below the great trochanter, there was an area two and a half inches in diameter completely spared by the rash. The contrast was still well-marked on 11.4.33 although the rash had faded considerably.

(3) A.M. aged eight months was admitted to a measles ward on 11.4.33. She had a generalised rash, somewhat morbilliform in appearance, but other signs were so indefinite that the diagnosis of measles was in considerable doubt. On 13.4.33, 10 c.c adult serum was given into the outer side of each thigh; Koplik's Spots were observed on 14.4.33. On 16.4.33 a well-marked measles rash made its appearance, the injected areas remaining clear, to an extent of three inches in diameter.

In a careful search of the literature, I have been unable to find any reference to skin tests having previously been

carried out with adult serum. The results of the above tests afford proof that the serum used contained measles antibody. This is not an argument based on the results of three cases, but an extension of the already accepted Debré Phenomenon.

COMMENTS AND CONCLUSIONS.  
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As a result of the work which has been outlined we are of opinion that adult serum contains sufficient antibody to be of definite value in the prophylaxis of measles. The reasons for such conclusion may be summarised as follows:--

- (1) In one hundred and thirty eight injected children there were twenty four cases of modified measles i.e. of measles which differed sharply from the mildest natural form. (Incubation period not notably increased)
- (2) In the Southlands group of cases we have complete evidence of a number of children having been protected by serum, developing an attack of natural measles when passive immunity had worn off.
- (3) The results of the skin tests afford evidence that the effects of adult serum injections are due to specific antibody.

Apparently 10 c.c of adult serum even when given very early in the period of exposure (reckoned from the day of appearance of rash of primary case) is not quite sufficient to protect young children completely and a greater dose should be employed where the aim is abortion of attack as in hospital wards.

Our impression that the choice between abortion of attack on the one hand and attenuation on the other is not a simple matter to be decided solely by such factors as age, date of injection and amount and nature of serum given, is in harmony with the work of Stocks on latent epidemisation. In assessing results it must be borne in mind that home cases are exposed to infection in many quarters during an epidemic,

which means one can not be so certain of the day of incubation as is possible in institution cases; this would seem part of the reason, at least, for discrepancy between home and institution results.

Since the passive protection conferred by serum is probably always short it is a very difficult matter to assess the value of injecting on a large scale children living at home during an epidemic because they are liable to contract measles a week or two after injection. Passive protection will always be of great value for the individual home case where there are special reasons calling for temporary protection; and for the protection of hospital wards. The success, therefore, which has attended the use of convalescent serum and which would probably also attend the employment of adult serum has not abolished the need for some means of actively immunising children to measles.

## APPENDIX ON THE ANALYSIS OF STOCKS.

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As a result of investigation of the very complete measles records of the Metropolitan Borough of St. Pancras for the period 1924-28, Stocks noted that in a city population epidemics come to an end long before attack by measles of all the children who have not previously suffered. He also found that neither the recurrence of the epidemic nor its highest point bore any constant relationship to the number of children not previously attacked.

Proceeding to compare the behaviour in an epidemic of children who had been recently exposed to a case of measles in their family with the behaviour of children in whose family there had been no such case, he found a marked difference in the mode of reaction. This difference could be explained by the operation of a process of "latent epidemisation" i.e. the effects of sub-infective doses; for this explanation he offered statistical proof. He wrote:--

"after an interval of about eleven months the attack rate in children still at risk who had been exposed to a case of measles in the same house was about one fifth of that expected . . . . a ratio intermediate between those found after intervals of three and eighteen months . . . . . The only explanation which seems possible for these results is that the majority of children intimately exposed to infection who escape contracting measles at the time become immunized, and that such latent immunity gradually disappears"

This means that the susceptibility to measles of those who

have not yet been finally protected by an attack, is subject to variation during the epidemic itself and during the inter-epidemic period. Such variation would seem to have an important bearing on the practical problems of measles prophylaxis, especially as no means has been devised for the production of an artificial active immunity to the disease. For these reasons it was considered desirable to add this appendix.



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