STUDIES

IN THE

PROPHYLAXIS OF MEASLES.

by

Thomas M. Hunter, M.B.,Ch.B., D.P.H.
Senior Assistant Physician,
City of Glasgow Hospital,
Knightswood.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

" Considering how destructive this disease is in some seasons ; considering how many die even with the mildest constitutional form ; considering how it hurst the lungs and eyes , I thought I should do no small service to mankind if I could render this disease more mild and safe in the same way that the Turks have taught us to mitigate smallpox. I suspected strongly that the cough , often so harassing , even of the mildest kind , was produced by receiving the infection mostly by the lungs and I hoped that the symptom would abate considerably if I could find a method of communicating the infection by the skin alone. "

Francis Home .

Medical Facts and Experiments.
Edinburgh.
1759.

P R E F A C E.

To one who is interested in the preventive aspect of medicine there is no more fascinating study than the investigation of new methods to attain an end as desirable as the prophylaxis of a deadly disease. Measles is one such disease the study of which is baffling but which nevertheless is yielding some first-fruits in tangible results. Every investigator is confronted with difficulties from time to time and it is in these moments that a friendly encouragement is appreciated out of proportion to the thoughts of the donor. It has been my good fortune to have this encouragement in full measure and I wish to record my appreciation of it. Dr.William Dow, the enthusiastic Physician Superintendent of Knightswood Fever Hospital, afforded me the facilities of the Hospital and the time required to investigate the cases; and Dr.A.S.M.Macgregor, the Medical Officer of the City of Glasgow, who was very interested in the work, placed at my disposal the suitable means for covering the amount of ground that is included in these investigations. I wish also to record my appreciation of the courtesy and attention which the nursing staffs of the many institutions have given without which the difficulty of compiling such a work would have been multiplied many times, if not put beyond the bounds of possibility. Sister Thompson, who was in charge of the measles ward which furnished the donors of the raw material, must come in for special mention - the time and the trouble taken in such preparations as were necessary at very awkward times being given cheerfully and ungrudgingly.

I N D E X.

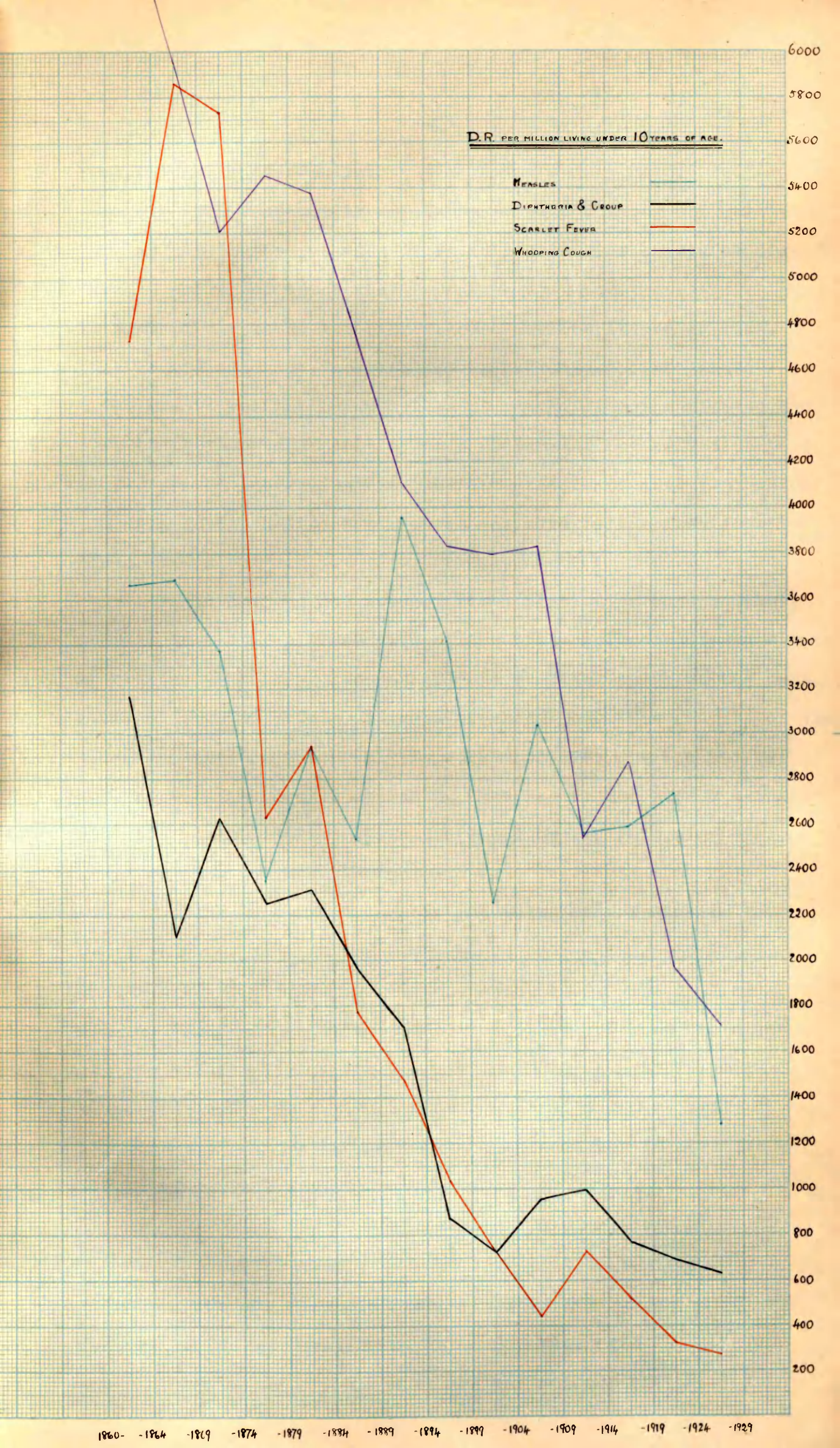
THE SUBJECT.

THE SUBJECT.

Thirty or forty years ago measles was a disease the mention of which provoked amusement whereas scarlet fever was regarded by all with the greatest anxiety. For some hitherto unexplained reason scarlet fever has been steadily losing its virulence but to-day measles has retained the position it held then and thus becomes the more serious menace to young life.

A glance at the graph shown here on the following page shows very clearly the variation in the Death Rates per million under ten years of the four different diseases as recorded in the Health Reports of the Medical Officer of the City of Glasgow since the year 1860. From this chart an idea can be gained as to the enormous decrease in mortality in the three diseases - whooping cough, scarlet fever, and diphtheria and croup. The fall in the figures for scarlet fever has been most dramatic - from 5860 in the period 1865-1869 to 270 in 1925-1929. Diphtheria and croup figures have fallen from 3165 to 623 in the same period, and whooping cough from 6480 to 1715 and those for measles from 3663 to 1280. It should be noted that this last figure is by far the lowest ever recorded for any five year period and is less than half the one immediately before. A fall almost as great occurred in the period 1900-1904 to be followed by a rise to the usual level and the same might occur again.

Though as will be demonstrated later there is no natural immunity to measles at any age - the numbers shown as death rates per million under ten years represent a fair index of the course of the disease. Despite the fact that the children of to-day are looked after more carefully than those in previous generations, there has been no continuous fall in the figures showing that up to the present the Public Health policy against measles has been


D.R. PER MILLION LIVING UNDER 10 YEARS OF AGE.
MEASLES
DIPHTHERIA & CROUP
SCARLET FEVER
WHOOPING COUGH
6000
5800
5600
5400
5200
5000
4800
4600
4400
4200
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
1860- -1864 -1869 -1874 -1879 -1884 -1889 -1894 -1899 -1904 -1909 -1914 -1919 -1924 -1929

almost totally ineffective.

The tendency is still too prevalent among not merely the lay public that measles is to be regarded as a trivial disease of childhood which must be encountered sometimes and which is most likely to be got over without serious injury or risk. This general lack of interest may be ascribed to two causes - to a failure to realise how many deaths result from the disease and also to the knowledge that efforts to prevent its epidemics have so far proved unavailing - a fatalistic state of mind into which too many Public Health Administrations have fallen from time to time.

No one who has studied Vital Statistics can be likely to take such a complacent view of the risks attaching to an attack of measles which ranks second only to whooping cough as the most fatal of the infectious diseases of childhood. The gravity of the disease cannot be too firmly impressed on everyone who has the interests of the people at heart. Measles is not merely a regional but a world problem, as is indicated by the following figures compiled from various sources.

The graph shown on the preceding page indicates the death rate per million under ten years of the four main diseases in the area of the City of Glasgow since 1860. The following figures for England during the period 1921-1928 show the mortality per million living (not merely under ten years) for three of these diseases. They also indicate generally the relative importance of measles and whooping cough and the comparative safety of scarlet fever.

Measles	-	422 per million living.
Scarlet Fever	-	77 per million living.
Whooping Cough	-	437 per million living.

Other figures are also instructive. Thus over a period of fifteen years the death rates in London have been

Measles	-	251 per million living.
Scarlet Fever	-	42 per million living.

while in the London Hospitals the case death rates have been

Measles - 10.6 per cent.
Scarlet Fever - 1.5 per cent.

It should be noted that during the last four years measles has caused eight times as many deaths as Scarlet Fever and one and a half times as many as Diphtheria.

Brownlee states that the average death rate in a series of 18,000 hospital cases was 9.1 per cent. while Rolleston in a similar series of 4314 cases had 414 deaths equivalent to a mortality of 9.6 per cent.

Measles has always been a universal disease which seemed to the casual observer merely a trivial illness which could not be prevented. The degree of susceptibility of human beings is shown by the fact that 96-98 out of every 100 children who have not had the disease, and who are intimately exposed to it, will promptly contract it. This leads to an almost universal history of a past attack in all in urban areas, Ker stating that out of a series of 14,000 people, 97.3 per cent. of those over 15 years had had it.

It has been well said that "Measles attacks without distinction but slays with discrimination". From all over the world where attention has been focussed on the problem, statistics can be gathered to show that the latter part of this description is very true.

SCOTLAND. In the years 1913-1922 the deaths from measles were 14,290 - a number which was more than eight times the number of deaths in the whole population from smallpox, typhus and typhoid fever combined during the same period. Of this number 13,292 were under five years of age, the disease being particularly fatal in the second half of the first year when deaths were more than one-fifth of the total.

The case mortality figures for 1925-1926 are interesting.

Glasgow	(first	year	of	life)	66	times	that	of	5-15	years.
Aberdeen	"	"	"	"	25	"	"	"	"	"
Renfrewshire	"	"	"	"	21	"	"	"	"	"
Birmingham	"	"	"	"	24	"	"	"	"	"

ENGLAND. Out of 1357 deaths in the period of six months ending May, 1931.

280	were under	one year	- 20.6%
575	" "	two years	- 42.4%
1249	" "	five "	- 92.0%

DENMARK. The period 1922-1927 gives the following figures:-

First month of life	6	deaths)	
2-3 " " "	26	")	First year - 398 deaths.
4-12 " " "	366	")	
Second year " "	292	"	
Third " " "	105	"	
Fourth " " "	41	"	
5-10 " " "	6	" (average)	

First year	5513 cases	398 deaths	- Mortality	7.2%
1-5 years	57579 "	479 "	- "	.83%
5-15 "	73157 "	107 "	- "	.15%

FRANCE. Herrman considers measles responsible for
2.4 per cent. of all deaths under ten years, and
6 " " " " " from one to three years.

Both in France and in England and Wales 90% of deaths from measles occur in group 0-4 years, the bulk of fatalities within the first year taking place in the period 9-12 months.

UNITED STATES. Metropolitan Life Statistics show a measles death rate of:-

84	per 100,000	in age	group	1-4	years.	
10	" "	"	"	5-9	"	
1	" "	"	"	10	"	upwards.

Forbes and Green in 1927 say that

More than 90% of deaths from measles occur under five years

and 75% " " " " " " two " .

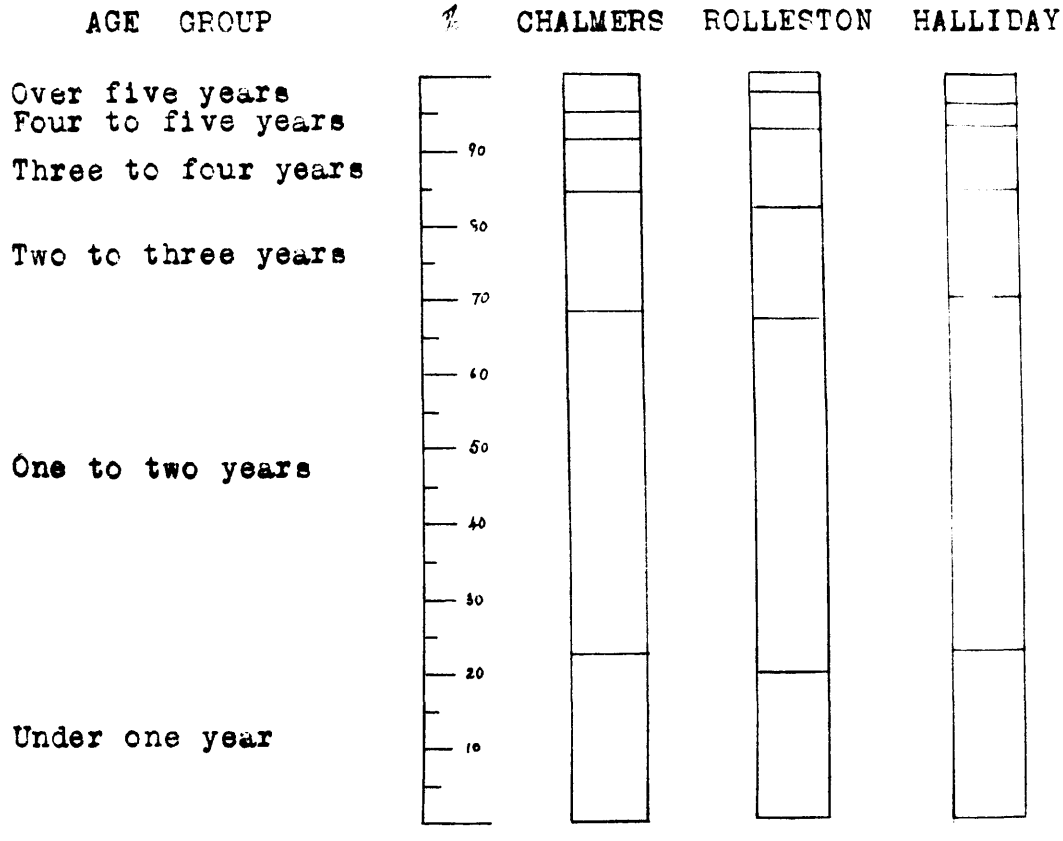
Summarising these figures and dividing them into the various age groups we can compile the following table:-

Age Group.	1913-1922. Scotland.	1931. England.	1922-1927. Denmark.	1927. United States.
½-1	20	20.63	40.4	)
1-2	)	21.74	)	) 75
2-3	)	)	)	)
3-4	)	)	)	)
4-5	) 73.01	) 49.67	) 48.7	) 15
5-6				
6-7				
7-8 up.				
Under 5	93.01	92.04	89.1	90
Over 5	6.99	7.96	10.9	10

Interesting as the above figures are, even of most interest are those of three individual epidemic years as recorded in 1908 by Dr.Chalmers of Glasgow, in 1912 by Dr.Rolleston of London, and in 1926 by Dr.Halliday of Glasgow.

Age Group.	Chalmers 1908.	Rolleston 1912.	Halliday 1926.
½-1	22.96	19.8	22.71
1-2	45.65	47.3	47.31
2-3	15.96	14.9	14.82
3-4	6.9	10.4	7.89
4-5	3.59	5.3	3.15
5-6	)	)	2.52
6-7	)	)	.63
7-8	)	)	.32
5-10	)	1.9	)
10-up	) 5.02	.3	) .63
Under 2	68.61	67.1	70.02
" 5	95.06	97.7	95.88
Over 5	5.02	2.2	4.1

The figures from all these seven sources indicate that the deaths from measles in the first five years of life form well over 90% of the total. The last three show a remarkable parallelism illustrated in the following diagram which indicates clearly the well marked constancy of the fatality proportions to the age group of the patient.



These figures are quite sufficient to show that the disease is one affecting mostly the first five years of life and that after the first year the mortality incidence varies inversely with the age of the patient. There seems to be no doubt whatever that the newborn infant in the great majority of cases has an inherited immunity from the mother butthat this passes off after a few months leaving the infant in a particularly susceptible state in the latter half of the first year. From the first year onwards there is first a gradual and then a rapid decrease in the mortality incidence until later in life the risks from an attack are almost negligible. This statement of course is applicable to the great majority of the people in the world though, as we will see, in scattered communities there is a lack of protection at all ages.

There are many stumbling blocks on the pathway of the study of the causation of measles and it continues to be one of the ever present communicable diseases that seem to baffle the efforts of preventive medicine. The period of infectivity is extremely limited but owing to the mode of onset numerous exposures may occur before the correct diagnosis of the patient's catarrhal symptoms has been established. With the exception of smallpox, measles is the most infectious of the fevers and, in contrast to smallpox, no protection such as that afforded by vaccination has hitherto been found. The infection is present in a very intense degree at the first onset of the catarrhal symptoms and as these precede the appearance of the characteristic rash by at least three days, this period passes in most before the true cause is recognised. Coughing in the catarrhal stage is the main way in which the infection is spread. Brownlee says truly that only one means of protection exists for any but those gifted with a special immunity and that is a previous attack.

In any country in which measles is more or less constantly present its occurrence in an adult is as rare as its

occurrence in childhood is common. The outbreak in the Faroe Islands, which was recorded by Panum of Copenhagen, showed that adults may be just as susceptible to the infection as are children. It was conveyed there from Copenhagen in 1846 after an interval of sixty-five years by a cabinet-maker who landed at Thorshavn the chief port incubating the disease. Two of his friends took it and these started the epidemic in which out of 7782 inhabitants no fewer than 6000 came down with the infection. Age was no bar and few escaped who were exposed to it - though it was noted that many over sixty-five years of age had an apparent immunity.

Again in 1874 the Fiji Islands had an epidemic when one of the native chiefs brought the disease with him from Sydney - his son and one of his retinue landing in the very infective stage. It is said to have carried off one third of the population in 1874-1875 and in an epidemic some years later thousands more died. At present, however, it occurs without any virulent symptoms and in general it is considered by those responsible for the health of the Pacific Islands that measles need no longer be feared.

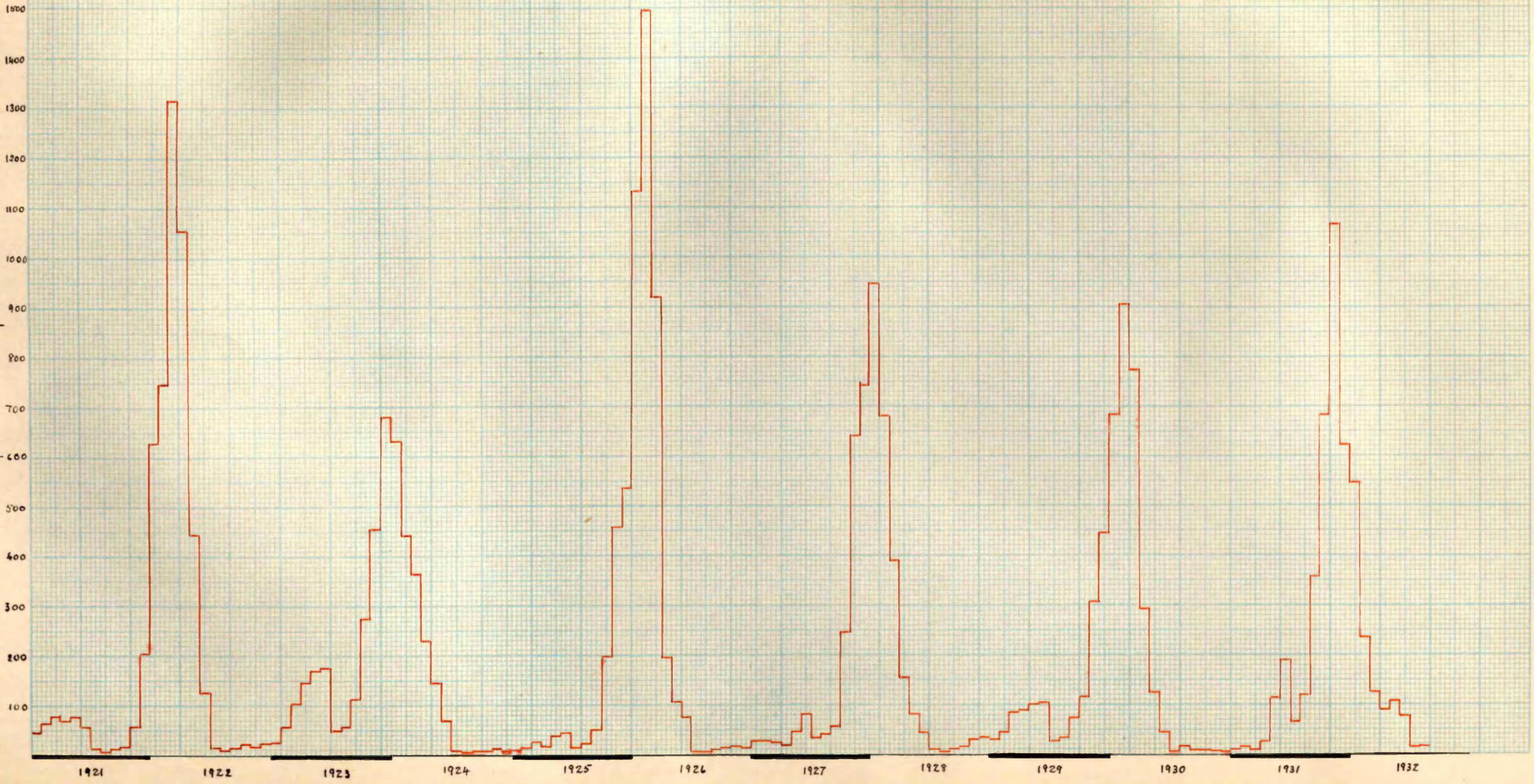
The natives of St.Kilda, who never suffered from illness while they resided on the Island, became the ready prey of measles in the comfort of their mainland settlement. Within a year of their removal from St.Kilda every member of the little colony that settled at Tulliallan, Kincardine, suffered - not even the patriarch of seventy four escaping. While they all lived on St.Kilda - indeed it is said in the whole history of the island - there was not a single case of measles, scarlet fever or whooping cough but in April, 1932, the whole colony suffered at the same time from severe attacks of measles.

Because of the extreme virulence of the infective agent and on account of the high mortality and devitalising

complications that are often entailed in a measles epidemic, some reliable prophylactic has long been sought. During a few weeks of an epidemic more babies may be lost than could be saved in a year by a baby clinic. In the present day immunological epoch in the history of medicine, it is matter for regret that one of the commonest infections, and one which contributes in a substantial degree to the mortality of the country, should to such an extent have baffled inquiry as to be accepted meantime by many Public Health Administrators as an inevitable evil.

Though the outlook for some mastery over its perennial incidence seems to be growing somewhat brighter, Measles meantime remains regulating itself by its own laws and determining the period of its recurrent outbursts by the number of immunes it itself has created. The immunity believed to be produced by sub-infective doses is short-lived - that which follows a survived attack is usually, if not always, lifelong. Each successive epidemic then adds an appreciable quota to the total number of immunes in the population and protects our country from such widespread epidemics as fell on the Faroes in 1846 and on Fiji in 1874.

Incidence of Measles in Glasgow. Numbers indicate Weekly Average in Monthly Periods.



A SHORT HISTORICAL ACCOUNT OF INVESTIGATIONS INTO THE AETIOLOGY AND SPECIFIC TREATMENT OF MEASLES.

A SHORT HISTORICAL ACCOUNT OF INVESTIGATIONS INTO THE AETIOLOGY AND SPECIFIC TREATMENT OF MEASLES.

The prevention of measles seems still an unsolved problem since strict quarantine is frustrated by the infectivity of the disease in the prodromal period. The prevention by prophylactic inoculation is a possibility but it must be preceded by isolation of the virus or a satisfactory method of obtaining it in a pure form whether or not it is definitely identified microscopically or culturally. It is interesting and instructive to trace how work in this direction has been carried out in the past and to estimate the state of our knowledge as to the aetiology of measles at the present time.

There seems to be no doubt but that the first scientific investigation into measles was performed in Scotland almost two hundred years ago. Francis Home of Edinburgh describes an attempt to actively immunise against measles by preventive inoculation, recording his work in this field in "Medical Facts and Experiments" in the year 1759. Stirred by Jenner's work on Smallpox and following a suggestion that had been made by Alexander Monro in the previous year he wrote as follows:-

> "Considering how destructive this disease is in some seasons; considering how many die with the mildest constitutional form; considering how it hurts the lungs and eyes, I thought I should do no small service to mankind if I could render this disease more mild and safe in the same way that the Turks have taught us to mitigate Smallpox. I suspected strongly that the cough often so harassing, even

of the mildest kind, was produced by receiving the infection mostly by the lungs, and I hoped that the symptom would abate considerably if I could find a method of communicating the infection by the skin alone".

His first attempt was on an infant of seven months. He incised the skin of a patient suffering from measles at a point where the eruption was most pronounced and soaked some cotton wool in the blood. Two incisions, deeper than those for vaccination against Smallpox were made in the child's arm and these were allowed to bleed for fifteen minutes. To the raw areas the soaked cotton wool was applied for three days. The child became ill on the sixth day and the eruption appeared on the eighth and lasted till the thirteenth day. Recovery was perfect. He inoculated twelve, in most with success, giving a mild form of the disease.

He also tried immunisation by the transplantation of nasal mucus on a swab of cotton from a child having measles to the mucous membrane of another child. He also used skin scales after the rash and reported measles following skin inoculation - analogous to Smallpox after variolation. The symptoms began earlier than in the classical disease and were much milder and of shorter duration.

In 1816 Themmen repeated these inoculations of Home but with negative results. Six years later, however, Speranza reported some success in seven cases.

In 1842 Katona got 93% success in 1122 inoculations carried out in Austria. A mixture of blood and the contents of miliary vesicles was used as a vaccine which caused fever in seven days with the usual prodromal symptoms followed by the eruption two or three days later, i.e. on the ninth or tenth day after inoculation.

In 1848 and in 1852 Mayr twice transmitted measles by nasal mucus. Catarrhal symptoms appeared in eight or nine days followed by fever and eruption in a few days. Blood inoculation however did not have any effect.

These confirmations of Home's experiments were the only positive results recorded though a great many other experimenters copied his method during the hundred years already covered. Their experience was contrary to that of Home so that he was discredited and the efficacy of his method was vigorously denied. The few confirmations seem to have had no general practical application for nothing further was done in the investigation of the modification of the disease.

In 1880 Babes investigating the bacteriology of the disease reported the presence of cocci in pairs and in short chains in the secretions of the conjunctiva, nose and bronchi and emphasised the role of the streptococci in measles.

In 1897 Folger reported two cases which were the first recorded descriptions of streptococcal septicaemia.

In 1901 Slawyk found streptococci in the blood in fifteen out of sixty-eight cases but since these were post-mortem they are not of any great value.

In 1904 Menschikow found a pneumococcus-like organism in the blood in nine out of sixty-one cases and also reported diplo-streptococci in measles sputum but he did not prove any aetiological relationship.

A very important step in tracing the actual cause of measles was taken in 1905 when Hektoen showed he could produce measles by injections. He produced the typical attack in two cases by small injections of blood which had been obtained from measles patients on the first day of the rash. After incubating for twenty-four hours with three to twelve parts of ascitic broth he injected four or five cubic centimetres subcutaneously. He

stated that on occasions there was no infective agent in the blood.

There was none 12-24 hours before the appearance of the rash.
It was always present on the first appearance of the rash.
There was none 24-30 hours after the appearance of the rash.

Hektoen reported that blood which was sterile from a bacteriological point of view could give measles and that sterile Berkefeld filtrates of the original blood could give measles. He concluded from this that the cause of the disease was a filtrable virus.

In 1909 Eckert got two cases of fulminant streptococcal sepsis in measles, and in the same year Lorey, who was the first to use blood agar extensively, found streptococci in the blood in 15 out of 115 cases but the stage of the disease was not mentioned nor whether the organisms were haemolytic in character.

Lathorpe was the first to mention a streptococcus which was non-haemolytic in character having isolated it in 1918 in 44 cases of otitis following measles.

In 1911 Anderson and Goldberger showed that the rhesus monkey was susceptible to the virus of measles in pre-eruptive and eruptive stages and that the virus was filter-passing. In 1921 Blake and Trask came to the same conclusion after experiments similar in nature. In 1921 Nevin and Bittman showed that rabbits reacted to injections of the virus, and in 1922 Duval and D'Aunoy obtained reactions in guineapigs.

In 1917 Ruth Tunnicliff isolated a diplococcus from measles cases and has since done a great deal of work in investigating its significance in the aetiology of the disease.

Sellards and Bigelow in 1921 obtained Gram-positive bacilli from the blood. Similar bacilli were reported by Kusama, Yokoyama and Ito from the kidney of a monkey injected with measles blood.

In 1923 Caronia in Italy recovered from measles patients

a small Gram-negative anaerobic coccus which he claims as the specific infective agent of measles producing some evidence in support.

In the following year Dougas recovered green-producing cocci from the blood.

In 1926 Ferry and Fisher in America reported another organism taking the form of a streptococcus which they claim to be the specific cause.

In the following year Duval and Hibbard recovered a diplococcus closely resembling that of Tunnicliff. At the same time Cary and Day claimed a short streptococcus as the aetiological agent.

Guardabassi in Italy in 1927 proclaimed the discovery of another totally different kind of agent in the form of an amotile filtrable granular formation 0.4 to 0.6u anaerobic in culture, but very few details were given.

A still different cause is shown by Degkwitz in some experiments published in 1927. He does not demonstrate the actual agent itself but says that it is one of the filtrable viruses which grows in a symbiotic combination with a variety of other organisms.

As can be seen from the above brief outline there is no general agreement as to the agent - the rival claims of the coccus and of the virus being put forward with all the bias of the individual investigator. In the portion which now follows the main points about some of these recent aetiological factors will be brought out in more detail, and it will be seen that, far from helping to clear up the mystery, they only seem to render it more unfathomable.

In 1917 Ruth Tunnicliff reported the discovery of a diplococcus from the blood, throat and eyes of early cases of measles - at first with difficulty from the blood, but latterly

almost without failure. The organism was anaerobic in the first culture but aerobic in character in the subcultures.

Smears from the original culture showed very small round sometimes flattened diplococci in pairs or in short chains - sometimes as clumps of cocci of varying sizes. Subcultures appeared larger as diplococci, sometimes as short or long chains, or clumps like staphylococci. The cocci at the ends of the chains were occasionally smaller than the middle ones. On other occasions there were large forms.

The organism was Gram-positive, passed through a Berkefeld N filter and was killed by exposure to a temperature of 57°C in forty-five minutes. On human blood agar plates after 24-48 hours the colonies showed as small dry greenish spots with regular margins surrounded by a greenish discoloration of the medium. Sometimes there was slight haemolysis after 48 hours. The colonies became more moist on cultivation. The growth on plain agar was slight, colourless and delicate. It was flocculent in both dextrose and plain broth leaving the supernatent fluid clear. It fermented dextrose, saccharose, maltose and lactose (occasionally) but did not ferment inulin, salicin, raffinose and mannite. The organism was not soluble in bile nor did it liquefy gelatin.

The sediment of a 20 cc. culture killed a rabbit in 24 hours. When injected into a monkey the leucocyte count rose from 4000 to 24000 on the following day and fell to 7000 on the eleventh day. Specific opsonins were present as the eruption subsided and the symptoms disappeared, and in immunised rabbits there was an increase in the opsonic power.

In 1922 she published reports on further work with the same diplococcus. She inoculated animals repeatedly and found that their serum contained increased agglutinins and opsonins and that there was increased agglutinin absorption. Injection

into rabbits gave Koplik's spots in 3-15th.day (generally 7th.) persisting for 1-3 days, followed in 1-5 days by the eruption (i.e. 7-18th.day, generally the 11th.day after injection).

She further stated that her diplococcus from the first rabbit caused Koplik's spots and an exanthem in the second rabbit, and that the seventh cultured generation gave a reaction in rabbits whereas the second generation of other organisms did not do so.

Much later - in 1928 - she reported that the diplococci in the infective stages of measles differed from those found in convalescence. This was done by using some immune serum from injected animals.

The phagocytic index of normal blood with the diplococci was stated by indicating the number out of 100 leucocytes which contained the diplococci after incubation. The phagocytic index of the immune serum was also found. The opsonic power of the immune serum was indicated by the ratio of the two.

$$\text{Opsonic Power of Serum} = \frac{\text{Phagocytic Index of Immune Serum}}{\text{Phagocytic Index of Normal Serum}}$$

If over 2 then the coccus was the measles coccus.

Tunnicliff, in further observations into the relationship of the green-producing diplococcus with measles, investigated the reaction of the skin to her organism. In 1925 she reported that Berkefeld filtrates of aerobic and anaerobic cultures in broth with or without ascitic fluid gave no cutaneous reaction when injected and that killed organisms suspended in salt solution also failed to give convincing reactions. Later, however, she used anaerobic dextrose broth cultures of the green-producing coccus killed by 0.5% carbolic acid and obtained a skin reaction. Using 0.2cc intracutaneously in rabbits there was an area of circumscribed induration 1-4cm diameter within 4-24 hours, persisting even for three days and leaving pigmentation and

desquamation. The practice adopted when human beings were used in the tests was to dilute the antigen obtained to such a degree that there was no reaction in the insusceptibles - generally when 1 to 40. The results were as follows:-

Positive in 100% of those who had not had measles.
Negative in those with measles after the rash.
Negative in 96% of those with a history of measles.

She also stated that:-

Antigen was neutralised by convalescent serum.
" " not " " normal serum.
" " neutralised " immune goat serum.
" " not " " normal goat serum.

Tunnicliff - following some work on similar lines by Ferry and Fisher - revised her opinion as to the production of toxin by the green producing diplococcus. She found that the filtrate of a 0.2% dextrose broth culture (six days at 36°C) gave no extracellular toxin but that a filtrate of a similar culture with the addition of 1% sheep blood (after six or seven days) gave a reaction in a dilution of 1 in 10. Following an intradermal injection of 0.1cc there appeared a circumscribed area of erythema 1cm. in diameter. This soluble or extracellular toxin (filtrate) unlike the intracellular toxin (killed culture) only gave a positive result in 50% of the susceptible cases.

This toxin gave the same results as the antigen when mixed with the different sera. It was neutralised by convalescent serum and by immune goat serum but not by normal human serum nor by normal goat serum. Boiling for one hour destroyed the toxin.

The toxin was injected into normal rabbits and into some which had had previous injections of the diplococcus with the result that the normals gave the skin reaction and those previously injected failed to do so.

Early in 1926 Tunnicliff reported the preparation of immune goat serum by means of intravenous injections of her diplococcus in a suspension in 10cc of salt solution. The

organisms were grown for 24 hours in tubes containing 10cc of ascitic fluid broth, centrifuged and suspended in the salt solution. After a series of injections of killed then living diplococci into these animals she collected the serum and claimed that it contained antibodies specific to the diplococcus. This serum was a typical antibacterial serum and not an antitoxin. In collaboration with Hoyne she published results which showed that the product was efficient in neutralising the effects of the intracutaneous injection of the green-producing diplococcus.

Cultures of Tunnicliff's coccus produced reactions in normal rabbits (Koplik's spots, temperature, rash) and immune goat serum prevented these occurring though normal goat serum did not do so. This serum was said to have neutralised killed cocci and the filtrates (intracellular and extracellular toxins) when these were used as intracutaneous tests. They also said that it gave the Debre phenomenon just like human convalescent measles serum.

Later the same two investigators reported good results when it was administered to measles contacts during the first three days but later than that it had little effect. Serum reactions occurred in 12-13%.

Halpern in 1928 reported 63% success and 37% attenuated.

Late in 1930, however, Barenberg gave 8cc. in 38 cases and got 17 severe and 21 modified measles, 6 having serum rashes and 11 having complications. He gives no details as to time of exposure but all the reports seem to agree as to the frequency of serum sickness and the lack of efficacy after the fourth day.

In 1927 Tunnicliff used horses, and together with White reported that the serum of these gave apparently complete protection in a few, incomplete protection in some, and no protection in others. It seems inconclusive evidence.

In 1923 Caronia announced that the micro-organism responsible for measles passes through an ultramicroscopic phase (filterpassing) in the cycle of development but later appears as a small diplococcus when cultivated under special anaerobic conditions on a special medium the preparation of which has not been described. He obtained cultures from bone-marrow, cerebrospinal fluid, and the naso-pharynx in pre-eruptive and eruptive stages, and also from the blood of rabbits injected with human measles blood. He stated that convalescent serum contained antibodies specific to it. He also prepared a vaccine from the coccus in the form of cultures which when inactivated or attenuated gave an immunity but when recently made caused typical but attenuated measles.

In the following year Ritossa found constantly in the urine when centrifuged minute paired bodies morphologically identical with Caronia's coccus. These were present during the disease, were scarcer later and absent in convalescents and in controls. Filtrates in special media gave turbidity like Caronia's coccus and the agglutination tests were positive.

In the same year Arloing and Dufourt obtained Gram-negative micrococci similar to Caronia's coccus in eight blood cultures but there were no control cultures made at the same time.

However, the number of investigators who have failed to obtain results similar to these outnumber by far those who corroborate. Szirmai and Jacobovios in 1926 repeated Caronia's work and were unable to confirm any claim. Hecht in 1926 said, "The reaction to the alleged measles toxin is the same in children who had had measles as in those with no history of measles".

In 1927 MacCartney found artefacts in the sterile non-inoculated culture medium closely resembling the organism of Caronia. Selma Meyer following Caronia's technique got similar bodies there, as well as in blood cultures from Chickenpox,

Chorea, Polyarthritis and from normal blood. The latter worker also injected rabbits with the uninoculated medium and found the same bodies in the liver and spleen as with the measles cultures. Fever and eruptions may be produced by the injecting of the medium alone. Arloing and Dufourt in 1924 raised the question as to whether these bodies were simply flocculated colloids. Takaki in 1926 suggested the autolysis of added animal organs.

Caronia convinced that he had found the causal organism of the disease proceeded on the usual lines of preparing a vaccine for active immunisation. He did this in two ways. He either treated the cultures of his coccus with carbolic thus killing the organism, or he mixed the coccus with convalescent serum thus neutralising its effects. His method of procedure was to give on alternate days three intramuscular injections of 2cc of a well developed culture (with the addition of 0.5% carbolic acid). This generally gave no febrile reaction but there was a slight local reaction. He stated that of 539 who had been exposed and were thus vaccinated 10 took measles - less than 2%.

Sindoni (Caronia's assistant) after eighteen cases reported that the disease was of less duration, of less severity and showed less complications than normal attacks. Annecchino in 1925 followed Caronia's procedure and of 41 thus treated and exposed none took measles.

Meyer on the other hand vaccinated thirteen in exactly the same way (i.e. three times) but they all took typical and not modified measles. Furthermore out of four cases (two injected by Sindoni and two by Meyer) though they took no measles then, no less than three developed measles spontaneously some time later.

Summing up then we find that Caronia's claims are

Supported by:-		Rejected by:-	
Arloing and Dufourt	- 1924.	Takaki	- 1926.
Ritossa	- 1924.	Szirmai and Jacobovics	- 1926.
Auricchio	- 1924.	Meyer	- 1926.
Sindoni	- 1924.	McCartney	- 1927.
Saliroli	- 1925.		
Annecchino	- 1925,		
and other Italians.			

In 1924 De Villa made some intracutaneous tests with the killed cultures of Caronia's coccus and found that:-

Cases with no history of measles gave	65%	Positive reactors.
Cases with history of measles gave	25%	" "
Cases after vaccination with cultures gave	No	" "

In March, 1926, the American investigators Ferry and Fisher announced the recovery of a streptococcus from the blood of measles patients in the acute stages of the disease. This organism which they called Streptococcus morbilli was a medium-sized Gram-positive, aerobic streptococcus, occurring in long chains in liquid media and in chains of varying length on solid media, which produced a small colony with a green halo on whole blood agar. It did not produce haemolysis of the red cells, was not soluble in bile, and did not liquefy gelatin. It fermented glucose, lactose, saccharose but did not ferment mannite, salicin or inulin. It produced an extracellular toxin which the authors claimed was specific to measles.

The blood and medium having been incubated plates were made, slopes planted and broth cultures inoculated. After incubating the broth for six days the culture was filtered - the product containing 4000 to 6000 skin test doses per cubic centimetre. After the necessary dilution 0.1 cc. was injected intracutaneously. The results were:-

Susceptibles - no history of measles	- 40% positive.
Insusceptibles - with history of measles	- Up to 3% positive.
Patients in pre-eruptive and early stages	- Positive.
Patients in later and convalescent stages	- Negative.

Toxin was destroyed by boiling or heating in steam for one hour.
It was neutralised by convalescent serum and by antitoxin.
It was unaffected by anti-scarlet-strept serum and by normal

horse serum.
Toxin injected after convalescent serum or antitoxin had no effect.

Ferry and Fisher also stated that:-

> Convalescent serum agglutinated Streptococcus morbilli. Normal serum did not agglutinate it.

In the following year Ferry showed that rabbits had typical local reactions after subcutaneous or intracutaneous injections of live or dead suspensions or of broth filtrates of the organism. These local reactions were frequently followed by a generalised rash and conjunctival congestion.

Cary and Day in the same year, 1927, got a green producing diplococcus from early tonsillar cultures in 93 out of 95 cases using sheep blood agar as the medium. Many growths were pure and the majority showed a great preponderance of the coccus. It was a Gram-positive aerobic streptococcus which may pass a Berkefeld N filter. Growth in Salicin medium differentiated it from Streptococcus viridans.

It was present in early cases in 98% throat cultures.
50% conjunctival cultures.
33% blood cultures.

Degkwitz did not demonstrate the causative organism but claimed that he could cultivate it in a medium. The virus was obtained by bleeding a typical case on the first day of the eruption and diluting with a special salt solution which had the same number of anions and kations and the same pH as blood. He subcultured this with symbiotic organisms - Tunnicliff's green-producing coccus or the pneumococcus - and finally filtered through a Berkefeld W filter. He stated in 1927 that though the injection of 1c.c. of 1/5000 dilution of the blood virus did not give measles in a susceptible child the same amount of the above mentioned culture when carried through fifteen generations over 78 days (one in three trillion of the original) caused a reaction. This reaction consisted of a rise in temperature, rhinitis and conjunctivitis

in 10-14 days with blue-red macules though not a typical measles eruption. A control series injected with the symbiotic organisms did not give a reaction. Both groups of patients were later injected with infectious measles blood and the virus group remained immune whereas the controls took typical measles attacks.

This work of Degkwitz confirms the view of Hektoen that measles is given by:-

Material sterile from a bacteriological point of view.
Sterile blood from acute measles cases.
Dilutions of acute measles blood through a Berkefeld filter.

Degkwitz inoculated sheep with Berkefeld filtrates of nasal secretions and of sputum of early measles and thereafter collected the serum in doses of 5c.c. which he called a unit. He advised that this serum was best given between the seventh and the eleventh days of exposure so that a mild attack and permanent active immunity was produced.

Many reports have been made as to its inefficiency in the prophylaxis of measles. Progulski and Redlich gave 10-20 c.c. at the time specified and concluded that it had no power to protect, attenuate or prevent complications and said that in most it gave unpleasant serum sickness and prolonged the incubation. Kochmann also condemned it as did Kaupe, Mosse, Rietschel and numerous others. In fact, out of over a dozen, the only investigator to confirm the good results of Degkwitz himself was Wiese. Moreover it is no half-hearted condemnation and many recommended its complete withdrawal from the market. Zoepffel for example, stated that all injected took measles, most had bad complications and almost all had serum sickness.

Summarised, the results of the injection of the Degkwitz sheep serum were as follows:-

CONDEMNED COMPLETELY.

Kochmann	- 1926.
Progulski and Redlich	- 1926.
Kaupe	- 1926.
Seligman Dingmann Alterthum	- 1926.
Rietschel	- 1926.
Noeggerath Oster Viethen	- 1926.
Erichman	- 1926.
Schlossman	- 1926.
Zoepffel	- 1926.
Baron	- 1927.
Silverman	- 1929.

SUPPORTED BY - Wiese.

Degkwitz in 1928 used monkeys, producing a rash (though not typical measles) by injecting his virus, and collected the serum from those showing a rise in temperature after such injections. He claimed that measles contacts did not contract the disease if given this immune monkey serum but that normal monkey serum had no such beneficial effect. There is not much literature about this serum - probably the poor results and summary dismissal of his claims for his sheep's serum being responsible for the absence of reports.

Considering the work of Degkwitz the main points he emphasised were:-

1. The virus lived for weeks at $0^{o}C$ in physiological salt solution with the same number of anions and kations and with the pH of blood.
2. Such cultures by skin inoculation gave quicker and milder measles with a shorter course.
3. Measles was produced from material bacteriologically sterile (blood, dilutions, filtrates).
4. Virus grew in plasma and the above solution (1 to 6 or 7) but symbiotic organisms were necessary.
5. The virus - bacteriologically sterile - gave in humans a reaction like measles and protected against later exposure.
6. Monkey serum (after injections of the virus) protected humans against measles.

The weight of epidemiological evidence indicates with great probability that the contagium, whatever its form, is present in the throat and nasal secretions in the fastigium and at the height of the eruption, and that it disappears or

becomes non-infective with the fading of the rash. The experience of Redlich coincides with that of Debre and Joannon who state that:-

> Contagium begins with the catarrhal symptoms.
> Stops with the fall in temperature.
> Ends with the full development of the eruption.
> They all consider carriers improbable.

As was first conclusively demonstrated experimentally by Hektoen in 1905 and now generally accepted as a proved fact, the unknown contagium is present in the blood stream during the late pre-eruptive and early eruptive stages of the disease. There is corroboration of this statement in the interesting case that is recorded by Harrell in the Journal of the American Medical Association, Volume 82, page 1812. The patient developed measles on the eighteenth day after the transfusion of blood from a donor. It was found that the donor had a typical measles rash two days after the transfusion. As there were no cases of measles in the hospital and as the donor was not at any time in contact with the recipient the infection must have been caused by the measles agent being present in the transfused blood. Bauguess later reported two similar cases which showed incubation periods of thirteen and fourteen days.

It cannot be denied that the cause of measles is a living agent but though various cocci, bacilli and protozoa have been claimed from time to time to be the specific cause the question as to its identity is still unsolved. Since the germ has not been positively isolated and identified all attempts at immunising by cultures or conserved substances have at present only theoretical interest. The use of so-called measles toxins is still in the experimental stage.

The suggestion has been made that the exanthem is caused by the contagium itself and not by its toxin since there is a definite and gradual progress of the rash from the uppermost part

THE VARIOUS AETIOLOGICAL CLAIMANTS.

Year.	Investigators.	Gram.	Filter-passer.	Type.	Form.	Appearance on Blood-agar.	Further details.
1917	Tunnicliff.	Positive.	Yes.	Anaerobe then Aerobe.	Diplococcus.	Green	Original culture:- Very small round, sometimes flattened diplococci, or short chains, clumps of cocci, varying sizes. Throat smear:- Similar with leucocytes and large epithelial cells.
1923	Caronia.	Negative.	Yes.	Anaerobe.	Coccus.		Recovered from blood, marrow, naso-pharynz, cerebrospinal fluid. Specific immune bodies in convalescence.
1926	Ferry and Fisher.	Positive.	No?	Aerobe.	Diplo-streptococcus.	Green.	Extracellular toxin produced neutralised by convalescent serum.
1927	Duval and Hibbard.	Positive.	Yes.	Aerobe. (facult. anaerobe)	Diplococcus.	Green.	Filter passer in blood. Subcultures are visible and do not pass filter.
1927	Cary & Day.	Positive.	Yes?	Aerobe.	Short streptococci varying in size.	Green.	Culture:- Minute pinpoint and green. Round. Later more vigorous growth. Non-contagious.
1927	Guardabassi.	Negative.	Yes.				Amotile filtrable granular formation 0.4 - 0.6u long. Giemsa pink. Grows best in concentrated broth - pH 7.2 (petrolatum).
1927	Degkwitz.	Not demonstrated. Grows in physiological salt solution with same anion, kation and pH as blood. It is filtrable. Bacteriologically sterile. Monkey serum after injection protects humans.					

of the body down over the trunk, arms and legs and no simultaneous appearance over the entire body as one might expect would be the case if the agent were in solution.

It might be remarked from the reports of the investigators noted that there seems to be a preponderance of evidence in support of the green-producing diplo-streptococcus but it is difficult to understand how such an organism which is present in enormous numbers in the discharges of eye, nose and throat during the catarrhal stages should be absent from the upper respiratory tract of cases during the incubation period of the disease.

Again, if measles is due to a diplococcus it would seem probable that, like diphtheria and scarlet fever, soon after the transfer it would begin to develop and produce symptoms. Their absence during the non-infective period and their abundance during the very infective stage seem to point in their favour but in almost all diseases due to bacterial infection there is a greater or lesser number of cases in which the infecting microbes persist. The absence of infectivity soon after the height of infection, so marked in measles though diplococci are still present in the throat, seems to be against their aetiological significance. It is suggestive also how measles is like smallpox, mumps and chicken-pox in having a long incubation when it is not communicable and then when convalescence is established it suddenly ceases to spread contagion. These three other diseases have long been regarded as being due to different kinds of virus and it is quite possible that the virus of Degkwitz should hold the premier place in any future investigation.

We have seen that many investigators have found that a toxic filtrate of a bouillon culture of organisms isolated by blood culture can give a transient erythema in susceptibles and no reaction in those with a measles history and therefore claim there is a specific and isolated organism of measles which produces

a toxin that may be used as an index of immunity to the disease. How can we reconcile this with the fact that when Long and Cornwall in 1927 made 47 blood cultures from 26 selected cases (in 12 in the pre-eruptive stage, in all in the early period of the rash and the rest later) only four growths were obtained - the result of contamination - and no toxin producing green streptococcus was isolated?

Then again it is a well known fact that bile insoluble green-producing cocci are practically constantly present in the throats of normal persons and are not uncommon in nasal cultures. Since green-producing cocci have not been found with great constancy they may well be an accidental invader of the blood during the catarrhal stage and their presence or absence there is merely a coincidence and not an essential part in the process of invasion by measles.

CONVALESCENT MEASLES SERUM.

Earlier in this work some figures were quoted from Denmark which showed particularly well how the wave of mortality from measles rises and falls with age. It has been proved without doubt that infants whose mother has never had measles may have no inherited immunity whereas those whose mother has had an attack are usually immune for three or four months, less certainly up to five or six and that even in the sixth and seventh months they have not entirely lost their inherited immunity.

While awaiting the discovery of the actual causal agent of the disease attention has been focussed on the action of the serum of convalescents. It has long been known that immunity after an attack is well marked and that in the great majority this immunity lasts for life. The persistence of this active

immunity throughout the life of the recovered patient immediately suggests the utilisation of the antibodies in the blood.

It is stated that thirty-five years ago a German physician used large amounts of convalescent serum in cases just beginning incubation with favourable results. The first definite results published, however, were those of Nicolle and Conseil in 1918 who had, in 1916 in Tunis, withdrawn 9-10 c.c. of blood on the third to sixth day of defervescence and after allowing it to clot had drawn off the serum, added a trace of phenol and injected subcutaneously into two susceptible contacts. The two cases thus treated remained immune though exposed to two measles cases later. The same authors reported two other cases in 1920.

In 1916 Park and Zingher injected 48 cases with convalescent serum - of 28 who got serum 1½-4c.c. six took measles (after 2, 7, 8, 15, 17 and 25 days) while of 20 who received 8c.c. none took measles.

In 1917 Richardson and Connor protected seventeen cases. In 1920 Degkwitz protected 172 cases. Since then many others have confirmed the beneficial results to be obtained from the injection of convalescent serum.

It is not always easy to withdraw blood from young patients and the use of vesicating agents to invoke the outpouring of serum into blisters has been advocated - a method used by Hugh Thomson of Glasgow many years ago. Modinos of Alexandria considered that owing to the difficulty of obtaining convalescent serum and to the difficulty of excluding tuberculosis, syphilis and malaria, such vesicatory ichor should be used. He reported in 1926 that it was much easier to get 10-15c.c. from a child of 6-10 years: that patients were readier to give serum thus: that malaria was excluded and that tuberculosis and syphilis (which are generally more prevalent in those over twenty years of age) are less common. He found that 3-5c.c. gave immunity in exposed

susceptible children. The dose recommended in "Médicine" (Paris) is 1c.c. for each year and 10c.c. up to 15 years.

Until the causal agent of measles is definitely isolated and identified, and until a reliable method of active immunisation is possible, the ideal to be aimed at is not so much to prevent measles as to keep it under control. Scientific opinion has gradually been turning away from the desirability of producing a passive immunity to that of producing an active immunity at an early period. To the little child of three years or less, and particularly to one already struggling with some other illness, an accidental exposure to infection with measles is a serious matter, and, if the disease could by any means be avoided till later in childhood when the mortality is much reduced then many thousands of lives would be saved for useful work in the community.

The onset of measles by means of such injections of serum can be deferred until the patient is of an age and in a suitable state of health when an attack is not fraught with the same danger.

In 1923 Debré and Ravina emphasised the greater value of modifying by serum to get a mild form of the disease rather than to completely prevent its development. This sero-attenuation gives a relatively lasting immunity whereas absolute sero-prevention confers only a transient passive immunity. To obtain an immunity that is at all lasting there must be a minimum of clinical manifestations of the disease. These may be a cutaneous eruption slight and transient, it may be, but unmistakable, together with a temperature for a few hours and perhaps some catarrhal symptoms.

Debré early drew attention to the fact that convalescent serum when injected into the subcutaneous tissues of a person in

the catarrhal stage of measles caused a local inhibition of the subsequent eruption. This phenomenon has been associated with his name and the degree of inhibition is an index of the strength of the convalescent serum so that if several sera are given in the same person the relative values of the contained immune bodies can be roughly estimated. Unlike the Schultz-Charlton test in the eruption of scarlet fever the injection of convalescent serum even in considerable doses does not produce blanching once the eruption has appeared. Since the serum is a homologous one it does not of itself give a local reaction nor does it produce any symptoms of serum disease.

The outstanding objection to convalescent serum is the difficulty in procuring a suitable and adequate supply when the occasion for its use arises. With rare exceptions it has been established that an attack of measles confers a lasting immunity, and, since as we have already seen the great majority of adults have at some time in their lives suffered from the disease, their blood must contain a certain amount of measles immune bodies. This very large and for practical purposes limitless source of protective serum has been used by many investigators, the dose for each age and stage being much larger than the dose of convalescent serum.

Adult whole blood or the serum obtained from it has been advocated as a routine measure to be adopted in the control of a measles epidemic. It is certainly universally available, it is free from the dangers and disadvantages of horse serum, it is easy to prepare and administer and the possibility of the presence of antibodies of diseases associated with measles may in fact show on future investigation that is is superior to convalescent serum. The larger doses which are necessary may mean that more punctures of the skin are required since if more than fifteen cubic centimetres are injected in the one spot there is apt to be some

discomfort and even necrosis of the tissues. If this is remembered the injections are well tolerated and there may be no temperature reaction.

One of the first cases in which the value of parent's blood was demonstrated was that recorded by Wolff in 1924. In July, 1923, a child (B.G.) of two and a half years took measles and H.G. (one year) did not develop it contrary to expectation. In the same family in May, 1924, an infant of five months took measles and still the child H.G. now one year, nine months remained unaffected. The explanation was that H.G. when eight days old had melaena and had had injected 30c.c. of the father's blood. It is interesting to note that the duration of passive immunity in this case was very much longer than that generally accepted for convalescent serum.

In May, 1925, Debré Joannon and co-workers reported good results in 200 cases, the dosage being about six times that of convalescent serum, and in the same year Kovacs got good results also. Munoyeno in 1926 and Von Torday in 1926 had but few failures. Townsend on the other hand in the same year said that 20c.c. neither prevented nor modified.

Nevertheless there seems some evidence that parent blood is efficacious in sufficient dosage and this should range from four to six times the corresponding dose of convalescent serum. There does not seem to have been much work done in this country in the way of utilising this enormous store of protective power and since few districts are as fortunate as Glasgow in having adult cases of measles this potential reservoir should form the bulwark for the country at large in the control of epidemics.

IMMUNISATION.

Up to the present the aim of Public Health Authorities has been to prevent measles but that this policy has been an absolute failure is shown by the fact that well over 90% of the adult population have a positive history. It is indeed doubtful wisdom to attempt eradication unless at the same time active immunisation is compulsory, since, if the policy were successful, the infection would undoubtedly return and finding virgin soil, would repeat the tragic epidemics of the Faroes and Fiji Islands. Since it is characteristic of measles that "it attacks without distinction but kills with discrimination" the aim should be not to abolish but to control the disease so as to postpone the attack to an age when the risks are very much less.

The discussion of immunisation against measles should include a brief survey of attempts that have been made at different times to produce an active immunity against the disease. These fall under the following heads:-

1. Application of nasal mucous secretion from measles patients to the nasal mucous membrane of young susceptible children.
2. Injections of very small doses of blood containing measles virus obtained from a patient in the early stage of the disease.
3. Injections of the various organisms or material claimed by the various investigators as the cause of measles.
4. Combination of the above with the injection of convalescent measles serum.

Francis Home of Edinburgh we have seen was the first to write about the immunisation against measles by using active nasal secretions and active measles blood. The first person known to have used the <u>serum</u> of active measles patients seems to have been Hugh Thomson of Glasgow who in 1890 held the post of

vaccinator appointed by the Faculty of Physicians and Surgeons, Glasgow. He blistered the patients in the acute stage, vaccinated contacts with the serum and demonstrated the practicability, the safety and success in producing a milder attack than that got by infection normally. The eruption was earlier (9th. to 10th. day) than the normal (12th.to 14th.day) with less bronchial affections and catarrhal symptoms. He further said that "inoculation seems to be the only way by which we can control and regulate the incidence of the disease". He suggested that these inoculations should take place during the months when respiratory troubles are less prevalent in order to lessen the risks - the first September or October after the child has attained the age of six months - advocating the inoculation for the prevention of an inevitable though future evil. Blood up to 18 days old gave measles but in one case when its age was 35 days measles did not result. He experienced the usual difficulties in carrying out his scheme due to the reluctance to make humans the subject of experiment, the want of faith in the proposed preventative and the fear of doing harm. It is worth noting in this connection how as in so many other ways history has the curious habit of repeating itself. About five years ago Professor Karl Leiner of Vienna introduced a similar method there but had to desist owing to the pressure of press propaganda. Apart from this very little was done in the field of immunisation till 1915 since when numerous investigators have approached the problem from different angles.

In 1915 Herrman noticed that young infants generally had some inherited immunity towards measles and that, if exposed to infection before the age of five months, they would not only remain protected at the time of exposure but would not develop the disease when exposed after months or even one to two years. He thought that he could produce the state of active immunity in

such subjects by giving them some active infectious material while thus protected. Accordingly he inoculated children of four to five months by swabbing their nasal mucous membrane with the diluted secretions of measles patients who were in the first day before the measles eruption came out. This procedure resulted in a reaction or an attack of attenuated measles and active immunity was thus established. This idea of his which seems to be perfectly sound from a scientific point of view is rather impracticable for general use for it is limited to young children who are temporarily immune for such an application of active secretion to a normal susceptible would cause a typical attack of measles. Even when limited to the class chosen many parents might - in fact undoubtedly would - object to allowing their children to be infected in this manner. Again the possibility of transferring other diseases at the same time would have to be considered. Of seventy-five subjects treated thus and observed for a period varying from four to eight years Herrman found that though sixty-two were subsequently exposed definitely to measles only five took the infection.

In 1918 as a consequence of his work with convalescent serum Nicolle put forward a somewhat similar scheme which could include all persons considered susceptible. Ten cubic centimetres of serum were injected first and this was later followed by an injection of one cubic centimetre of active measles blood or by the application of active measles secretions. This second part of the treatment was repeated later to increase the immune power of the body.

In the same year in America Richardson gave fifteen cubic centimetres of convalescent serum and swabbed with the virus contained in naso-pharyngeal secretion, the results being satisfactory resulting in an abortive subcutaneous measles eruption.

Hiraishi and Okamoto in Japan in 1921 withdrew blood from a patient, between the stage of Koplik's spots and the height of the eruption, into 2% citrated saline and injected into the interscapular region of susceptibles 0.0001c.c. to 0.005c.c. After inoculation some of the forty-four cases were treated at intervals by either larger amounts of measles blood or by pharyngeal smears. Within nine weeks of inoculation 29 took measles and 15 did not, so that they considered the amount of immunity conferred by this method was negligible.

In 1927 Debré, Joannon and Papp used as antigen blood at the onset of the eruption, which was filtered, diluted and sterilised by antiseptic. A dilution of 1/800 subcutaneously in children of two to four years gave no reaction but only leucocytosis on the third or fourth day, leucopenia on eighth to tenth day, then leucocytosis later, this being considered an extremely attenuated form of measles. Three weeks later another injection of 1/400 gave fever on the seventh to tenth day, inflamed mucous membranes and occasionally a slight eruption. Hundreds were given this with no morbid reaction. Immunity persisted for several weeks. At present, however, this is only in the stage of experiment.

Reference has already been made to the claims for the different organisms reported as the cause of measles. The experiments have been performed on animals of different kinds and though results show the production of immune bodies to the individual organism concerned the results after injection of active measles material in those thus immunised are not as conclusive. Much more must be done before any reliance can be placed on such methods of immunisation as has been put forward, for the only suitable subject for measles immunisation is the human.

THE PREPARATION of CONVALESCENT SERUM

THE PREPARATION OF CONVALESCENT MEASLES SERUM.

The preparation of convalescent measles serum is very simple according to the various workers who have reported on the subject, but any record of the details of the technique and of the difficulties likely to be encountered in the process are difficult to find in the literature. The method used in the present investigation had really to be evolved by degrees.

First of all the patient was selected on admission to the ward and the details and the course of the illness were recorded. On a separate sheet - a copy of one of which can bee seen at the end of this section. The chief points considered were the age - young adults of eighteen years and upwards being preferred to those just over ten years - and the type of the attack. This attack had to be typical and unmistakable, stress being placed on the presence of Koplik's spots. There had to be no clinical evidence of tuberculosis nor syphilis and no history of malarial attacks. Other details were taken and an analysis of these will be given further on in this section.

The first sample of blood was drawn off with aseptic precautions in the ward and carried over to the laboratory where clotting was allowed to take place. The serum was later withdrawn into sterile tubes and as it was slightly tinged with corpuscles it was put in the centrifuge and spun after which it was stored in the ice-chest. After a day or so the surface showed a film which when shaken up, broke easily to form a cloud, and the obvious deduction was that there had been some contamination. The tubes were laid aside so that the growth would continue but only a moderate amount formed - not much more than when first observed. This milky material was taken by platinum loop, films

were made and the emulsion was put on a serum slope - one from each tube - and these incubated. The films were fixed and a distinct deposit was seen. A control spot of staphylococci was then placed on the slide and both spots were stained. Examination under the microscope revealed well stained controls but nothing else. After two days in the incubator the serum slopes showed no evidence of growth and smears from their surfaces were also negative as shown by a stained specimen under the microscope.

This seemed rather peculiar and as no reference could be found in the literature at hand the matter demanded further investigation. Contamination was obviously the first thought in the mind. It was considered that, as the serum stood to separate and as no preservative had been added, micro-organisms might be responsible and so anything that hastened the final process would be an improvement. Citration of the blood seemed advisable since a larger amount of useful fluid might be obtained from the limited amount of blood, and besides this advantage the whole process could be carried through at the one time.

For the second batch therefore, tubes were used containing sterile sodium citrate solution so that the final concentration would be between 0.3% and 0.4%. These were brought after sterilisation into the ward from the laboratory and used as before, the mouths being flamed in the usual manner.

Here also a film was observed to form after a short interval and a deposit also was noted. The film was rather white in colour and under the microscope it was suggestive of a fatty emulsion. This immediately suggested that it might be due to the absorption of fat in the diet and that if a longer period were allowed to elapse from a meal this film might be avoided. The deposit now present had to be explained. Contamination again suggested itself. The technique was considered faulty and was further improved. Since the resulting process was the one

followed throughout the rest of the work it will be described here in detail.

Large test-tubes to hold 25c.c. were thoroughly cleaned, dried and sterilised by dry heat and 3c.c. of 2.5% solution of Sodium Citrate were added. The whole was now wrapped in butter paper and kept upright. Sterilisation was effected by an hour's steaming in the Koch apparatus.

Test-tubes were chosen to fit the centrifuge and cut down to the right height, a mark being made on the glass at the level of 10c.c. fluid so that the tubes would balance when blood was added up to the mark. They were each fitted with a plug of cottonwool through which a metal pin had been thrust and thus even centrifuging at a speed of 4,000 revolutions could not throw the plug into the fluid. These tubes when thus completed were also wrapped in butter-paper, sterilised by the hot air oven method - an hour at 170°C. - and stored for use.

Little bottles to contain 5c.c. were cleaned thoroughly. The bottles mostly used were those containing Burroughs Wellcome Dick Test fluid and those containing the Insulin product of the same firm. They were plugged with cottonwool and wrapped in butterpaper. Since the mouths of these varied in size they were grouped in five sizes - B.1, 2, 3 and 4. They also were sterilised in the hot air oven at 170°C. for an hour.

Rubber stoppers to fit the above bottles were grouped in the same way so that there was no attempting to fit the wrong plugs thus lessening the risks of contamination. These stoppers were boiled for 20 to 30 minutes or more for sterilisation just prior to use.

A pair of ordinary dissecting forceps were boiled for twenty minutes in soda solution before being used to place the sterile rubber stoppers in the filled bottles.

Trikresol was added to sterilised water to make a 2.5%

solution, or rather an emulsion, since it was found impossible to get the amounts to become homogeneous.

The cannula, needles and syringes were boiled for 20 minutes before use to render them sterile.

The patient having been selected, his arm was exposed and the most suitable vein chosen. The skin was washed with ether and with spirit, the vessel engorged by applying a tourniquet and the area again washed with ether and spirit. The sterile large bore needle was then inserted into the vein and blood withdrawn into a sterile syringe. The needle was left in the arm, the syringe disconnected and the 20c.c. blood ejected into the tube of sterile citrate solution which was thereafter immediately plugged and inverted once or twice. The syringe was then re-applied and the operation repeated until the required quantity of blood had been withdrawn. The needle puncture was then sealed with collodion. The butter paper in which these tubes were wrapped was only removed when the syringe was three-quarters full of blood so that the chance of contamination by bacteria was reduced to the absolute minimum.

This citrated blood was removed to the laboratory and since each tube was sufficient to fill two of the 10c.c. sterile centrifuge tubes only two of these were opened at a time. The blood was spun till the plasma was clear - 3500-4000 revolutions for four or five minutes. This plasma was withdrawn by the sterile syringe and canula and was immediately put into the final bottles in doses of 5c.c. To each of these small bottles was added 1c.c. of the 2.5% Trikresol and the boiled rubber stoppers were applied by means of the sterilised forceps. In this process also the butterpaper wrapping was not removed from the centrifuge tubes until the blood was ready for decanting, and the little 5c.c.bottles were not exposed till the centrifuge tubes had been spun.

Each little 5c.c.bottle had affixed to it a label on which was a number indicating the particular donor from whom the contained serum or plasma had been obtained. A separate sheet of which a replica is given later contained the details of the donor and of his illness.

A sample of blood from each of the donors was sent to the Public Health Laboratory where the serum tests for syphilis were carried out by Dr.Wiseman and his staff. The history of the patient was elicited and the chest examined to exclude the possibility of tuberculosis. Malaria was also excluded.

Several bottles of the second batch were heated at 56°C. for twenty minutes on each of three days but clinical results showed no appreciable loss of efficacy in the action of the serum treated thus.

When the third batch of plasma was made, particular attention was paid to the different stages in the preparation but still no obvious source of contamination was found. It was noticed that when centrifuged at first the plasma had a somewhat greenish tinge and that it was not perfectly clear like the serum but showed some faint opalescence. After some time the greenish tinge was replaced by yellow which persisted throughout the process. Two bottles were taken, the first containing plasma only and the second plasma and trikresol. Both became progressively denser with very little difference, the second being, if anything, a little more rapid. A certain stage was reached after which on standing in the ice-chest no further increase in opacity took place. On leaving for some days in the cold there gradually separated to the bottom a fluffy deposit which, however, did not form a layer as organisms would have done but remained rather like a billowy cloud. The upper surface of this deposit was not horizontal and was easily disturbed. There was a clear fluid above this cloud forming roughly a quarter of the liquid. On attempting

to get the deposit thrown down the centrifuge was used, but, instead of clarifying, the muddiness returned to a uniform density throughout the liquid.

The fourth batch of plasma was prepared under a still more improved technique. The trikresol on being added to the surface of the plasma caused the upper portion to become quite milky in appearance but this milkiness disappeared on the bottle being shaken up slightly. A sample bottle of this lot was taken when the usual muddiness had developed well, and, after flaming the bottle lip, a portion was added to a test-tube of broth. Immediately on the addition of the plasma the broth turned milky and opaque. This tube was then incubated at 37°C. and examination after a period showed an absence of bacterial contamination.

Being now convinced that the technique was as far as could be ascertained faultless from a bacteriological point of view a control test was performed.

Three tubes of Hartley's broth were taken. To the first was added a loopful of an ordinary throat culture (bacilli, cocci etc.). Into the second and third was put sufficient of trikresol to make it of a finished strength of 0.5%. The second tube had now added to it a loopful of the same throat culture. The third tube was left not inoculated. These three tubes were incubated for 36 hours at 37°C. with the object of finding the action of the trikresol on organisms and media.

At the end of that time the first tube was milky and opaque macroscopically and teeming with organisms microscopically. The second tube and third tube seemed to be the same to the naked eye but under the microscope the second tube showed some organisms. The third tube was sterile.

The question as to the organisms in the second tube was next considered. Were they merely the loopful which had been

added or had they multiplied slightly? A portion of this inoculated culture medium was added to a fresh tube of broth so that the concentration of trikresol would be about 0.08% (One c.c. inoculated medium to five c.c. broth). This fourth tube with the other three was incubated at 37°C. and it was thought that this would show whether the organisms were merely inhibited from rapid growth or had been killed by the 0.5% trikresol. At the same time a rough test of density of organisms was made by inoculating sterile water of an amount equal to the original broth tube with a loopful of organisms, boiling it to distribute these more or less uniformly and staining. This showed a much greater density of organisms than was present in the original test-tube of broth.

After incubating for two days at 37°C. the fourth tube was found to be perfectly clear and on microscopic examination no organisms were found. To see if this concentration of trikresol (0.08%) inhibited growth, a fresh loopful of the original broth culture was added and the resultant mixture incubated for 12 hours. At the end of that time the medium was opalescent and examination under the microscope showed abundant micro-organisms.

From the above experiment it was decided that trikresol in a concentration of 0.5% killed micro-organisms so that even if any had obtained access to the convalescent serum in the course of preparation - which is very doubtful - they would not merely have been inhibited from multiplying but would have been killed by the trikresol.

At this period of the work there was a falling off in the number of cases of measles. The ground now was cleared and the technique was considered to be sufficiently well developed to warrant its being established. At this period of the work there was a falling off in the number of cases of measles and about two

months elapsed before another case was admitted, it being thought best that no one should be a donor who had not reached the age of ten years. This fifth case was a boy of twelve and it was thought to draw off 60c.c. but his blood seemed to clot very readily and only 40c.c. could be obtained.

The sixth donor was a boy of eleven years and here the blood though fluid when ejected from the syringe into the citrate solution was found to have clotted when later examined in the laboratory. In this case an attempt to retain the clot in the test-tube by a sterile glass rod when decanting into the centrifuge tube caused a slight tinging of part of the serum. It is of interest to note that on the addition of the trikresol there formed within half a minute a hairlike cloud which settled later to the bottom. This was considered due to the precipitation of the protein of the broken red corpuscles by the trikresol and would seem to shed some light on the nature of the so-called muddiness which has been mentioned before in this section.

The seventh donor was a disappointment in two ways. The presence clinically of old healed tuberculosis in the chest precluded the use of her serum for humans but in view of the possibility of later using animals it was thought the serum might be of use in that connection. Only 40c.c. had been obtained when the needle was found to be blocked by clotted blood. Enough serum was obtained from this to form a basis for any such animal experiments. An X-ray examination of this donor confirmed the diagnosis of old-standing tuberculosis but although no activity was found clinically nor shown radiologically the theoretical risks were considered too great to run. It was hoped that more suitable donors would appear before the demand for serum was too great.

The eighth donor was satisfactory, the total amount of blood obtained being 120c.c. Here there occurred clotting in

several of the tubes, the citrate being incomplete in action. This was put down to the loss of time in connecting and in disconnecting the needle and syringe so it was decided to get a two-way tap to speed up the process. In the cases following this tap was used with the result that more blood was obtained in a shorter time with less risk of clotting taking place. Some of the blood specimens, however, became solid despite the rapidity of the withdrawal owing to the increased coagulation speed of the individual so that in every case it was necessary to use the utmost dispatch to avoid cessation of the flow.

During the collection of the serum there were one or two very interesting facts elicited. As has been stated the blood sometimes clotted during the withdrawal and the serum was only separated with difficulty. At other times the blood was fluid when ready for the centrifuge tubes though there was occasionally the beginning of a clot present. Now it was noted that in such cases the spun plasma was of a nature suggesting oiliness and that, on the addition of the Trikresol and after shaking, the imprisoned air bubbles did not rise as usual to the surface. There appeared to have formed a gossamer network of fibrin which penetrated throughout the fluid. The introduction of a sterile platinum needle with slight movement caused this network to adhere to the metal and by gentle rotation the entire fibrin could be removed without more than one drop of the plasma. It was noted, however, that this removal did not entirely clear the fluid nor did it make any great difference in the resulting opacity which developed.

Occasionally there was a loss of a small centrifuge tube of blood when spinning at speed. Here the tube was found generally to be one of the new ones made to replace the breakages incidental to the thorough cleaning each tube underwent between each use. These new tubes were latterly tried in a spin with

water to see if they would withstand the great pressure involved in spinning at 3000-4000 revolutions per minute.

All the adults who were thought suitable for tapping had a blood withdrawal performed but in some the results were disappointing, particularly in Donor No.19, where no veins were seen or palpated and only 12cc.blood could be obtained.

Another difficulty encountered in the process was caused by the difference in gauge of the nozzles of the different syringes. One in particular did not fit the needle very well and the continual slipping, as well as being annoying, allowed some of the valuable material to remain untapped.

At the beginning of the work the Public Health Laboratory test consisted in doing the Wassermann reaction alone. If the result was negative then the batch of bottles obtained from that donor was added to the stock. This was the routine adopted in the cases of donors up to No.25, when as a result of the Copenhagen Conference's recommendation in the matter there was an additional test done - the Kahn test. Donors No.1-26 had negative Wassermann tests. Donor No.27 had a positive Kahn but no Wassermann so that the serum in that case was rejected for clinical use. It was not thrown out, however, but was kept for later laboratory tests. All the donors from No.28 to No.39 had negative Wassermann and negative Kahn tests so they added to the useful store. Now there were two specimens sent in on the same day from Donors No.40 and No.41 and the results of these were that each had a negative Wassermann but that they both had a positive Kahn. These were both rejected for use on contacts despite the negative result of the more established test. Some workers in England have used sera that have given a positive Wassermann result at first followed by a later negative but I do not think that such a course should be countenanced. THERE SHOULD NOT BE THE SLIGHTEST SUSPICION OF ANY DISEASE IN THE DONORS. Of

those donors remaining there was only one, No.47, who gave a positive Kahn test - the Wassermann not being performed.

Thus out of the fifty-four cases who acted as donors there were only four who gave a positive result to the Kahn test. In two of these the result of the Wassermann test was negative and in the other two that test was not performed. This result I consider very satisfactory when it is said that the presence of venereal disease in the general population is very much more than this would seem to indicate.

Several other potential donors were refused owing to the presence or strongly suspected presence of tuberculosis. Only one such - No.7 - was tapped and this occurred at the beginning of the series when the supply of good donors was poor.

The dangerous nature of measles in the adult is shown by the case of a member of the nursing profession. On admission there was a typical measles attack with some signs of catarrh in both lungs. The temperature returned to normal in three days but only stayed so for little over a day when it rose rapidly and she became very ill, the chest showing much catarrh and impaired resonance on the right side. The temperature began to swing, the patient sweated, and a troublesome cough developed. The presence of tuberculosis (suspected on admission) was again brought forward and the spit now present when examined showed swarms of tubercle bacilli. She looked like a case of acute phthisis and the muscles began to waste visibly but this phase of the process became less evident in a short time though the activity still remained pronounced. An X-Ray plate showed the presence of active tuberculosis and also revealed calcareous glands in the root of the right lung. She was later transferred to a phthisis hospital in a very poor state of health both physically and mentally. This case with its cheerless prognosis illustrates very forcibly

the fact that measles in an adult can be a very serious disease indeed.

On the two following pages there are tables showing at a glance the outstanding points about the donors and it is interesting to note some details about them. Contractions are as follows:-

P.I.D.	-	Previous Infectious Diseases.			
W.C.S.M.Gm.	-	Whooping-cough, Chickenpox, Scarlet Fever, Measles and German Measles respectively.			
E.	-	Eyes - Normal, Suffused, Discharging	-	N	S D
K.	-	Koplik's - Unknown, Present, Absent	-	?	P A
R.	-	Rash - Faint, Moderate, Bright	-	F	M B

The following pages do not give the occupation of the donors but this was also noted at the time of the withdrawal of the blood. Glasgow is in a very fortunate position as regards the area which it drains, for, unlike many other big cities, many of the new inhabitants come from the outlying districts where measles is not common. Most of these donors too are of the age of twenty or more when they come to Glasgow to find employment. By far the greater number are Highland girls entering domestic service - in the series here these constituting exactly half of the total. As a centre of education Glasgow attracts others - nurses in training contribute eleven and students at college contribute seven. Thus:-

Domestic Servants	-	27
Nurses	-	11
Students	-	7
Scholars	-	2
Sailors	-	2
Policeman	-	1
Waitress	-	1
Grocer	-	1
Hospital Maid	-	1
Labourer	-	1
Total,		54

Out of the fifty-four cases under consideration there were no fewer than forty who gave a history of having had an attack of whooping-cough. This showed that this disease is very prevalent even among those who are isolated from the other

DETAILS OF THE DONORS.

No.	NAME	AGE	HOME	STAY	P.I.D.	E	K	R	DAY	TEST	WASS.	KAHN	BLOOD	PLASMA	DOSES
1.	Margaret McDonald	23	Tiree.Argyll	-	W	S	?	B	Twelfth	I 10402	Neg	-	60	18	3
2.	Morag Campbell	23	Port Ellen.Islay	2y	W	D	?	B	Eighth	I 10786	Neg	-	80	50	10
3.	Lachlan McCrimmon	24	Skye	-	.	D	?	B	Seventh	I 11215	Neg	-	15	10	2
4.	Angus Morrison	25	Harris	1y 6m	W	S	P	B	Eighth	I 11414	Neg	-	90	50	10
5.	Ian Colquhoun	12	Glasgow	-	W M	D	?	B	Eighth	I 14536	Neg	-	40	20	4
6.	Robert Mitchell	11	Glasgow	-	M	D	P	B	Ninth	I 15033	Neg	-	65	41	8
7.	Kate McCrae	40	Portree.Skye	-	W C	D	P	B	Eighth	I 15034	Neg	-	40	24	4
8.	Alex.Sutherland	26	Applecross.Ross.	3y10m	.	D	P	B	Seventh	I 16897	Neg	-	120	65	13
9.	John Bremner	31	Orkney	4y	.	S	P	B	Eighth	I 17407	Neg	-	120	65	12½
10.	Marion McAulay	24	South Uist.	4y	W C S	D	P	B	Seventh	I 17406	Neg	-	160	105	21½
11.	Flora McLeod	23	Skye	3y	W C	S	A	B	Ninth	I 17408	Neg	-	80	48	9
12.	Margaret James	20	Mull	3w	W C S	D	P	B	Eighth	I 17611	Neg	-	140	87	17
13.	Margaret McDonald	21	Applecross.Ross.	1y 4m	.	D	P	B	Seventh	I 17985	Neg	-	130	82	16
14.	Joan McDonald	20	Uig.Stornoway	2y	W C	S	A	F	Seventh?	I 18034	Neg	-	60	32	6
15.	Mary Campbell	20	Skye	2m	W	N	A	M	Seventh	I 18191	Neg	-	60	33	6½
16.	Christina McFadyen	19	Barra	2m	W	S	A	M	Seventh	I 18192	Neg	-	120	71	14½
17.	Christina Mathieson	30	Stornoway	1m	W	D	P	B	Seventh	I 18227	Neg	-	110	90	18
18.	Norman McLeod	28	Stornoway	-	.	S	P	B	Seventh	I 18228	Neg	-	140	83	16½
19.	Kirsty McLeod	21	Scalpay.Harris.	2y	W	D	P	B	Seventh	I 18229	Neg	-	13	7	1½
20.	Annie McLeod	21	Uig.Stornoway	2y	W	D	P	B	Ninth	I 18394	Neg	-	80	50	10
21.	Kate McIsaac	19	Lochmaddie.N.Uist.	2m	W	D	P	B	Seventh	I 18395	Neg	-	40	26	5
22.	Isa McLeod	26	Stornoway.	5y	.	D	P	B	Twelfth	I 18600	Neg	-	120	70	14
23.	Flora Beaton	29	Strath.Skye.	6y	W	N	A	F	Eighth	I 18844	Neg	-	105	58	11½
24.	Janet McLean	21	Cornaig.Tiree.	3y	.	D	A	B	Eighth	I 18894	Neg	-	80	43	8½
25.	Kate McLeod	24	Benbecula	1y	W	D	P	B	Ninth	I 18037	Neg	Neg	65	48	9½
26.	Jessie Beaton	28	Lochboisdale.S.Uist	3y	W Gm	D	P	B	Seventh	I 19064	Neg	-	76	33	6½
27.	Margaret Mathieson	29	Lochinver.Sutherland	2y 6m	W	D	P	B	Eighth	I 19063	-	Pos	40	24	5

D E T A I L S O F T H E D O N O R S.

No.	NAME	AGE	HOME	STAY	P.I.D	E	K	R	DAY	TEST	WASS.	KAHN	BLOOD	PLASMA	DOSES
28.	Sarah White	25	Symington.Lanark	1m	C S	D	P	B	Seventh	I 19173	Neg	Neg	100	59	11½
29.	Margaret McNeil	24	Stornoway	3y	W	D	P	B	Sixth	I 19174	Neg	Neg	120	72	14½
30.	Peggy McDonald	21	Harris	2y	W	D	P	B	Eleventh	I 19247	Neg	Neg	40	23	5
31.	Sheena Campbell	21	Lochgoilhead	3m	W	D	A	B	Eighth	I 18035	Neg	Neg	90	50	10
32.	Kate McLeod	30	Skye	4m	W C S	D	P	B	Eighth	I 18036	Neg	Neg	120	66	13
33.	Mary McLeod	19	Glendale.Skye	8m	W	D	A	B	Seventh	I 18038	Neg	Neg	120	64	12
34.	Flora Campbell	22	Stornoway	6y	W	S	P	B	Eighth	I 18039	Neg	Neg	120	62	12
35.	Cathie McInnes.	19	Sleat.Skye	2y 6m	W S	D	P	B	Seventh	I 18040	Neg	Neg	40	25	5
36.	Christina McLeod	25	Waternish.Skye	2m	W	D	P	B	Eighth	I 18043	Neg	Neg	140	85	17
37.	Mary White	21	Peebles	1y 9m	.	D	P	B	Eighth	I 18042	Neg	Neg	40	26	5
38.	Johanna McKenzie	21	Kilmuir.Skye	1y 5m	W	D	P	B	Seventh	I 18044	Neg	Neg	140	85	17
39.	Marion McArthur	24	Achmore.Stornoway	2y	W	D	P	B	Eighth	I 18041	Neg	Neg	100	55	11
40.	Christina McDonald	26	Lochmaddie.N.Uist	3y	W	S	P	B	Eighth	J 1066	Neg	Pos	40	23	4
41.	Morag Gillies	20	Leacklee.Harris	10m	.	D	P	B	Seventh	I 18045	Neg	Pos	100	62	12
42.	Mary Montgomerie	19	Stornoway	1m	W	S	P	B	Seventh	J 1282	Neg	Neg	140	80	16
43.	Christina McLeod	41	Stornoway	6m	.	D	P	B	Seventh	J 760	Neg	Neg	140	85	17
44.	Margaret Campbell	28	Ardnamurchan	3w	W	D	P	B	Seventh	J 761	Neg	Neg	120	72	14
45.	Julia Kennedy	22	Tiree	6m	W	D	P	B	Thirtieth	J 762	Neg	Neg	160	98	19
46.	Kate McLeod	23	Stornoway	-	W	D	P	B	Fourteenth	J 763 2419	Neg	Neg	60	37	7
47.	Chrissie McRury	23	North Uist	2y 6m	W	D	P	B	Eighth	J 764	-	Pos	100	61	12
48.	Annie Mullen	18	Co.Sligo.Ireland	1y11m	.	D	A	B	Seventh	J 765	Neg	Neg	120	77	15
49.	Annie Boyd	30	Penbecula	7y	W	D	P	B	Seventh	J 2803	Neg	Neg	120	70	14
50.	Euphemia McKenzie	20	Broadford.Skye	2y	W S M	D	A	B	Eighth	J 2804	Neg	Neg	120	76	15
51.	Henrietta McLeod	20	Lochinver.Sutherland	10m	W	D	P	B	Nineteenth	J 2805	Neg	Neg	20	10	2
52.	Rhoda McKinnon	24	Tarbert.Harris	3y	W Gm	D	P	B	Nineteenth	J 2806	Neg	Neg	160	95	19
53.	Mary McLennan	22	Skye	3y	W	D	P	B	Eighth	J 2808	Neg	Neg	160	70	14
54.	Alexina McDonald	21	Skye	1y 6m	.	N	A	M	Eleventh	X	Neg	Neg	80	40	8

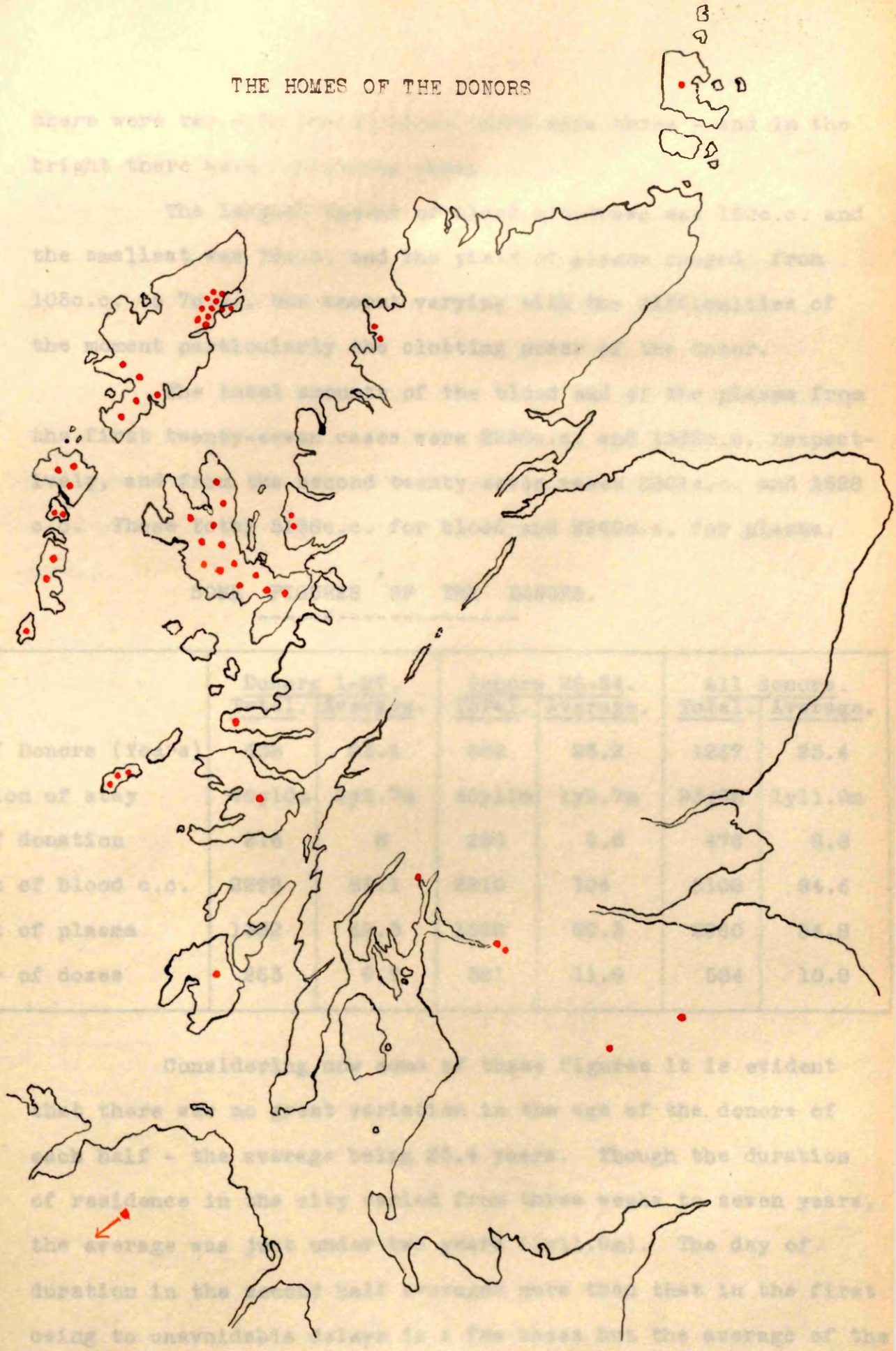
infectious diseases. The next in order - and a very long way behind - was chickenpox, this having attacked only seven of the fifty-four. Scarlet fever had only attacked six of them. Two gave a definite history of an attack of german measles while three said they had had a previous attack of measles. One case of very good measles gave a history of having had a previous attack and, since she had been treated for this in Knightswood Hospital and as the date of the attack was also known, the Journal was searched for particulars. The description found there was that of an attack of german measles and not of measles - no Koplik's spots, no eye symptoms but enlarged glands - so that the only case giving a history of a previous attack that could be verified turned out to have been been wrongly labelled.

The map on the following page clearly shows the distribution of the homes of the donors. Note that the Inner and Outer Hebrides contribute between them forty-two out of the fifty-four.

The duration of the stay of each donor in Glasgow before taking measles was noted. In a few at the beginning this detail was omitted but in forty-five cases it was known. The period varied greatly, the shortest being three weeks and the longest being seven years. In practically all, it was found by careful questioning that the exposure to measles which caused the attack was the first to which the donor had been subjected. This illustrates clearly the susceptibility at all ages.

The different signs on admission were noted. Thus Koplik's spots were not noted in the first four as they were not under the writer's personal supervision, but in the remaining fifty cases they were present in thirty-nine and absent in eleven. The eyes were normal in three, suffused in ten and discharging in the other forty-one. In all there was a rash, the intensity ranging from faint through moderate to bright. In the faint group

THE HOMES OF THE DONORS



Skye	13	Ross-shire	2
Stornoway	11	Glasgow	2
Argyll and Islands	7	Orkney	1
Harris	5	Barra	1
South Uist	4	Symington	1
North Uist	3	Peebles	1
Sutherland	2	Co.Sligo.Ireland	1

TOTAL 54.

there were two - in the moderate there were three - and in the bright there were forty-nine cases.

The largest amount of blood withdrawn was 160c.c. and the smallest was 12c.c. and the yield of plasma ranged from 105c.c. to 7c.c., the amount varying with the difficulties of the moment particularly the clotting power of the donor.

The total amounts of the blood and of the plasma from the first twenty-seven cases were 2298c.c. and 1332c.c. respectively, and from the second twenty-seven cases 2801c.c. and 1628 c.c. These total 5108c.c. for blood and 2960c.c. for plasma.

SOME FIGURES OF THE DONORS.

	Donors 1-27.		Donors 28-54.		All donors.	
	Total.	Average.	Total.	Average.	Total.	Average.
Age of Donors (Years)	638	23.6	629	23.2	1267	23.4
Duration of stay	46y10m	2y2.7m	46y11m	1y9.7m	93y9m	1y11.9m
Day of donation	216	8	260	9.6	476	8.8
Amount of blood c.c.	2298	85.1	2810	104	5108	94.6
Amount of plasma	1332	49.3	1628	60.3	2960	54.8
Number of doses	263	9.7	321	11.9	584	10.8

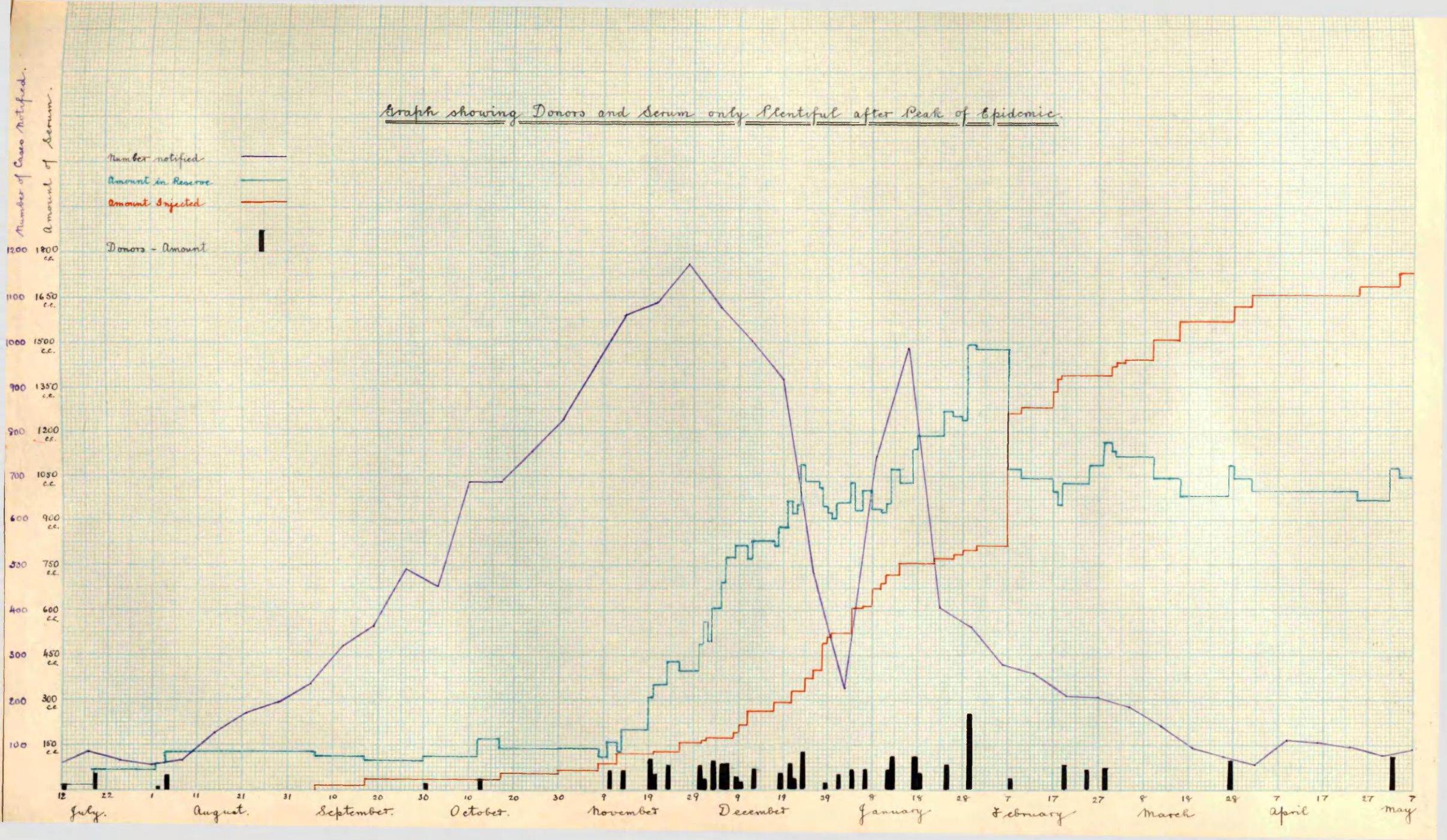
Considering now some of these figures it is evident that there was no great variation in the age of the donors of each half - the average being 23.4 years. Though the duration of residence in the city varied from three weeks to seven years, the average was just under two years (1y11.9m). The day of duration in the second half averaged more than that in the first owing to unavoidable delays in a few cases but the average of the whole group was 8.8 days.

There was a difference in the amounts of blood withdrawn in each half for as time went on the difficulties incidental to the process became less obtrusive and there were fewer

losses of the raw material. The average withdrawn from the second half was nearly 20c.c. more than that of the first half while the resulting amount of plasma exceeded by more than ten c.c. - that is by more than two doses. In all there were over five litres of blood withdrawn from the fifty-four donors and the plasma obtained measured almost three litres.

The graph following shows that the amount of serum and the number of donors only rose after the peak of notifications had been reached and this illustrates one of the practical difficulties in the use of convalescent serum during an epidemic period.

Graph showing Donors and Serum only Plentiful after Peak of Epidemic.



The following page shows a specimen form on which the details of the various donors were noted at the time of the donation of the blood. At the bottom there is shown in diagrammatic form the number of 5 c.c. doses obtained and the results of each individual dose. The number in the square indicates the group in which the dose was used.


indicates a test dose retained in store.


indicates complete protection.


indicates a very attenuated attack (doubtful case)


indicates a primary attenuated measles.


indicates a primary mild attack.


indicates a secondary attenuated measles.


indicates an attenuated attack on later occasion.


indicates a normal attack of measles.


indicates a rejected dose.


indicates a dose still in store.

MEASLES DONOR No. 10. WARD. III JOURNAL REFERENCE. B 25 p 2.

NAME. Marion McAulay (Nurse) AGE. 24 VACC. +

ADDRESS. Stobhill Hospital. Prev.Infect.Dis. Whooping Cough
Chickenpox
Scarlet Fever.

DURATION OF STAY HERE. Four years

PREVIOUS RESIDENCE. South Uist.

DATE OF ADMISSION. 9.11.31. DAY OF DISEASE. Second.

ADMISSION. Koplik's spots. Present.
~~Absent~~.

Rash. Day of appearance. 8.11.31.
Brilliant. Face & chest.
Moderate. Abdomen.
~~Faint~~.

Eyes. ~~Normal~~.
~~Suffused~~.
Discharging.

Cough. ~~Present~~.
Absent.

COURSE OF ILLNESS.

Normal.

First day of normal temperature. 13.11.31.

DATE OF DISMISSAL. 26.11.31.

In Hospital. Pneumonia. Absent.
~~Present~~.

Eyes. Normal.
~~Chronic conjunctivitis~~.
~~Corneal ulcer~~.

Other complications.

Any other notes.

DONATION OF BLOOD. Day of normal temperature. Seventh
Date. 19.11.31.

Result of Wassermann. Negative
Result of Kahn.
Date of the tests. 20.11.31.
Serial number of the tests. I 17406.

Any evidence of tuberculosis. No.

Amount of blood. 160 c.c.

Amount of plasma. 105 c.c.

Notes.

Store	15 Reid	15 McGavin	15 Hamilton	16 McInnes	16 McKay	16 Robertson	16 McInat	16 Spence	16 Monk
16 Emery L	16 Emery R	17 Haggerty	17 Bruce	17 Cook	17 O'Donnell	17 Nichol	17 Williams	17 Thomson	17 Austin
17 McGlashan			15 Collins						

E X T R A C T

of

C A S E R E C O R D S.

In the pages which follow an account is given of a number of instances of cross-infection occurring in the wards of Knightswood Fever Hospital and in many other institutions in and near the City of Glasgow. In giving the day of exposure the rule followed has been that adopted by Zingher of America where the day of the first appearance of the real measles rash is considered as being the fourth day in which active dissemination of the causative agent has been produced by the infecting patient. In other cases the exact day of exposure is known even to an hour as in the case of Little (Group 3) who, through an erroneous history from the outside authorities, was admitted direct to the active measles ward and had good contact there. While admitting that the former method of calculation may be rather inaccurate, at any rate it affords a standard for the different groups of patients in each case of cross-infection so that uniformity may prevail as far as is possible in order not to invalidate any deductions on the score of inaccurate premeses.

CASE RECORDS.

Before going into detail with the different cases under consideration it would be helpful to show the form in which they were recorded. The following pages, therefore, illustrate a typical group and show the amount of ground covered with each patient under observation. It may be stated here that the rule was to consider every child who had not had an attack of measles to be susceptible to the disease, and therefore to be a suitable case for the injection of serum. In a few of the cases the history of an attack was afterwards found to be wrong but since measles itself is practically characteristic in its rash and its concomitant symptoms, these mistakes were very few in number. These cases form controls and they show quite clearly that the infective agent was present in a virulent form.

At the beginning of the work the amount of the serum or plasma was very limited and in order to get the maximum result of injecting it, only those cases of measles crossing our own wards were considered. Later, however, as the supply became greater, the opportunity of utilising it outside Knightswood Hospital was taken. Before this could be done there were some inquiries for serum but we could not meet the demand much as we would have liked to have done. When the reserve amount became abundant there was no question of refusing to utilise it and all the cases occurring were treated with the usual dose.

The scope of the investigation was that of the Health Department of the City of Glasgow. Every child who had serum injected was reported on, and the results, whatever they were, were noted as carefully as possible. The chief indications of an attenuated attack were given to those who had charge of the patients so that as few mistakes as possible would occur in the detection of very modified attacks. Despite these instructions, however, it was found that in a very few cases the signs of such

aberrations from the normal were not appreciated at their true value by those in charge. All such cases have been included in my returns as attacks even of the mildest degree.

Before giving an account of the various groups in the series it would be best to have an idea as to the exact terms of description used and the picture that they should bring to the mind. The results of the injections were classified under four headings so that some comparisons might be made at the end of the work.

Complete protection. This term does not require any explanation.

Attenuated attacks. The patients who took attacks designated thus showed no Koplik's spots and no fever (except perhaps a rise of temperature lasting for one or two four-hourly readings), and little or no catarrhal symptoms. The rash which appeared varied from the just discernable to a fairly definite one and took the form of discrete pinpoints in small areas, more papular in type and certainly never a typical measles exanthem. It generally appeared on the face and occasionally included the body but very seldom appeared on the limbs. Under this heading there did not occur any complications.

Mild attacks. This term included those cases that were a little more definite than an attenuated one but less so than a normal. As a rule there was some cough associated with such cases and more fever in height or length together with suffusion of the eyes and a rash less indefinite than in the preceding group. Here also there were no complications.

Normal attacks. These cases had all the classical signs and symptoms.

A further subdivision was made as regards the case of measles from which the patient was presumably infected.

Primary cases were those who developed the disease after the

original exposure - that is at the end of one incubation period. Secondary cases developed from one of these primaries or from a coincident normal or control case whose history was erroneous. Tertiary cases were those who developed measles from a totally different source perhaps weeks later - the most interesting group of all - indicating the duration of protection.

It is impossible in the space available to give a complete record of all the cases but on considering the various infections there are many points that can be discussed in detail. At the end of this section there are some pages which show in a summarised fashion the results obtained and it is in explanation of these that the following notes should be considered. The routine was to put all contacts, whether or not they had had serum, on four-hourly temperature readings with a view to finding if the temperature were affected, and, if so, the diagnostic significance that might be placed on such readings.

The work necessitated travelling all over the City of Glasgow to the various institutions affected by the disease. These outbreaks occurred in an irregular manner but in Stobhill Hospital where the disease had caused much trouble administratively the effect of the use of serum had a remarkable effect in limiting the outbreaks. It should be noted that though the institutions affected by measles were scattered the method of collecting data and the standard of observation though necessarily varying at times, were practically constants. In this list Stobhill Hospital figures largely but it was observed that the origins of the different exposures were newly admitted children and were not those who had been given injections of convalescent measles serum. On the pages following this list of institutions there is shown a specimen report on Group 4 a cross-infection of a ward in Knightswood Hospital which will indicate in some detail the various points noted about each patient.

The cases were:-

GROUP.		SERUM.	NO SERUM.
1	Knightswood, Wd.1.	3	6
2	Knightswood, Wd.9.	3	1
3	Knightswood, Wd.9.	4	1
4	Knightswood, Wd.1.	1	6
5	Knightswood, Wd.7.	5	-
6	Knightswood, Wd.9.	1	1
7	Scotstoun House.	6	3
8	Knightswood, Wd.7.	1	1
9	Orphanage.	4	-
10	Oakbank Hospital.	1	-
11	Stobhill Hospital 42.	3	1
12	Robroyston Hospital.	3	-
13	Scotstoun House.	5	-
14	Stobhill Hospital 42.	10	-
15	Robroyston Hospital.	5	2
16	Stobhill Hospital 42.	8	-
17	Shieldhall Hospital.	9	1
18	Robroyston Hospital.	5	-
19	Sick Children's Hospital.	3	-
20	Mearnskirk Sanatorium.	15	-
21	Stobhill Hospital 42.	4	-
22	Belvedere Hospital 8.	3	-
23	Baird Street House.	12	-
24	Robroyston Hospital.	11	1
25	Stobhill Hospital 42.	1	-
26	Knightswood Hospital 1.	6	-
27	Belvedere Hospital.	8	-
28	Oakbank Hospital.	1	-
29	Mount Blow House,	3	2
30	Robroyston Hospital.	3	2
31	Belvedere Hospital.	3	1
32	Knightswood Wd.10.	4	-
33	Stobhill Hospital 42B.	6	-
34	Stobhill Hospital 42B.	5	1
35	Knightswood Wd.6.	9	-
36	Stobhill 1B.	1	-
37	Mount Vernon.	6	1
38	Stobhill Hospital 33.	4	1
39	Salvation Army House.	14	-
40	Stobhill Hospital 42B.	8	-
41	Stobhill Hospital 42B.	5	-
42	Stobhill Hospital 42B.	5	-
43	Stobhill Hospital 42.	6	-
44	Stobhill Hospital 42B.	7	-
45	Stobhill Hospital 42.	3	-
46	Stobhill Hospital 42.	5	-
47	Stobhill Hospital 42B.	5	-
S	Bearsden.	1	-
W	Maryhill Barracks.	1	-
Total comparable cases,		245	32
C	Caldwell House.	89	-
GRAND TOTAL,		334	32

Specimen report on a cross-infection of a ward. I.

GROUP 4.

Margaret Brownlie. Age 5 years. P.I.D. Nil.

Admitted 12.55 p.m. 27th.October, 1931, as Laryngeal Diphtheria. Ill since 22.10.31. Sickness, sore throat and croupy cough.

On admission:- Well nourished girl very sharply ill. Face flushed. Tongue coated and moist. Cervicle glands palpable. Both tonsils much enlarged and well patched especially on posterior aspect. Naso-pharynx clean and congested. Heart and abdomen normal. Lungs normal but breathing distressed at times. Troublesome short croupy cough and marked indraw present. Culture for Klebs-LoefflerPOSITIVE. Put in steam tent and given 24,000 units anti-diphtheritic serum. Throat fomented.

28.10.31. Face flushed. Tonsil patches breaking up.

29.10.31. Morning. Some suggestion of mottling on face. Eyes clear palpebral conjunctiva injected, Koplik's spots present. Later measly rash appearing on left side of the neck and on upper chest. Later still the rash appeared on body and limbs. Definite typical measles eruption. A little spot still on left tonsil.

30.10.31. Bright generalised measles rash. Voice husky.

Investigation into the histories of all the patients in the ward showed that three were susceptible to infection, i.e. they had not had an attack of measles. Two of these three were left as controls as they were quite healthy but the third patient who had already been observed (E.Johnstone, Group 1) was considered a very suitable case for any protection that the convalescent serum might confer. When first injected she was a poorly nourished child suffering from old-standing eye trouble and though she was now in a better condition the state of the eye was not yet satisfactory and an infection might easily lead to irreparable damage to the sight. She was given an intramuscular injection of 5 c.c. from Donor No.4, the age of this serum at the time being 86 days. It was given at 4.30 p.m. on 29th.October, so that the patient had been exposed for two days.

Specimen report on a cross-infection of a ward. II.

GROUP 4.

Elizabeth Johnstone. 5 c.c. serum on 29.10.31. (Second day).

22.11.31. Marked photophobia. (This girl had had bad eyes since her admission months before and had had several attacks of photophobia). Short dry cough verging on croup heard. Her normal nasal discharge became more profuse. She was off food and was restive.
23.11.31. Seemed rather listless and cross, eyes worse, discharging (Routine washout of eyes). Cough worse but softer. Suspicion of rash behind ears.
24.11.31. Slight mottling on face. Less but quite definite on trunk - discrete on limbs. She seemed brighter and eyes were less sore. Eating well. No Koplik's spots.
25.11.31. Rash fading and much less evident. Still slight cough.
26.11.31. Slight staining on face. She was brighter.
27.11.31. Back to her normal self.

Marie Brown. No serum.

12.11.31. Little croupy cough.
13.11.31. Temperature up to 101.6 and 100. Cough. Injected eyes.
14.11.31. Blotchiness on face and trunk, tongue coated, tonsils enlarged and speckled, throat congested, post-nasal discharge. Eyes slightly discharging, few Koplik's, troublesome cough. Fairly comfortable.
15.11.31. Rash bright and general. Eyes discharging. Troublesome cough.
16.11.31. Rash very bright. Eyes and cough as before.
17.11.31. Rash fading. Eyes still discharging.
18.11.31. Heavy looking. Nasal and post-nasal discharge. Pulse and respiration increasing. Cough still.
19.11.31. Still drowsy and restless. Croupy cough troublesome. Right gland enlarged. Right ear discharging.
20.11.31. Chest signs suggestive of pneumonia on right side.
22.11.31. Cough not quite so troublesome.

Ival Ferrier. No serum. Discharged early. Mother's report:-

15.11.31. Catarrhal symptoms started.
17.11.31. Spots first seen coming out on nose and chin (morning). Spread later on to the back.
18.11.31. Doctor called in -- Measles (? day of rash).

These three were in the same ward as the original case of measles, and were at first the only ones to be very closely observed. In the adjoining ward there were other four patients who had not had measles but there was no great chance of them

having been exposed to the acute case. However, even though the only means of a transfer of the infective agent was by a door that never was open the contagium attacked the two who were far from the communicating door. The infective case, Brownlie, as is shown in the accompanying sketch, was fairly near the door and the fact that the adjoining ward was crossed in this way illustrates once again the extreme infectivity of measles.

Specimen report on a cross-infection of a ward. III.

GROUP 4.

Eileen McElvenny. No serum.

8.11.31. Face flushed.
9.11.31. Throat sore. Fretful.
11.11.31. Throat painful. Colour changeable.
12.11.31. Typical prodromal rash bright on face and behind ears. Koplik's spots present.
13.11.31. Prodromal still showing on face and ears. Very faint on back and trunk. More Koplik's spots. Later, rash fading on body and face.
14.11.31. No rash visible. Eyes very suffused. Later, faint rash on face.
6 p.m. Face swollen with brilliant rash. None on body. Many Koplik's spots.
15.11.31. Faint rash on face. Eyes more suffused. Faint rash on body. Later brilliant on face and behind ears, but faint on body.
16.11.31. Brilliant rash on face, bright on back and trunk, faint on limbs. Later, brilliant all over and very blotchy. Koplik's spots going. Stools green.
17.11.31. Pyramidon given. Rash still bright and blotchy.
18.11.31. Left ear discharging profusely. Rash fading. Later, right ear discharging profusely. Rash gone.
19.11.31. Ears discharging.
Ears discharging profusely for weeks with temp.
26.12.31. Mastoid operation was performed. Slow recovery.

James McLauchlan. No serum.

13.11.31. Rise in temperature to 99 and 102.
14.11.31. Very faint blush on chest and arms. Face flushed.
15.11.31. 8 p.m. Eyes suffused. Few Koplik's spots. Faint rash on trunk and face, more on brow, and body practically free. Spots on neck and behind ears.
16.11.31. Less evident rash but some suggestion of mottling on brow, face and chin. More Koplik's spots.
17.11.31. Morning. Brilliant rash on face.
Evening. Brilliant on body and limbs.
18.11.31. Good general rash, face, body and limbs.
19.11.31. Fading on trunk - brilliant on lower limbs.
20.11.31. Rash completely gone. Improving.

Donald McDonald. No serum.

6.11.31. Dismissed well.
30.11.31. Reported well and free from measles.

Ian McLauchlan. No serum.

10.11.31. Dismissed well.
27.11.31. Seen at "GATE". Known to have been free from measles.

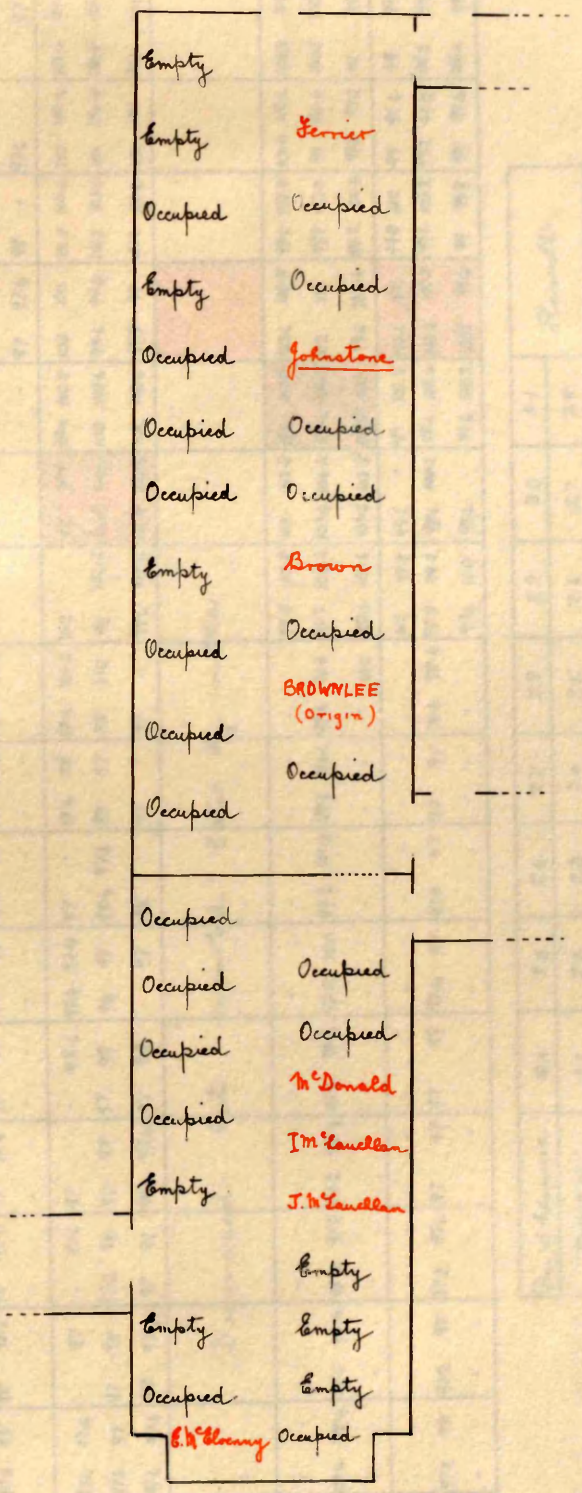
Specimen report on a cross-infection of a ward. IV.

GROUP 4.

Knightswood Fever Hospital

Ward 1.

Susceptibles in red.
Injected underlined.



GROUP 4.

Knightswood Fever Hospital.

Ward 1.

Specimen report on a cross-infection of a ward. V.

Day of Exposure		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		Result.
DATE		Nov 5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		
		AM	PM																															
E. Johnstone SERUM	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	97	97·6	97·6	97·4	97	97·2	97·8	See continuation.
	6	97·4	98	98	98·8	98	97·6	97	98·6	98	97	97	98	97·6	97	98	97·4	97·6	97·4	97	97	97	97	97·6	97·4	97·4	97	98	98·4	97	98·6	97	97·6	
	10	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	97	97·4	98	1	97·6	.	.	97	
M. Brown	2	97·4	97·4	.	97	.	97·6	97	.	.	98·6	97·4	97·4	97	.	98·4	98	98·4	101·6	102	.	102	101	100·6	100·8	100	100	101·8	100·6	100	100·4	101·4	101·6	Measles
	6	97·4	97	97	98	97·2	98	97	98	97	99	98	97	98·4	97·6	98	97	98	100	99	102·2	101·8	100·4	100	100·6	99·6	99·4	101·2	102·4	101	100·8	100·8	101·2	
	10	97·6	97·4	97	97·6	97	98	98·4	97·4	97	98	.	97	98	.	97	.	97	.	99·6	102·6	101·4	100·8	102	100·6	99·8	99	101·2	101·6	102	101	101	101	
J. Ferrier	2																																	Measles
	6			Dismissed but reported later by mother.																														
	10																																	
E. McElvenny	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	99·8	102·8	102	102·8	103	103·8	102·6	100·8	99·2	102·8	101·4	100·6	100·8	100	Measles
	6	97·4	98·4	101·6	98·4	98·2	97·2	97·2	98·4	97·6	99·6	98·8	100	99·2	101·2	99·4	101·6	98·4	103	99·2	104·2	103·4	104·4	103·4	104·8	102	103	99·8	103·2	99	100·4	100·2	100·6	
	10	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	100	102·4	102·6	103·2	103·8	103·8	103	99·4	102·4	101·2	102·6	99·8	99·2	101	99·6	
J. McLauchlan	2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	102	99·8	99·2	.	99	100·2	100·4	101	99·8	100	99	99·6	99	99·2	Measles
	6	97·2	98	97·2	98	97·2	97·6	97	97	97	99	97·4	97	97·8	97	97	97	98·6	98·4	98·8	99·2	98·4	100·2	98·4	101·4	100·2	100·8	99·6	100·2	99·2	99·2	100·2	98	
	10	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	97·4	100	99·2	.	99·6	100·2	100·8	99·4	99	99·8	99	99·4	100·6	99·2	

continuation

Day of Exposure		24	25	26	27	28	29	30	31	Result.
DATE		21	22	23	24	25	26	27	28	
E. Johnstone SERUM	2	97·6	.	98·6	.	.	97·8	99·8	98	98	97·6	98·6	.	97·6	97	97·6	98	Very attenuated measles
	6	98·6	97·2	98	98·6	97·4	98·4	99	97·6	98·4	97·6	99	97·2	98·4	98	97	98	
	10	97·6	.	98·4	98	98·8	98·4	97·4	.	.	.	97·4	.	97·4	.	97	98	

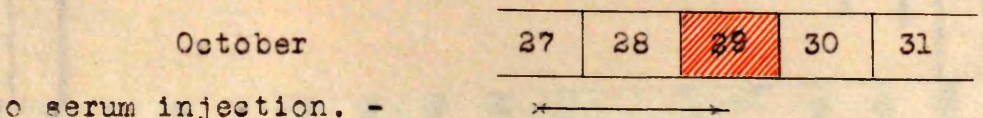
Day of rash in red.

G R O U P 4.

Knightswood Fever Hospital.

Ward 1.

Name.	Age.	Ward.	Serum	Donor	Day	Age of serum.	Fever.	Catarrh.	Koplik.	P rash.	Rash	Results.
M.Brown	2y	S	-	-	-	-	16	15	17	-	18	Measles
E.Johnstone.	2y 8m	S	5cc	4	2	86	27/13	25/11	0	-	27/13	Attenuated measles.
I.Ferrier.	4y 6m	S	-	-	-	-	?	18	?	-	20	Measles.
D.McDonald.	1y10m	A	-	-	-	-	-	-	-	-	-	No measles.
I.McLauchlan.	5y 6m	A	-	-	-	-	-	-	-	-	-	No measles.
J.McLauchlan.	4y	A	-	-	-	-	16	18	18	18	20	Measles.
E.McElvenny.	4y	A	-	-	-	-	12	15	15	15	18	Measles.(Severe)



From exposure to serum injection. -

GROUP 1. The temperatures of the contacts were taken four-hourly from the tenth day of exposure but in spite of this precaution the first sign of the infection occurring in the patient Jenkinson was the catarrh on the fifteenth day causing a slight cough, followed on the next day by suffused eyes and Koplik's spots. On these points alone he was transferred to an observation ward and that evening he had the beginnings of the prodromal rash - all these being accompanied by a normal temperature. It was not indeed until the following day at 10 a.m. that the temperature rose at all. This was not what one would expect to find judging by the textbooks and the delay in the fever till the 16th. day of exposure was also unusual. The prodromal rash - a lenticular eruption of widely scattered spots brownish in colour - was described by Pickering Pick in 1926 as occurring in 50% of cases. It is in a way suggestive of measles but closer inspection makes one doubt the diagnosis. Once seen, however, it is fairly easily recognised, but the exact verbal description is not easy.

It is difficult to explain why Rennie, who was, if anything, in closer contact than Jenkinson, should not catch the infection directly but should take it from McLeod, that is, on exposure to a second case. The times of the first real measles rash in the contacts in Group 1 were almost a constant (17,18,17) and this time 17 days was the same time exactly from the catarrh of McLeod to the rash of Rennie, so that it is only reasonable to conclude that Rennie was a contact case of McLeod.

Since these cases all occurred in a diphtheria ward, in consequence of the claims of some continental workers as to the efficacy of Anti-diphtheritic serum in the prophylaxis of measles, the details of the injections each contact had had were noted. Jenkinson, who took measles on the first exposure had had Anti-diphtheritic serum only twelve days before contact, whereas Rennie, who escaped the first contact, had had Anti-

diphtheritic serum 42 days and Anti-scarlet-streptococcal serum 32 days before. This seems to indicate that Anti-diphtheritic serum has no effect on the measles infection but leaves open the question as to the prophylactic action, if any, of Anti-scarlet-streptococcal serum.

Of the two who were given measles convalescent serum in the same ward none took measles but of the four without it three developed the disease - the fourth being a boy of ten who, though his history was negative, might have had it before.

GROUP 2. Here again two cases were susceptible and the one that got the serum remained free whereas the other developed measles. This cross-infection took place in one of the scarlet fever wards of the Hospital and the description of the case developing measles is not without interest.

Jean Taylor. 2 years of age. No serum was given.
Exposed to a case with the rash on 17.9.31.
She was normal and perfectly well till 29.9.31.

29. 9.31. 6 p.m. Temperature normal. 7.30 p,m. Temperature 100°. Eyes very heavy and very measly looking though no distinct rash. Palpebral conjunctiva injected but bulbar clear. Koplik's very scanty. Faint lenticular eruption on body not macular measles nut like the prodromal rash of Jenkinson (Group 1).

30. 9.31. Restless night. Watery eyes and short cough. Forenoon. Rash slightly more pronounced. Koplik's spots marked. Right eye suffused - left apparently normal.

TRANSFERRED.

Evening somewhat similar. Slight rash on face.

1.10.31. Bright typical measles rash on face - less on trunk. Evening - good rash on trunk.

2.10.31. Typical eyes and rash. Beautiful measles.

3.10.31. Rash fainter. Right ear discharging profusely.

4.10.31. No discharge from ear.

15.10.31. Dismissed well.

GROUP 3. In this case Hughes was given 5 c.c. convalescent serum on the fourth day of exposure but showed signs of modified measles notwithstanding. This result was contrary to what was expected and the reason for this partial failure was sought. The main reasons for failure in the results from the use of serum are insufficient dosage, bad timing of injections, excessive age

of the serum, poor health of the patient and poor quality of the serum. The dosage in this case was adequate since similar doses had protected other cases; the fourth day was the one on which others had thrown off the infection at that time; and the general health of the patient was excellent. There only remained the age and the quality of the serum. The same serum No.2 had given good results before but these had been obtained when it was 61 days old. The dose used in this case was aged 90 days and was from one of those bottles which had been heated to 56°C. for twenty minutes on three different days. Either of these factors might be responsible for the partial failure though the complete success of an identical dose eight days later indicates the possibility of another factor.

There is no doubt but that the attack which Hughes developed was less severe than a normal one; it took longer to show; there was practically no constitutional disturbance (the child played and was bright all the time) no Koplik's spots were seen though carefully sought and the catarrhal symptoms were slighter than normal. The absence of any reaction whatever on the part of Woods might be explained by the difference in ages. Woods at six years of age was almost bound to have had subminimal doses of infection and the amount of protection afforded ny the convalescent serum would be sufficient to turn the balance in his favour. Hughes at one year was without this advantage and so was exposed to the infection to a greater degree.

The original case of measles was transferred to an isolation ward from a scarlet ward. On the same day there was admitted a boy suffering from scarlet fever with a history of exposure to measles outside the Hospital and he was put with the original in a little ward of two beds. It was later found that the new patient had not really been exposed and had no history of an attack. He seemed a healthy boy and it was considered that

in his present state a modified attack might be obtained. Accordingly he was left in the closest contact until the eighth day of exposure when 5 c.c. were given intramuscularly. (No.2h 98) Apart from a slight flushing four days later he showed no signs of infection though these were looked for carefully. He was dismissed free on the 30th. day of exposure. Many of the cases who had been injected and who remained free while under observation were requested to report to the Hospital if at any time through the winter they developed the disease. This child was one of the few who did so. His mother reported that he had a measles rash on 31.12.31, and that the whole body was covered. He was in bed for three days but had no eye symptoms and no complications of any sort. He therefore had an attenuated attack on the 75th. day after the original exposure. This shows that the effect of the serum is not evanescent though for complete protection the time of utility is limited.

GROUP 4. This is the group selected for the complete report as shown in some previous pages. As can be seen from the notes there, one of the susceptible contacts in the same ward was dismissed but notes as to his attack were sent by his mother. The other two were followed closely and the non-injected took measles with the rash on the fifteenth day - the injected case showing the rash on the twenty-fourth day. Now, since the serum had been given on only the second day of exposure, it was expected that complete protection might be assured, especially since the same child had escaped in Group 1 with serum on the second day then. Despite this she took the infection - in a very attenuated form to be sure, but that she took it at all was rather disturbing. She was an interesting case who had been admitted with pneumonia a very long time before and who had had very weak eyes since before admission. As she had a profuse nasal discharge which contained Klebs-Loeffler bacillus she was transferred to the

diphtheria ward. Here the eyes still gave trouble and when she was exposed in Group 1, it was thought that at all events she must be protected from measles as that disease would most probably ruin her sight completely. She was protected. This time though the eyes were much improved they were still troublesome and it was again feared that ulceration might ensue. There was no cause for concern - she was not in the least distressed with the attack. She had been on the list of those awaiting tonsillectomy and she had the operation on the eighth day of the second exposure. The rash appeared on the nineteenth day after operation. This would seem to suggest that had the throat been left no attack would have followed, but with the formation of new raw areas the virus of measles still present was able to increase till it was just sufficient to overthrow the effect of the 5 c.c. measles convalescent serum thus producing an attenuated attack.

With these three cases it was thought that that cross-infection had ceased. However, in the adjoining ward a little girl showed some signs of early measles and shortly after that another patient also showed signs of contracting the disease. The notes that had been taken on the occurrence of the original case showed that there were four children in the adjoining ward who at the time had not had measles. Of these two had been dismissed and the other two who had remained in hospital contracted the disease. Some investigation revealed that both the dismissals had escaped the infection up to a period of 32 and 35 days after their exposure. The little girl who took measles had a very severe attack, developing double otitis media which persisted with high temperature for weeks, ultimately requiring a mastoid operation; but the boy took an ordinary sharp uncomplicated attack and was dismissed well on the thirtieth day after exposure. The girl who developed the double otitis had had her tonsils and adenoids removed on the same day as the other patient

- eighth day of exposure - and this certainly seems to have had some influence in opening the pathway of infection to the middle ear.

GROUP 5. The only point in this Group is that one of the injected who was given serum on the third day showed a measles rash on the sixth day of the presumed exposure. Since this is quite out of the realms of possibility she must have been in contact with another case outside and must have been incubating the disease on admission. The appearance of the rash on the third day after injection seemed a good chance of testing the phenomenon of Debré. He said that injection of convalescent serum shortly before the rash inhibited it locally. This serum had been given into muscles of the thigh and there was no sign of any prevention, but there might have been no leakage of serum along the track of the needle and so the serum might have had no chance to show this effect. Several of the children injected here were very ill but no bad effects

GROUP 7. This was the first in the series that did not occur in the Knightswood Hospital itself. Measles broke out in a Convalescent Home in connection with the Child Welfare Scheme in the City, and serum was given to six susceptibles on the first day after the rash - three receiving serum 99 days old and three 42 days old. These were all the cases thought to be liable to the disease but two others took it though a positive history had been given. Later still another child took measles from one of those of the first exposure and though she was not a contact of the original of this outbreak she is included here for convenience. All three given serum aged 99 days took measles - one on first exposure and the others on exposure to a later or primary case. The primary one had a very attenuated attack while the controls showed a typical course. The two secondaries took very slight measles and neither was in the least bit upset or ill. The third

control who was exposed to one of these secondaries took a severe attack and ran a temperature for a considerable period.

GROUP 11. By this time the practice was to give all susceptibles the benefit of the serum and so no controls were left deliberately. Three children were given the serum in this instance but one was omitted and she took a good measles attack. The Doctor in the Ward in Stobhill Hospital where the cases occurred had heard of serum prevention and in trying to prevent the onset of the disease had given this last case 5 c.c. of the mother's blood. This was not sufficient and it had no effect on the course of the attack.

GROUP 15. This exposure occurred in Robroyston Hospital and all five susceptible contacts were given serum. Two remained free, one had a typical attack of measles, one a primary attenuated and one a secondary attenuated attack. Much later one of those kept free took an attack of measles and showed the rash 45 days after this exposure and 17 days after the other exposure. This last attack was slightly modified but not to a very great extent showing the evanescence of the protection conferred. The one showing pure measles was really in the invasive stage when the serum was administered, with suffused eyes, temperature 100°, slight croupy cough and a suggestion of Koplik's spots in a mouth deeply congested but there was no rash to be seen on the body or behind the ears. As it was considered that she was developing measles only part of the serum was given intra-muscularly, the last portion being administered subcutaneously with a view to finding if the phenomenon of Debré could be produced. The attack that followed was not in any way modified and there was no local inhibition of the rash at the point of injection.

A little girl, Stirling, in the same ward, did not get serum as she had a history of having had measles. However, she developed the disease and so formed a valuable control. Another

child also took it - she also having been left alone since there had been no actual contact. When she took the disease inquiries were made and though she had been in a ward by herself all the time, by careful questioning it was found that after all the injections had been given the suspicious case, McLauchlan, had been removed from her Ward and before being transferred to a free Hospital had passed one night in the room occupied by this little girl. There is no doubt but that the disease was transmitted then, the incubation period coinciding perfectly with previous experiences in that direction.

GROUP 16. Here there were three different cases of origin, the times of exposure being 4, 6 and 7 days. Only one child showed that the infection had prevailed and that occurred after an injection on the fourth day. This case had a temperature on the 14th. day of exposure with eyes and nose discharging but on the following day he was normal. On the 22nd. day he had a slight rash with no rise in temperature and with no discharge from eyes nor nose. He never appeared ill and there were no complications.

GROUP 17. Shieldhall Hospital was the scene of this outbreak, two different origins being known causing exposures of 5 and 10 days. Of the nine who were given serum only one took measles and that in an attenuated form. As in many of the other cases the temperature was up only for two four-hourly readings, no Koplik's spots were seen and there was no sign of a rash below the nipples. The rash in this case lasted only six hours - a tribute to the observation of the nursing staff there. In this case there occurred another of the controls which were noted as they arose. A domestic servant of 24 years was in the same ward but was dismissed on what was the tenth day of exposure being at that time quite well. Later word was received that she had developed measles after dismissal. Her sister was in Knightswood -

in fact she was Donor No.45 - but there was no contact at all since the donor was in hospital during the period available for dissemination of the virus. Through her and a friend information was collected about this case who never had had measles before. She took a good attack lasting for several days but with no complications.

GROUP 18. This was another exposure in Robroyston Hospital where the serum did not give the good results that it gave elsewhere. Out of five cases injected only two remained perfectly free. Two took an attenuated attack with the rash on the 12th. day while the third on the 13th. day gave a rise in one four-hourly reading with the suggestion of a faint rash for an hour or so. Doubtful as this case is, I think that it ought to be included in the series as an extremely attenuated form of measles. It is interesting to note that this last case was, at the time of the faint eruption, in the next cot to that of one of the other attenuated attacks when the rash there was good. He was observed for the time necessary for the development of measles from this second exposure but did not show any reaction whatever. From this then there is some evidence that measles had attacked him and given him some active immunity.

GROUP 20. Mearnskirk Hospital was the institution attacked here. Owing to observation room being fully occupied a case was admitted directly to the treatment ward and it happened that this case was incubating measles. As it was at Christmas time all the patients were mixed more than was usual so that infection was widespread. Altogether fifteen patients were exposed who had not lad measles and it is gratifying to record that on no instance was the disease contracted. Since all these children exposed were sufferers from tuberculosis much trouble might have ensued had measles gained a footing there.

GROUP 21. This was a very interesting instance of cross-

infection, for, occurring in Stobhill Hospital where so many others had been, an opportunity of testing the duration of the protective power was possible. There were six cases who had not at any time had measles but out of these there were two who some time previously had been given an injection of the serum with beneficial results. Accordingly it was thought that they might be left alone this time to see what would take place, so that if it did not actually prevent an attack it might modify it highly and so give an active immunity. The other four were given serum in the usual way. These last four remained free and of the other two one only showed any reaction. On the 41st. day after serum had been administered and the 18th. day of this second exposure a slight rash appeared. The child was not ill but there was some discharge from nose and eyes; the rash was faint on face, neck and trunk, none being seen on the limbs. There were no complications and the temperature at all times was normal.

GROUP 22. Belvedere Hospital was the scene of this cross-infection. All three cases were exposed for ten days before word was received about the outbreak. The usual small dose of 5 c.c. was given but little hope of complete protection was considered. One remained free; one took an attack of scarlet fever on the 14th. day of exposure to measles and was transferred to observation; the other seemed free also. The scarlet rash came out on the 14th. day with a temperature of 103.8^{o} and a sore throat. Two days later a measles rash appeared through the still-present scarlet rash but there were no Koplik's spots to be seen though they were searched for with care. Four days later the temperature was down to normal. The third case who had escaped the first chance of infection was brought down by the second. On the 31st. day of the original exposure and the 19th. of the second there appeared a rash with short cough but no Koplik's spots. Photophobia with some suffusion but no conjunctivitis was present. The rash soon

faded and at no time was the child ill. The case with the scarlet fever attack is difficult to estimate as regards the degree of severity of attack owing to the coincidence of diseases but the absence of Koplik's spots and of eye symptoms and the short duration of fever show at the least some mitigation of the disease. The other case escaped the first exposure as the period passed with no sign of reaction but took measles at the distance of an incubation period from the attack of the scarlet fever case. Since that patient was removed from contact on the onset of the scarlet fever and since the measles rash did not appear till two days later this illustrates very forcibly the extreme infectivity of the disease in the first part of the invasion period.

GROUP 23. The origin of the outbreak here caused seventeen to be exposed. Though six of these were children who had had an attack of measles they were given some serum as it was thought better to minimise the risks of serious results in an institution devoted to tuberculosis children. This time the serum was administered with a different view so that some were given more than others. Some were given 5 c.c. that might totally prevent infection while others were given smaller doses with a view to getting an attenuated attack (these latter being in a much better state of health than the former). This opportunity was taken as the notes available would be especially good. The serum was given on the sixth day of exposure in doses of 5 c.c., 3.4 c.c. and 1.7 c.c. The results were at first very misleading though the serum in all was from the same donor in order to avoid any added factor. Eleven cases had a negative history of measles and of four given 5 c.c. all took primary attenuated attacks; of three given 3.4 c.c. one took attenuated primary attack and the other two remained free; of four receiving 1.7 c.c. three took mild measles and one remained free. Of the six with a positive history one who received 1.7 c.c. took mild measles thus showing the

history of measles was inaccurate. Analysing the figures further it is seen that when the dose, donor and day are the same there is a variation with the age of the patient. Of the three receiving 3.4 c.c. the two older were protected, and of the four getting 1.7 c.c. the oldest remained free from measles. A feature of these cases was the fact that there was no typical measles rash, those eruptions resulting being more of a discrete papular type than a macular exanthem. None of the children was really ill and thought almost all of the cases took an attack it was of a very attenuated type and this was after all the end in view at the time of injection.

GROUP 24. In this case there were two separate cross-infections considered, the days of exposure being five and nine days respectively, with eight patients in the first Group and three in the second. In the first Group there were two who took primary attenuated attacks the onset being definitely delayed, and a third took a secondary mild form of measles later, the rash appearing on the 31st. day of the original exposure and the 16th. day of exposure to the later case. Out of the three in the second group who had been in contact for nine days before serum was given, there was one who took attenuated measles. Another of the unwitting controls occurred here, but the details of these attacks in full will be shown later in the work. In some of the cases there seems to have been more protection from the injection than might be expected from the reports of some other workers but that the infection was actually present in a virulent form has been demonstrated clearly from time to time in the series under consideration.

GROUP 29. This case occurred in Mountblow House at Dalmuir West, another institution in connection with the Child Welfare Scheme in the City. Three little children who were liable to take measles were exposed and they were given an injection of

5 c.c. serum for protection. They were observed for some time but owing to an outbreak of chickenpox they were sent home before the expiry of the incubation period. They were traced later through the Public Health Department of the City and it was found that none had developed measles. Here again another of the fortunate controls occurred as one of the nurses who had attended the children in question took measles with a typical attack followed by pleurisy. It is interesting to note that one of the three who remained free later became the origin of another outbreak in a third Home for Children. (Group 37).

GROUP 31. Measles broke out in one of the Scarlet Fever wards in Belvedere Hospital exposing three children who had not had an attack. Of these three there was one who took a primary attenuated attack while the other two remained perfectly free. There was one little boy who had a positive history of measles and on that account was left alone when the other injections were given. Later, at the end of the usual time, he developed measles of a good type and thus forms a contrast to the attenuated attack after serum.

GROUP 32. This is remarkable for the unusual occurrence of measles of an attenuated type after serum given on the fourth day of exposure. Four cases got injections from Donor No.25 and only one remained free, the others developing attenuated attacks after a prolonged incubation period. The one who remained free was eight years old and the contact in her case was not as close as in the others. Since so many had been totally protected by a similar dose of the fourth day it is possible that the serum from that donor was not as powerful as the normal convalescent serum. The attacks were attenuated, one being to such an extent that unless careful watch had been kept for the slightest aberration from the normal its onset would have been most certainly overlooked.

GROUP 33. Six patients here were given the injection on the

sixth day of exposure. Two of them took attenuated attacks showing the rash on the 22nd. day while a third took a secondary attenuated attack on the 27th. day (20th.) day of exposure. The rashes in all three were not typical measles eruptions but highly modified, though there was some temperature elevation. There were no Koplik's spots to be seen at any time here.

GROUP 34. In this instance the serum was administered on the fourth day. In one case, Baillie, there appeared on the following day a slight rash on the neck with discharging eyes and an elevated temperature. It was particularly noted that the area over the site of the injection showed not the slightest suggestion of a rash while all round there was a definite measles eruption, the free area extending $1\frac{1}{2}$ inches by 3 inches. There was no other effect to be seen - the attack being in all respects a normal one. Another child developed a rash five days after the original and must have been in the invasion period when injected as his temperature was up. He took a severe attack with broncho-pneumonia and died on the day following the appearance of the rash - a very acute measles. Another interesting patient in the Group under review was one who ran a temperature and on the eighth day of exposure to the measles case showed a good punctuate scarlet rash for which she was transferred to Belvedere Fever Hospital. Her right ear discharged and the cervical glands also became purulent and required incision later. There was no great change in the discharges until the 26th. day of exposure when harsh crepitant rales indicated broncho-pneumonia - a condition from which she died three days later, never having shown any sign of measles. There was still another patient considered here, a little boy of three months, who was not given serum as it was thought that he would have sufficient inherited immunity. On the 19th. day he showed a brilliant measles rash with ?Koplik's spots and discharging eyes. Shieldhall Fever Hospital received this case

and the report there stated that there was a morbilliform rash on face, neck and trunk, but none on the limbs. The spots were mostly discrete - not typical measles - and faint, faded soon and left no staining. It is worthy of note the similarity of the attack in this very young child to the type of attack after the injection of measles convalescent serum. The inherited immunity had not worn off sufficiently to render the child susceptible to a real severe attack but yet there was not sufficient left to prevent the onset of the disease. In Shieldhall the Doctor stated that he was doubtful of its being an attack of measles at all, but then he had not previously seen attenuated measles.

GROUP 37. This case of cross-infection occurred in the third of the Homes connected with the Child Welfare Scheme of Glasgow, Mount Vernon House. The origin was the same little girl who was mentioned in Group 29 as having been dismissed from Mountblow on account of an outbreak of chickenpox there. She must have been exposed to a later case for on the 39th. day of the original exposure she showed a rash of measles. There were no eye symptoms, no Koplik spots and no temperature. The rash when examined on admission to Ruchill Fever Hospital was fading (this was the day of its appearance) and the child was never at any time ill. This was undoubtedly an attenuated attack of measles. Six susceptible contacts were given a protective dose of the serum and four remained perfectly free. One took an attenuated attack with no rise in temperature, no Koplik's spots, no eye symptoms and only a faint discrete measly rash on trunk and limbs. Another case showed a rise in temperature on the 21st. day and on the following day was removed to Belvedere as chickenpox. The rash was papular on the trunk, especially on the back, and there were no nose nor eye symptoms. On the next day again the rash came out on the forehead and behind the ears raising the question of measles. The Doctor here also had had no experience of attenuated measles to

guide him in the diagnosis. The temperature remained normal. To my mind this was a case of very attenuated measles. The temperature was up for only one four-hourly reading, the rash was very suggestive and the fact that no vesicles developed clearly excluded chickenpox. The day of exposure also was a factor that indicated the great probability of this being measles of a very attenuated type.

A girl in the same ward as the original case, who, owing to a history of a previous attack had not been given serum, showed on the 15th. day a rise in temperature with a cough. Two days later the eyes became red and suffused and a discrete measles rash appeared which later became quite raised and brilliant. The eyes and nose discharged, the rash became generalised and rhonchi appeared at the base of the right lung. Three days after this the rash began to fade. This then was a good typical attack of measles resulting from exposure to a definitely attenuated attack, showing that the influence of the serum is on the body of the recipient and not on the causal agent of the disease itself.

GROUP 38. Here there were four patients who were given serum and of these three remained perfectly free of the disease. The other showed a rash on face and body but no Koplik's spots and no catarrh. The rash was more a papular one and not at all bright. There was neither eye symptom nor temperature. There was a girl in the same ward who was said to have had measles and who on this account did not get an injection. She developed a measles rash on the 13th. day and was transferred as an ordinary case of measles.

GROUP 39. This is one of the outbreaks that command attention in the demonstration of the good results from the serum. Measles occurred in the Salvation Army Home for Children in Pollokshields and of fourteen susceptibles exposed and injected, not one took the disease.

GROUP 40. This cross-infection occurred in the same ward in Stobhill Hospital as all the previous ones, in this instance eight children being injected. Here there were four who did not survive long enough to be included in the series as they died from the trouble for which they had been admitted. When one considers the number of children who were extremely ill and who therefore were liable to be an easy prey to measles one is struck by the small number who succumbed during the period of observation. None of the other four children showed the least sign of infection, remaining normal throughout.

GROUP 41. Five little patients were exposed here and serum was given on the seventh day. One died from another illness before the observation period was up; two remained free while the others took measles of a modified type. One showed a moderate rash with eye and nose discharges but the exanthem did not last long. This child had from his admission a pulmonary condition that did not clear up completely so that the exact type of measles attack is difficult to determine. It was more of a mild than an attenuated type. The second patient who did not remain free showed a very indefinite rash on the body and neck unaccompanied by either eye or nose discharge. This rash appeared on the 14th. day but the temperature only rose for two four-hourly readings on the 16th. day.

GROUP 43. Out of six cases who were given an injection of 5 c.c. of the serum only one showed signs of having developed the disease. On the fourteenth day the temperature rose and the eyes discharged, a rash appearing on the abdomen and legs. Later the rash developed and the temperature remained high. Difficulty arose with the swallowing and a croupy cough appeared. Diphtheria was suspected and the appropriate serum administered. There appeared later a patch of pneumonic consolidation at the right apex. A consultant to the Hospital (Stobhill) examined the

throat which appeared quite clean as far as ordinary examination showed and found there was membrane covering the vocal cords. The throat culture was negative but this, of course, does not exclude diphtheria. Two days before death, which took place on the 23rd. day, there was a certain amount of indraw.

GROUP 45. Out of three cases who were given serum on the seventh day one took measles. On the nineteenth day there was a rise in temperature and the patient was not well. She had been admitted with pneumonia and this had never quite settled. On the 24th. day a faint rash appeared on the neck and limbs - very slight on the body. Eyes were discharging but this was not a new feature. This case was not seen personally and the Doctor in charge notified the case as one of german measles. From the details supplied, especially as eyes were involved and there was some pulmonary trouble, it is more likely to have been measles. The faintness of the rash shows that it was in some degree attenuated and the report, "eyes discharging as before", would seem to show some pre-existing trouble there. While the presence of an unresolved pneumonia complicated the estimation of the intensity of the attack - the lengthening of the incubation period lent weight to the view of modification. Perhaps the best type classification would be "Mild measles".

GROUP 46. Five patients here had an injection of the serum on the eighth day of exposure. One died during the period of observation and one took a primary attenuated attack. On the 22nd. day this last showed a very faint ? measles rash on face and neck at night, with slightly watery eyes. Though this case also was notified as german measles it is another case of an attenuated measles, the eye symptoms, the incubation period, the absence of enlarged glands and of temperature all being suggestive of the attacks with which by this time one was quite familiar, though to anyone not so accustomed the diagnosis of the lesser

disease would seem justifiable.

All the other groups not included in the foregoing pages have been complete successes as far as the prevention of attacks of measles of any type are concerned. More detail of those attacks that did result could be given, but it will be sufficient to take only a few, which, from the same exposure on the same day, have had exactly the same opportunity of contracting the disease. The next few pages are therefore devoted to illustrate this point.

Comparison of an attenuated attack with a coincident normal attack.

GROUP 24.

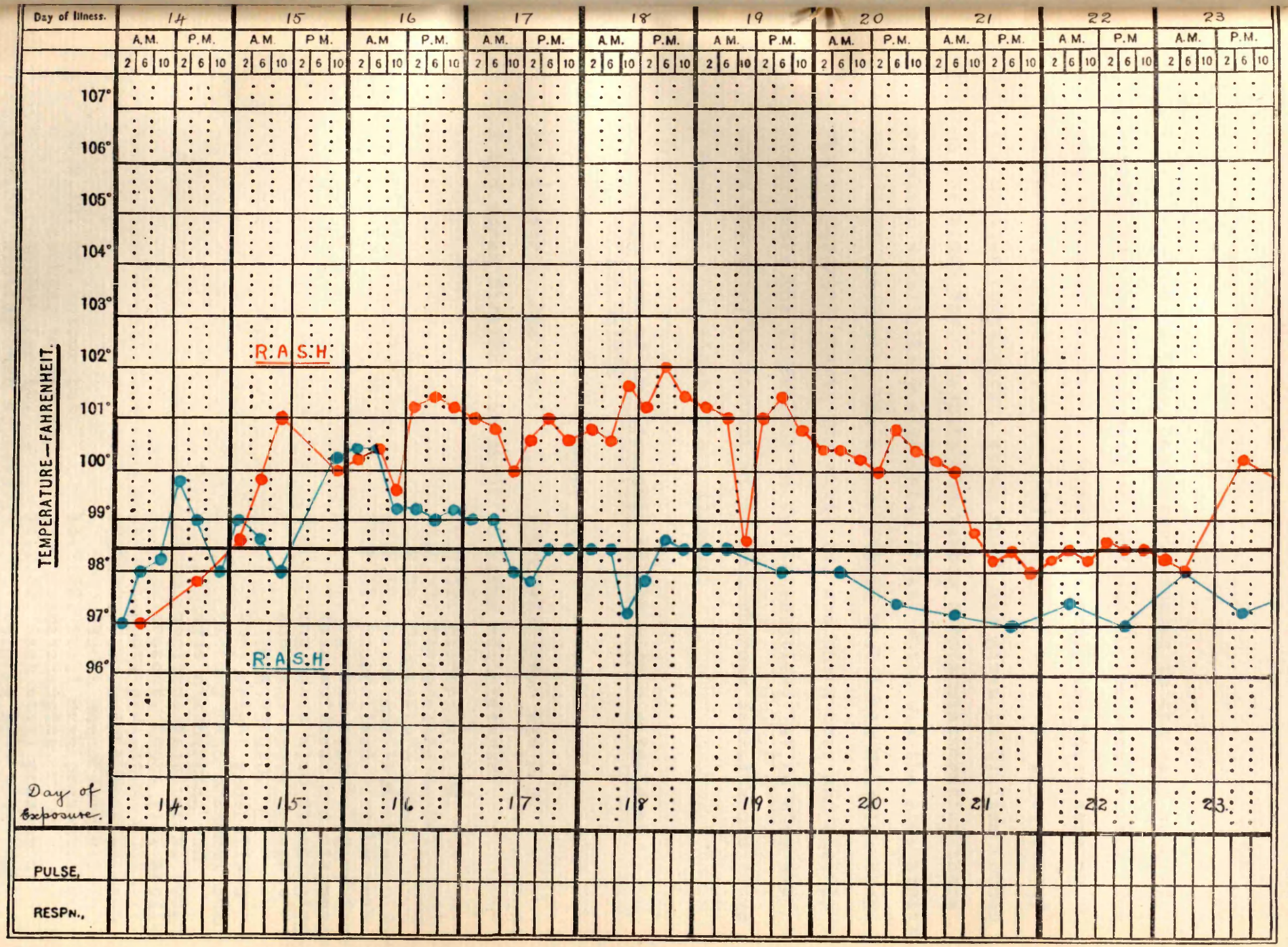
William Louden. Age 2 y.3 m.	Annie Naismith. Age 3 y.
5 c.c.serum 8/1/32. (9th.day).	No serum administered.
13.1.32. Evening temp. 99.4	12.1.32. Temperature 97 97.
14.1.32. Temp.99. Listless, measles rash, no Koplik's, no eye or nose discharge. TRANSFERRED. Very discrete bright rash on face and lower limbs, faint spots on trunk, none on arms. Only slightly ill. No Koplik's spots, pale membranes. Very comfortable.	13.1.32. Temperature 97 99.6 14.1.32. Temp.101. Cross. Eyes red and watery. Discharge from nose. Sneezing. Faint rash coming on neck and shoulders. Koplik's present. TRANSFERRED. Bright generalised rash present. Eyes and nose discharging. Sharply ill.
15.1.32. Rash faded. WELL.	15.1.32. Sharply ill. Rash very bright. Eyes discharging. Temps. 100.4 101.4 16.1.32. Ill. Restless and cross. Breathing distressed. Discharges. 101 101. 17.1.32. Rash and discharges same. Dusky colour. 100.6 102. 10 c.c. anti-scarlet serum. 18.1.32. Rash bright on face, less on trunk. Eyes and mouth sore. Temps. 101 101.4 19.1.32. Face flushed. croupy cough. Breathing distressed. Temps 100.4 100.8 Some 12,000 Anti-diph.units. 20.1.32. Rash fading. Eyes, nose and mouth still sore. Temps. 100 98.4 21.1.32. Brighter now. Normal temperature.

Group 24.

Serum on the ninth day.

William Louden.
(Attenuated Measles.)
5 c.c. serum.

Annie Naismith
(Measles)
No serum.



Both of these cases were exposed to the same case of measles for the same length of time and in the same degree. The ages were very similar as regards the group and there were no differences which could be made out other than the injection of the measles convalescent serum which was given to William Louden on the ninth day. Despite the rather late administration there resulted a definitely attenuated attack which was the more striking when contrasted with the severe attack that Annie Naismith took. The temperature charts for these two are shown over and clearly demonstrate the difference in the intensities. At no time was there any worry on account of Liuden, whereas Naismith did cause concern at the height of her illness.

Comparison of an attenuated attack with a coincident normal attack.

GROUP 31.

Isa Stewart. Age 5 y.	John McMillan. Age 3 y.
5 c.c.serum 31/1/32 (5th.day).	No serum administered.
	7.2.32. Temperature 99.
	8.2.32. Temperature normal.
	9.2.32. Temperature normal.
	10.2.32. Cross and irritable.
	11.2.32. Generalised blotchy rash appeared especially on face. Eyes suffused and discharging. Nose also discharging. Koplik's spots present. TRANSFERRED. Very bright generalised blotchy rash present. Both eyes discharging and swollen. Face puffy. Cough present. Looks ill. Koplik's spots present.
	12.2.32. Very bright measles rash almost haemorrhagic.
13.2.32. Off colour but nothing to see to account for it.	13.2.32. Still rash present. Eyes discharging
14.2.32. Blotchy rash appeared, not marked at first but later fairly good and generalised. Eyes slightly suffused and puffy. No discharge from eyes or nose. No cough and no Koplik's spots.	14.2.32. Rash still present as before. Eyes show some discharge.

Isa Stewart (Contd.)

TRANSFERRED.
Quick return to normal
and no complications.
CHILD WAS NEVER ILL.

John McMillan (Contd.)

15.2.32. Rash fading. Eyes still suffused. No complications.

These cases were exposed to a case of measles in the Scarlet Fever wards in Belvedere Hospital where a case of Scarlet Fever developed a measles rash three days after admission. They were both exposed in the same degree and their ages were not very much different. It is worthy of note that all who saw both these children were struck by the difference in the intensity of the attacks, there being a great contrast in the comfort of the one with the discomfort the other had to suffer. Certainly there was not very much temperature disturbance in the non-protected case but he looked miserable whereas the girl was not at any time in the least distressed.

Measles is one of the diseases that spread with lightning rapidity in a susceptible population. A doctor recently related how one cough from a child at a little party in his house was the cause of the entire company of children contracting the disease, and several similar illustrations of the intensity of the infection occurred in the series. Thus the patient, Blair, in Group 15 passed only a few hours in the same room as the patient McLauchlan, when the latter was in the invasion period before the appearance of the rash. That short time was sufficient. Even more striking is the case of Mary Quail in Group 22, who resisted the virus of the acute original measles but not of the second. An injection coincident with hers was given to the patient Thomson who on the 14th. day of exposure developed a scarlet fever rash and was therefore transferred from the ward. While the scarlet rash was at its height there appeared a measles rash through it, so that the two eruptions were present at the

same time. Quail therefore was out of contact with this measles case for two full days before the rash developed but nevertheless contracted the disease. The extreme infectiousness of measles in the early invasion stage could not be better illustrated than in this case.

Another point of interest in the results of the injections was shown in Group 7. Here a child, Evelyn Jordan, was given serum and remained protected from the original exposure but took measles from a normal attack in a patient with an erroneous history. There is not the slightest doubt about the extreme attenuation of the disease in her case - the only signs being a very faint rash and a slight cough. She never was ill. Notwithstanding this great modification she was the cause of another little child taking a severe attack of measles - Alice Wilson. This girl Wilson was sharply ill showing a brilliant rash together with broncho-pneumonia. She later became very croupy and at two different times was given 12,000 units Anti-diphtheritic serum. She ran a temperature from the eleventh till the thirtieth day of exposure, whereas the child responsible for her illness had a rise for only a day and a half. This shows that there is no radical change in the character of the virus of measles when subjected to the action of convalescent serum - any alteration in the type of attack resulting from the assistance given by the serum to the natural defence mechanism of the body tissues.

Another very interesting point occurred in Group 34. This did not take place in a child who had had serum but in one who did not get serum. Several cases who were susceptible contacts had been given serum at the age of three months. Since there was the possibility that in any event they would have remained free after exposure without the assistance of the injection this child of three months, John McEwan, was left alone. His inherited immunity was to be tested. The eyes began to

discharge on the eighteenth day and a bright rash appeared on the following day. There were no mouth signs (no Koplik's spots). The rash was absent on the limbs and the spots were mostly discrete not typical measles, faint, faded soon and left no stains. The temperature was normal throughout. One cannot but be struck by the great similarity to a case of attenuated measles after the injection of convalescent serum. It is quite reasonable to say that the inherited immunity took the place of the passive immunity of the convalescent serum in modifying the attack. The case also shows that even at the age of three months a child is not perfectly protected by nature from measles.

Caldwell House. A case of measles occurred in the Home for mental defectives situated at Caldwell House, several miles from the City of Glasgow, the patients in which were mostly drawn from Glasgow itself. The writer does not think much reliance should be placed on the individual histories supplied, though undoubtedly there must have been many, especially of those in the second decade, who had never been in contact with measles before, having spent the greater part of their lives in surroundings precluding exposure to the disease. Their records, however, have been kept separate from the rest of the measles exposures in order not to interfere with those with definitely authentic histories so that the results of the full investigation are therefore free from any suspicion. That some were definitely susceptible, however, is shown by the fact that one out of the eighty-nine injected developed measles of an attenuated type.

A most interesting point emerged from those injections at Caldwell House. The fact that convalescent serum is a homologous serum precludes the development of any reaction in the injected contact. Here the second person injected was one of the attendant nurses who later assisted in preparing the areas for

the injections, and consequently was under observation continually during a period of two hours after her own injection. The injection point (here the deltoid insertion) began to tingle within a quarter of an hour and there gradually appeared an ever increasing circular area of infiltration oedema passing from shilling size to crown size until when last seen personally it was over four inches in diameter. To begin with there was a tingling sensation but later with the development of the larger area this feeling disappeared. By the next morning the arm was normal and no oedema nor other sign was noted.

Examination of the literature was singularly disappointing as regards records of this occurrence, the only writer mentioning it being Robert Debré, who, together with Pierre Joannon, wrote in "La Rougeole. Epidemiologie, Immunologie, Prophylaxie, 1926" on p.229, as follows:-

"Ces accidents consistent en oedème local avec gonflement parfois considérable et toujours douloureux, apparition d'une zone rouge et chaude, assez étendue, autour du point d'inoculation. Ces symptômes apparaissent souvent dans les premières heures qui suivent l'inoculation et durent de vingt-quatre à quarante-huit heures. A ces troubles locaux s'associent parfois des signes généraux: fièvre qui s'élève à 38°, 39°, et même dans un cas à 40°, malaise, agitation et insomnie, et dans un cas, chez un nourrisson, inappétence et vomissements. Ces troubles sont passagere et disparaissent au bout de quarante-huit heures, sauf une légère gêne de la marche qui peut persister pendant un jour ou deux".

This case was the only one in the entire series in which there was any reaction at all and until I found this reference I had considered it in the nature of a reaction, through a special sensitiveness, to the small amount of the trikresol contained in the serum injected. In the above mentioned book

on measles, which contains an extremely good and interesting account of the different phases of the subject, the serum did not have any antiseptic added so that the reaction was not due to that factor. Nine contacts were given serum from the same donor without showing any local sign so there may be some idiosyncracy present in the individual to account for it. It occurred then in only one out of 353 injections, i.e. in about 0.28%.

THE DEBRÉ PHENOMENON.

During the investigation into the action of convalescent serum there occurred several cases in which the serum had been given very late in the incubation period or during the invasion stage of the disease. Bearing in mind the reaction known as the phenomenon of Debré, close attention was paid to such patients in order to find if, and under what circumstances, this took place.

In Group 5, the first of these special cases, the serum was administered on the third day of exposure to the original measles but three days after the injection there appeared a measles rash showing that the little patient had been incubating measles on admission. As this was not known the injection had been given as usual into the Vastus Lateralis muscle and no attempt was made to leave any subcutaneously. When the measles rash came out a close search of the area of injection did not reveal any difference in the rash even around the actual puncture opening. Of course the depth of the injected serum might be sufficient to account for the absence of inhibition of the eruption.

Group 15 furnished the second of these special cases. The patient was showing signs of measles at the time of the injection. She had suffused eyes, a rise in temperature to 100°, a short croupy cough and the suggestion of Koplik's spots in a

deeply congested mouth though no rash was seen behind ears or on the body. The serum was given mainly intramuscularly but the latter part was administered subcutaneously. This patient was later transferred to Knightswood Hospital and was closely watched for the exanthem. The measles rash appeared all over the body and also on the thighs, there being no difference in the injected area, showing that the serum had no effect on the rash when injected one day before the visible rash appeared. (It has been reported that Ultra-Violet Rays show the skin rash before normal light reveals it).

In another case not considered in the series of cross-infections, a chance was offered for the phenomenon. The child in question was sent in as a case of pneumonia and was seen in the ambulance on admission. Since it was said to have been in the same house as a case of measles and since there were some spots present very like Koplik's spots, instead of being sent to the pneumonia ward it was admitted to an observation ward. On the evening of admission some serum from Donor 11 was taken in an Agla syringe, and, by an intradermal needle, about 0.2 c.c. was injected in three places on the abdominal wall. The first and the third were good intradermal injections, but the second, owing to the struggling of the child, was given under the skin. A close watch was made in this case also for any sign of influence of the serum but two days passed and still there was no sign of a rash. The injections were given about 9 p.m. on 23/12/31, within an hour of admission and it was not until the morning of 26/12/31, that the measles rash began to appear on the neck. The body at this time was quite free from the rash but by evening there was a typical eruption present. For a distance of more than one inch around each of the injections there was not the slightest sign of any eruption though beyond this radius there was a brilliant rash. Throughout the duration of the rash in this child there

was never any alteration from the normal in the areas concerned. There did not seem any difference in the effect of the subcutaneous injection when compared with the two intracutaneous injections. This then was a very good example of the phenomenon of Debré. (Margaret Rooney - Ward Two - 23/12/31). It is interesting to note that the serum was given two and a half days before the measles rash appeared. N.B. The first case was at three days from the rash and the intramuscular injection did not have any effect on the skin eruption.

Opportunity was taken on other occasions where the patient looked as if he were incubating the disease or being invaded by it but there was no resulting attack. Here as in the large series of injections there were no signs of any reaction to the serum either locally or generally.

EFFECT OF OTHER TYPES OF ANTISERA.

In a few of the cases of cross-infection in the wards of Knightswood Hospital the susceptible contacts by reason of the original disease had been given injections of anti-serum. Thus all cases in the diphtheria ward had had serum while some in the scarlet wards had also been injected. Some diphtheria patients had also had anti-scarlet serum owing to having been exposed to cross-infection with that disease. In view of the fact that many continental workers have claimed some striking results from the injection of serum of various kinds - even normal horse serum - an analysis of these few cases might be interesting. The complete list is as follows:-

	TYPE OF ANTISERUM.			
Name.	Measles.	Diphtheria.	Scarlet Fever.	Result.
McElvanny, H.	5c.c.(2a)	20,000 (10b)	-	Free.
Chambers.	5c.c.(2a)	20,000 (26b)	-	Free.
Jenkinson.	-	20,000 (12b)	-	Measles.
McLeod.	-	16,000 (39b)	4c.c. (32b)	Measles.
Rennie.	-	16,000 (42b)	2:4c.c.(41:32b)	Measles.
Wylie.	-	20,000 (72b)	1c.c. (51b)	Free.
Johnstone.	5c.c.(2a)	24,000 (12b)	-	Free.
Ross.	-	20,000 (62b)	4c.c. (51b)	Measles.
Barr.	-	20,000 (73b)	8c.c. (51b)	Free.
Brown.	-	24,000 (3b)	-	Measles.
Ferrier.	-	20,000 (40b)	-	Measles.
Johnstone.	5c.c.(2a)	8,000 (1a)	-	Att.Meas.
McElvanny, E.	-	12,000 (44b)	-	Measles.
McLauchlan.	-	16,000 (22b)	-	Measles.

2a = Two days after. 3b = Three days before exposure.

From the above results there does not seem to be any protection in the anti-diphtheritic serum since even a dose of 24,000 in the case of Brown only three days before exposure was not sufficient to prevent the onset of measles. It is interesting to note that two cases who got anti-scarlet serum and no measles serum failed to contract the disease but it is not justifiable to say from this that it protected the contacts since a larger dose at a shorter interval failed to do so. It seems clear that these other sera are of no great value and should not be used for the purpose of preventing the onset of measles. There was no case in the series where normal horse serum had been injected, but there is no reason to suppose that it would have had any greater effect than these other sera which contain, in addition, known anti-bodies.

T A B L E S

Indicating the

FACTORS AND RESULTS

in

EACH INDIVIDUAL CASE.

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K E Y .

Column 1. Number of Group.

2. Name of Patient.

3. Age of Patient.

4. Exposure in Same or Adjoining ward

5. Amount of serum injected.

6. Number of Donor.

7. Age of serum in days when injected.

8. Day of exposure when serum injected.

9. Day of exposure fever appeared.

10. Day of exposure catarrh appeared.

11. Day of exposure Koplik's spots appeared.

12. Day of exposure prodromal rash appeared.

13. Day of exposure measles rash appeared.

14. Results after injection.

15. Results in non-injected patients.

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Result of the serum	Result of no serum		
1.	McElvenny	1y 8m	S	5cc	2	49	2	-	-	-	-	-	Free	-	-	-
	Chambers	4y 6m	S	5cc	2	49	2	-	-	-	-	-	Free	-	-	-
	Jenkinson	6y 8m	S	-	-	-	-	16	14	15	15	17	-	-	-	Measles
	McLeod	2y10m	S	-	-	-	-	14	17	18	17	18	-	-	-	Measles
	Rennie	3y	S	-	-	-	-	?	29/16	?	30/17	31/18	-	-	-	Measles
	Wylie	10y	S	-	-	-	-	-	-	-	-	-	-	-	Free	-
	Johnstone	2y 6m	A	5cc	2	49	2	-	-	-	-	-	Free	-	-	-
	Ross	3y	A	-	-	-	-	13	15	?	15	17	-	-	-	Measles
	Barr	5y	A	-	-	-	-	-	-	-	-	-	-	-	Free	-
2.	Carroll	9y	S	5cc	3	47	4	-	-	-	-	-	Free	-	-	-
	Taylor	2y	S	-	-	-	-	15	15	15	15	17	-	-	-	Measles
	Roberts	1y	A	5cc	2	61	4	-	-	-	-	-	Free	-	-	-
	Scott	1y	A	5cc	2	61	4	-	-	-	-	-	Free	-	-	-
3.	Woods	6y	S	5cc	2	90	4	-	-	-	-	-	Free	-	-	-
	Hughes	1y	S	5cc	2	90	4	20	17	0	16	20	-	Pri.Att.	-	-
	Connelly	4y	S	-	-	-	-	?	?	?	?	14	-	-	-	Measles
	Lyttle	4y 6m	S	5cc	2	98	8	-	-	-	-	-	Free	-	-	-
	Martin	4y	S	5cc	4	93	3	-	-	-	-	-	Free	-	-	-
4.	Johnstone	2y 8m	S	5cc	4	86	2	27/13	25/11	0	-	27/13	-	Sec.Att.	-	-
	Ferrier	4y 6m	S	-	-	-	-	?	18	?	-	20	-	-	-	Measles
	Brown	2y	S	-	-	-	-	16	15	17	-	18	-	-	-	Measles
	McElvenny	4y	A	-	-	-	-	12	15	15	15	18	-	-	-	Measles
	McLauchlanI	5y 6m	A	-	-	-	-	-	-	-	-	-	-	-	Free	-
	McDonald	1y10m	A	-	-	-	-	-	-	-	-	-	-	-	Free	-
	McLauchlanJ	4y	A	-	-	-	-	16	18	18	18	20	-	-	-	Measles
5.	Gallacher	6m	S	5cc	4	96	4	-	-	-	-	-	Free	-	-	-
	Cowan	11m	S	5cc	4	96	4	-	-	-	-	-	Free	-	-	-
	Murray	2y 2m	S	5cc	6	29	6	-	-	-	-	-	Free	-	-	-
	Kelloch	2y 4m	S	5cc	4	98	6	-	-	-	-	-	Free	-	-	-
	McDonald	1y	S	5cc	5	41	3	Incubating measles at the time					-	MEASLES	-	-
6.	Strain	1y 6m	S	5cc	3	96	3	-	-	-	-	-	Free	-	-	-
	Carson	9m	S	-	-	-	-	-	-	-	-	-	-	-	Free	-
7.	Brown	1y 3m	S	5cc	4	99	5	19	19	0	-	20	-	Pri.Att	-	-
	Healy	1y	S	5cc	4	99	5	29/15	29/15	0	-	30/16	-	Sec.Att	-	-
	Jordan E	3y 2m	S	5cc	4	99	5	28/14	30/16	0	-	31/17	-	Sec.Att	-	-
	Jordan W	4y10m	S	5cc	5	42	5	-	-	-	-	-	Free	-	-	-
	Wilson	1y 6m	S	-	-	-	-	11	10	?	13	15	-	-	-	Measles

	Name	Age	Ward	Serum	Donor	Age	Day	Fever	Catarrh	Koplik	Prod.	Rash	Result of the serum	Result of no serum		
7.	Beattie	3y 3m	S	5cc	5	42	5	-	-	-	-	-	Free	-	-	-
	Hillcoat	3y 3m	S	5cc	5	42	5	-	-	-	-	-	Free	-	-	-
	Dunn	2y 2m	S	-	-	-	-	13	14	16	17	18	-	-	-	Measles
	Cameron	3y 9m	S	-	-	-	-	17	17	18	-	20	-	-	-	Measles
8.	McGonnigle	2y 7m	S	5cc	6	39	5	-	-	-	-	-	Free	-	-	-
	Black	4y 6m	S	-	-	-	-	-	-	-	-	-	-	-	Free	-
9.	McAllister	9y	S	5cc	6	45	6	-	-	-	-	-	Free	-	-	-
	McDonald	12y	S	5cc	6	45	6	-	-	-	-	-	Free	-	-	-
	Beggs	11y	S	5cc	6	45	6	-	-	-	-	-	Free	-	-	-
	Williamson	13y	S	5cc	6	45	6	-	-	-	-	-	Free	-	-	-
10.	Clarke	3y 8m	S	5cc	8	21	7	-	-	-	-	-	Free	-	-	-
11.	McIntosh	1y	S	5cc	8	22	12	-	-	-	-	-	Free	-	-	-
	Keane	1y 3m	S	5cc	8	22	8	-	-	-	-	-	Free	-	-	-
	Lang	11m	S	5cc	8	22	8	-	-	-	-	-	Free	-	-	-
	Petrie	2y	S	-	-	-	-	?	?	?	?	17	-	-	-	Measles
12.	Johnstone	2y10m	S	5cc	8	28	5	-	-	-	-	-	Free	-	-	-
	McQueen	11m	A	5cc	8	28	5	-	-	-	-	-	Free	-	-	-
	Davidson	1y 2m	A	5cc	8	28	5	-	-	-	-	-	Free	-	-	-
13.	Cosgrove	4y 6m	S	5cc	8	29	5	-	-	-	-	-	Free	-	-	-
	Henderson C	3y 5m	S	5cc	8	29	5	-	-	-	-	-	Free	-	-	-
	Henderson C	2y 2m	S	5cc	8	29	5	-	-	-	-	-	Free	-	-	-
	Kidd	1y 3m	S	5cc	8	29	5	-	-	-	-	-	Free	-	-	-
	Matthews	1y 9m	S	5cc	8	29	5	-	-	-	-	-	Free	-	-	-
14.	Tracey	4y 1m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	Buchanan	4m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	Law	3m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	Ralston	3m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	McGill	4m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	Boyle	4m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	McVey	3m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	Smith	1y 3m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
	Mundy	6m	S	5cc	9	28	6-9	Died during incubation period.					-	D I E D	-	-
	Campbell	11y 1m	S	5cc	9	28	6-9	-	-	-	-	-	Free	-	-	-
15.	Reynolds	1y	S	5cc	9	34	4	-	-	-	-	-	Free	-	-	-
	Collins	1y 3m	S	5cc	9/10	28	4	45	-	-	-	45	-	Ter.Att.	-	-
	Reid	2y 6m	S	5cc	10	28	4	23/13	24/14	0	-	24/14	-	Sec.Att	-	-

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Results of the serum		Result of no serum	
15.	McLeish	3y	S	5cc	10	28	4	13	-	(16?)	-	17	-	Pri.Att.	-	-
	McLauchlan	2y	S	5cc	10	28	4	Injected in late invasion period.					-	MEASLES	-	-
	Stirling	3y	S	-	-	-	-	11	14	-	-	14	-	-	-	Measles
	Blair	11m	S	-	-	-	-	15	-18	18	-	18	-	-	-	Measles
16.	McInnes	2y	S	5cc	10	31	7	-	-	-	-	-	Free	-	-	-
	McKay	11m	S	5cc	10	31	7	-	-	-	-	-	Free	-	-	-
	Robertson	1y 1m	S	5cc	10	31	7	-	-	-	-	-	Free	-	-	-
	McQuat	1y 5m	S	5cc	10	31	7	-	-	-	-	-	Free	-	-	-
	Monk	11m	S	5cc	10	31	7	-	-	-	-	-	Free	-	-	-
	Spence	4y	S	5cc	10	31	6	-	-	-	-	-	Free	-	-	-
	Emery L	4y	S	5cc	10	31	4	-	-	-	-	-	Free	-	-	-
	Emery R	2y	S	5cc	10	31	4	25	0	0	-	22	-	Pri.Att.	-	-
17.	Haggerty	1y 9m	S	5cc	10	35	5	-	-	-	-	-	Free	-	-	-
	Bruce	3m	S	5cc	10	35	5	-	-	-	-	-	Free	-	-	-
	Cook	4y	S	5cc	10	35	5	-	-	-	-	-	Free	-	-	-
	O'Donnell	2y 6m	A	5cc	10	35	5	-	-	-	-	-	Free	-	-	-
	McNicol	8y	A	5cc	10	35	5	-	-	-	-	-	Free	-	-	-
	Williams	3y 6m	S	5cc	10	35	5	18	0	0	-	18	-	Pri.Att.	-	-
	Thomson	1y 7m	S	5cc	10	35	10	-	-	-	-	-	Free	-	-	-
	Austin	2y	A	5cc	10	35	10	-	-	-	-	-	Free	-	-	-
	McGlashan	4y	A	5cc	10	35	10	-	-	-	-	-	Free	-	-	-
	Kennedy	24y	S	-	-	-	-	?	18	?	-	21	-	-	-	Measles
18.	Stevenson	2y 6m	S	5cc	11	37	4	-	-	-	-	-	Free	-	-	-
	McGie	1y	S	5cc	11	37	4	10	0	0	-	12	-	Pri.Att.	-	-
	Duff	8m	S	5cc	11	37	4	-	-	-	-	-	Free	-	-	-
	Gallacher	1y 7m	S	5cc	11	37	4	10	0	0	-	?13	-	?Pri.Att	-	-
	Mills	1y	S	5cc	11	37	4	10	12	0	-	12	-	Pri.Att.	-	-
19.	McDiarmid	3m	S	5cc	11	38	5	-	-	-	-	-	Free	-	-	-
	Hughes	5m	S	5cc	11	38	5	-	-	-	-	-	Free	-	-	-
	McLauchlan	8½	S	5cc	11	38	1	Died during incubation period					-	D I E D	-	-
20.	McDonald	2y	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Ferguson	2y 4m	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Richards	15y	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Shields	7y 6m	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Williamson	7y	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Russell J	5y	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Result of the serum		Result of no serum	
20.	Russell M	3yllm	S	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Cuthbertson	3y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Taylor	3y 6m	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Tracey	3y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	McKinlay	5y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Murray	5y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	McGuire	3y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Robertson	1y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
	Wilkie	5y	"	5cc	12	35	4	-	-	-	-	-	Free	-	-	-
21.	Gray	4m	"	5cc	14	28	4	-	-	-	-	-	Free	-	-	-
	Innes	4m	"	5cc	14	28	4	-	-	-	-	-	Free	-	-	-
	McCusker	4m	"	5cc	14	28	4	-	-	-	-	-	Free	-	-	-
	Wilson	8m	"	5cc	13	29	4	-	-	-	-	-	Free	-	-	-
	McIntosh	1y 1m	"	-	-	-	-	0	18	0	-	18	-	-	-	N.B. Atten.)
	Keane	1y 4m	"	-	-	-	-	-	-	-	-	-	-	-	-	(Free N.B. -
22.	Quail	3y	"	5cc	14	29	10	29/17	31/19	?	-	31/19	-	Sec.Att.	-	-
	Thomson	7y	"	5cc	15	27	10	12	?	0	-	16	-	Pri.Mild	-	-
	McColl	0y	"	5cc	14	29	10	-	-	-	-	-	Free	-	-	-
23.	Buchanan	1y 6m	"	5cc	16	32	6	17	17	?	-	19	-	Pri.Att.	-	-
	Johnstone	1y 6m	"	5cc	16	32	6	14	15	0	-	15	-	Pri.Att.	-	-
	McCabe	2y 2m	"	5cc	16	32	6	13	13	0	-	13	-	Pri.Att.	-	-
	Bell	1y 7m	"	5cc	16	32	6	16	15	?	-	16	-	Pri.Att.	-	-
	Shevlin	1y 2m	"	3.4	16	32	6	10	9	?	-	13	-	Pri.Att	-	-
	Murphy	2y 6m	"	3.4	16	32	6	-	-	-	-	-	Free	-	-	-
	Cadder	6y 5m	"	3.4	16	32	6	-	-	-	-	-	Free	-	-	-
	Lynn	2y 1m	"	1.7	16	32	6	13	12	?	-	14	-	Pri.Mild	-	-
	McMillan	2y 9m	"	1.7	16	32	6	9	9	?	-	14	-	Pri.Mild	-	-
	Brown	2y 2m	"	1.7	16	32	6	13	8	?	-	14	-	Pri.Mild	-	-
	Molinari	3yl0m	"	1.7	16	32	6	-	-	-	-	-	Free	-	-	-
	Bole	2y 5m	"	1.7	16	32	6	14	12	?	-	15	-	Pri,Mild	-	-
24.	Paul	10m	"	5cc	12	46	5	-	-	-	-	-	Free	-	-	-
	Napier	1y	"	5cc	15	36	5	-	-	-	-	-	Free	-	-	-
	Wright	9m	"	5cc	15	36	5	26/11	?	0	-	31/16	-	Sec.Mild	-	-
	Coeffield	3y	"	5cc	15	36	5	-	-	-	-	-	Free	-	-	-
	Young	8m	"	5cc	15	36	5	-	-	-	-	-	Free	-	-	-
	Routledge	1y	S	5cc	15/16	36	5	22	22	0	-	22	-	Pri.Att.	-	-

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Result of the serum	Result of no serum		
24.	Kelly	10m	S	5cc	16	36	5	16	0	?	17	19	-	Pri.Att.	-	-
	Grier	4y	S	5cc	16	36	5	-	-	-	-	-	Free	-	-	-
	Naismith	3y	S	-	-	-	-	14	15	15	-	15	-	-	-	Measles
	Louden	2y 3m	S	5cc	16	36	9	14	0	0	-	15	-	Pri.Att.	-	-
	McGurley	1y 4m	S	5cc	17	34	9	-	-	-	-	-	Free	-	-	-
	Gallacher	5m	S	5cc	17	34	9	-	-	-	-	-	Free	-	-	-
25.	Gill	2y	S	5cc	17	36	5	-	-	-	-	-	Free	-	-	-
26.	Howieson	8y	S	5cc	17	37	4	-	-	-	-	-	Free	-	-	-
	Crichton	12y	S	5cc	17	37	4	-	-	-	-	-	Free	-	-	-
	Cassells	8y 6m	S	5cc	18	36	4	-	-	-	-	-	Free	-	-	-
	Hamilton	4y 6m	S	5cc	18	36	4	-	-	-	-	-	Free	-	-	-
	Hassin	2y	S	5cc	24	22	4	-	-	-	-	-	Free	-	-	-
	Swanson	2y 2m	S	5cc	24	22	4	-	-	-	-	-	Free	-	-	-
27.	Cowan	8y 8m	S	5cc	17	40	5	-	-	-	-	-	Free	-	-	-
	Clarke	5y 1m	S	5cc	17	40	5	-	-	-	-	-	Free	-	-	-
	Kirkwood	2y	S	5cc	18	39	5	-	-	-	-	-	Free	-	-	-
	Ward	2y 6m	S	5cc	18	39	5	-	-	-	-	-	Free	-	-	-
	Nimmo	4y 7m	S	5cc	20	37	5	-	-	-	-	-	Free	-	-	-
	Nisbet	1y 9m	S	5cc	20	37	5	-	-	-	-	-	Free	-	-	-
	McGhee	17y	A	5cc	21	36	5	-	-	-	-	-	Free	-	-	-
	McEwan	12y	A	5cc	21	36	5	-	-	-	-	-	Free	-	-	-
28.	Miller	1y 2m	S	10cc	17	48	9	Died during incubation period					-	D I E D.	-	-
29.	Ferris	1y 7m	S	5cc	17	52	6	-	-	-	-	-	Free	-	-	-
	Russell	4y 6m	S	5cc	18	51	6	0	39	0	-	39	-	Ter.Att.	-	-
	Thomson	2y11m	S	5cc	25	37	6	-	-	-	-	-	Free	-	-	-
	McLean	-	S	-	-	-	-	-	-	-	-	-	-	-	Free	-
	Smith	19y	S	-	-	-	-	17	17	?	-	20	-	-	-	Measles
30.	Fallon	1y 1m	A	5cc	20	51	5	-	-	-	-	-	Free	-	-	-
	McDonald	10m	A	5cc	21	50	5	Died during incubation period					-	D I E D.	-	-
	Dunlop	5m	A	5cc	28	36	5	-	-	-	-	-	Free	-	-	-
	McCafferty	7m	A	-	-	-	-	-	-	-	-	-	-	-	Free	-
	McMillan	3m	A	-	-	-	-	-	-	-	-	-	-	-	Free	-
31.	Stewart	5y	S	5cc	20	54	5	18	19	0	-	19	-	Pri.Att.	-	-
	McCafferty	2y 6m	S	5cc	24	42	5	-	-	-	-	-	Free	-	-	-
	Gillespie	4y	A	5cc	29	39	5	-	-	-	-	-	Free	-	-	-
	McMillan	3y	S	-	-	-	-	12	16	16	-	16	-	-	-	Measles.

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Result of the serum	Result of no serum		
32.	Clarke	3y	S	5cc	25	52	4	14	0	0	-	19	-	Pri.Att.	-	-
	Sheerin	1y 5m	S	5cc	25	52	4	17	0	0	-	21	-	Pri.Att.	-	-
	Neilly	1y 8m	S	5cc	25	52	4	23	0	0	-	?22	-	?Pri.Att.	-	-
	McIlveen	8y 1m	A	5cc	25	52	4	-	-	-	-	-	Free	-	-	-
33.	Hanlon	5m	S	5cc	28/29	56	6	21	21	?	-	22	-	Pri.Att.	-	-
	Boyle	6m	S	5cc	28	56	6	-	-	-	-	-	Free	-	-	-
	McCaffrey	1y 8m	S	5cc	28	56	6	26/19	26/19	?	-	27/20	-	Sec.Att.	-	-
	Murray	3y	S	5cc	25/26	57	6	0	0	0	-	22	-	Pri.Att.	-	-
	Lennox	5m	S	5cc	28	56	6	-	-	-	-	-	Free	-	-	-
	Greary	5m	S	5cc	28	56	6	-	-	-	-	-	Free	-	-	-
34.	McGarry	1y 2m	S	5cc	25	59	4	9	9	-	-	9	-	MEASLES	-	-
	Masterton	5m	S	5cc	28	56	4	-	-	-	-	-	Free	-	-	-
	Thomson	2y	S	5cc	28	56	4	Temps. from Scarlet and Pneumonia.					Free	-	-	-
	Baillie	2y	S	5cc	28	56	4	5	5	-	-	6	-	MEASLES	-	-
	Melvin	1y 6m	S	5cc	13	79	4	-	-	-	-	-	Free	-	-	-
	McEwan	3m	S	-	-	-	-	0	18	?	-	19	-	-	-	Measles.
35.	Higgins	8m	S	5cc	13	80	3	-	-	-	-	-	Free	-	-	-
	Morrison	5m	S	5cc	13	80	3	-	-	-	-	-	Free	-	-	-
	Neilson	7m	S	5cc	13	80	3	-	-	-	-	-	Free	-	-	-
	Guthrie	10m	S	5cc	13	80	3	-	-	-	-	-	Free	-	-	-
	Cairns	6m	S	5cc	13	80	4	-	-	-	-	-	Free	-	-	-
	Courtney	10m	S	5cc	45	30	4	-	-	-	-	-	Free	-	-	-
	McLay	11m	S	5cc	45	30	4	-	-	-	-	-	Free	-	-	-
	Ramsay	6m	S	5cc	45	30	4	-	-	-	-	-	Free	-	-	-
	Boyle	6m	S	5cc	45	30	4	-	-	-	-	-	Free	-	-	-
36.	McAllister	9m	S	5cc	13	81	6	-	-	-	-	-	Free	-	-	-
37.	Cray	3y 1m	S	5cc	13	92	5	-	-	-	-	-	Free	-	-	-
	Whiteford	1y 7m	S	5cc	13	92	5	-	-	-	-	-	Free	-	-	-
	Smith	2y 1m	S	5cc	18	86	5	0	0	0	-	25	-	Pri.Att.	-	-
	Forsyth G	1y 3m	S	5cc	18	86	5	-	-	-	-	-	Free	-	-	-
	Callaghan	1y 9m	S	5cc	31	61	5	-	-	-	-	-	Free	-	-	-
	Forsyth W	2y 7m	S	5cc	31	61	5	0	0	0	-	22	-	?Pri.Att.	-	-
	O'Henley	4y 3m	S	-	-	-	-	15	15	?	-	17	-	-	-	Measles.
38.	Cook	2y	S	5cc	13	92	7	-	-	-	-	-	Free	-	-	-
	Whicher	3y 1m	S	5cc	13	93	8	0	0	0	-	11	-	Pri.Att.	-	-
	Hardie	2y 1m	S	5cc	18	87	8	-	-	-	-	-	Free	-	-	-

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Result of the serum	Result of no serum		
38	Easton	2y 1m	S	5cc	18	87	6	-	-	-	-	-	Free	-	-	-
	McAllister	7y	S	-	-	-	-	?	0	?	-	13	-	-	-	Measles
39	Wilson	3m	S	5cc	18	95	6	-	-	-	-	-	Free	-	-	-
	Martin	7m	S	5cc	18	95	6	-	-	-	-	-	Free	-	-	-
	Johnstone	6m	S	5cc	18	95	6	-	-	-	-	-	Free	-	-	-
	Freemen	4m	S	5cc	18	95	6	-	-	-	-	-	Free	-	-	-
	Hall	4m	S	5cc	22	89	6	-	-	-	-	-	Free	-	-	-
	Smith	4m	S	5cc	23	83	6	-	-	-	-	-	Free	-	-	-
	Harvey	3m	S	5cc	23	83	6	-	-	-	-	-	Free	-	-	-
	Mann	5m	S	5cc	23	83	6	-	-	-	-	-	Free	-	-	-
	Docherty	3m	S	5cc	23	83	6	-	-	-	-	-	Free	-	-	-
	Hazlett	5m	S	5cc	22	89	6	-	-	-	-	-	Free	-	-	-
	Little	4m	S	5cc	22	89	6	-	-	-	-	-	Free	-	-	-
	Currie	4m	S	5cc	22	89	6	-	-	-	-	-	Free	-	-	-
	Cameron	4m	S	5cc	29	78	6	-	-	-	-	-	Free	-	-	-
	Cleary	1y10m	S	5cc	29	78	6	-	-	-	-	-	Free	-	-	-
40	Jamieson	5m	S	5cc	22	95	6	-	-	-	-	-	Free	-	-	-
	McDonald	4m	S	5cc	22	95	6	Died during observation period					-	D I E D.	-	-
	Johnstone	5m	S	5cc	22	95	6	Died during observation period					-	D I E D.	-	-
	Forbes	3y	S	5cc	22	95	6	-	-	-	-	-	Free	-	-	-
	McVey	6m	S	5cc	22	96	6	-	-	-	-	-	Free	-	-	-
	Deane	5m	S	5cc	13	107	6	-	-	-	-	-	Free	-	-	-
	Forsyth	10m	S	5cc	22	95	6	Died during observation period					-	D I E D.	-	-
	McCleneghan	8m	S	5cc	22	95	6	Died during observation period					-	D I E D	-	-
41	Moley	2y 3m	S	5cc	26	97	7	8	10	?	-	11	-	Pri.Mild	-	-
	Louden	10m	S	5cc	26	97	7	-	-	-	-	-	Free	-	-	-
	Kelly	6m	S	5cc	26	97	7	16	0	0	-	14	-	Pri.Att.	-	-
	McIntyre	4m	S	5cc	28	96	7	-	-	-	-	-	Free	-	-	-
	Brookhouse	1y 1m	S	5cc	30	91	7	Died during observation period					-	D I E D	-	-
42	Burtcher	3m	S	5cc	31	88	7	-	-	-	-	-	Free	-	-	-
	Hume	10m	S	5cc	31	88	7	-	-	-	-	-	Free	-	-	-
	Graham	9m	S	5cc	31	88	7	-	-	-	-	-	Free	-	-	-
	Masterton	6m	S	5cc	31	88	7	-	-	-	-	-	Free	-	-	-
	Harvey	2y 2m	S	5cc	31	88	7	-	-	-	-	-	Free	-	-	-
43	Orr	10m	S	5cc	32	89	7	-	-	-	-	-	Free	-	-	-
	Weatherall	1y 6m	S	5cc	31	92	7	-	-	-	-	-	Free	-	--	-

	Name	Age	Ward	Serum	Donor	Age	Day	Fever.	Catarrh.	Koplik.	Prod.	Rash	Result of the serum	Result of no serum		
43	Nicholson	5m	S	5cc	24	103	7	-	-	-	-	-	Free	-	-	-
	Martin	1y 1m	S	5cc	18/19	117	7	-	-	-	-	-	Free	-	-	-
	Carstairs	1y 6m	S	5cc	37	75	7	14	14	?	-	14	-	Pri.Att.	-	-
	Boyle	7m	S	5cc	23/24	103	7	-	-	-	-	-	Free	-	-	-
44	Franks	6m	S	5cc	30/45	87	8	-	-	-	-	-	Free	-	-	-
	Bryne	9m	S	5cc	45	87	8	-	-	-	-	-	Free	-	-	
	Cearns	1y	S	5cc	48	66	8	-	-	-	-	-	Free	-	-	-
	Fotheringham	3m	S	5cc	48	66	8	-	-	-	-	-	Free	-	-	-
	Hall	4m	S	5cc	48	66	8	Died during observation period					-	D I E D	-	
	Lloyd	3m	S	5cc	48	66	8	-	-	-	-	-	Free	-	-	
	Higgins	1y 6m	S	5cc	48	66	8	-	-	-	-	-	Free	-	-	-
45	Esplin	4m	S	5cc	25	136	7	-	-	-	-	-	Free	-	-	-
	McDuff	9m	S	5cc	29	133	7	19	-23	?	-	24	-	Pri.Mild	-	-
	Nolan	6m	S	5cc	38	108	7	-	-	-	-	-	Free	-	-	-
46	Eadie	1y10m	S	5cc	48	75	8	-	-	-	-	-	Free	-	-	-
	English	1y 7m	S	5cc	48	75	8	0	22	?	-	23	-	Pri.Att.	-	-
	Collins	1y 2m	S	5cc	48	75	8	Died during observation period					-	D I E D.	-	-
	McMillan	1y 5m	S	5cc	48	75	8	-	-	-	-	-	Free	-	-	-
	McCabe	1y 8m	S	5cc	48	75	8	-	-	-	-	-	Free	-	-	-
47	Taylor	1y	S	5cc	38	115	7	-	-	-	-	-	Free	-	-	-
	McKinnon	4m	S	5cc	48	82	7	-	-	-	-	-	Free	-	-	-
	Jamieson	8m	S	5cc	48	82	7	-	-	-	-	-	Free	-	-	-
	McLauchlan	1y 1m	S	5cc	48	82	7	Died during observation period					-	D I E D.	-	-
	Turnbull	2y	S	5cc	48	82	7	-	-	-	-	-	Free	-	-	-
S.	Margaret	1y 3m	S	5cc	24	17	5	-	-	-	-	-	Free	-	-	-
W.	Taylor	1y 2m	S	5cc	13	97	9	-	-	-	-	-	Free	-	-	-
C.	Eighty-nine	-	S	5cc	Various		5	Only one took an attenuated attack of measles out of the eighty-nine cases								

A N A L Y S I S
of the
R E S U L T S.

ANALYSIS OF THE RESULTS OF THE INJECTIONS OF SERUM.

The scope of the investigation comprised fifty instances of exposure involving three hundred and forty five patients. A glance at Table 1, on the following page shows the distribution of these under different headings. One group of eighty nine occurring in a mental home has been excluded owing to the possibility of error in the history of no previous attack but the other forty nine groups can be considered, as far as possible, free of error in this respect, as great care was taken in extracting histories. That a large number of these 89 were really acceptable for use is shown by the fact that one developed an attenuated attack of measles at the usual period.

The care in extracting histories is shown by the fact that only eleven were given serum who had had a previous attack of measles - cases mostly about whom information was not available at the time of injection.

Out of the remaining 245 cases there were twelve who died in the observation period and who therefore are disregarded. Since there were many other diseases affecting these children, who for the most part were in-patients in institutions, it is fortunate that there were so few who succumbed to the other disease during the period.

After removing these ineligibles from the total injected there thus remained 233 patients inoculated with convalescent measles serum about whom there is no doubt, the definitely known susceptibles. Out of this number there were 185 who entirely escaped infection, equivalent to a protection rate of 80 per cent. In 36 cases the attack was attenuated. It will be observed that 28 of these contracted the infection from the original case of measles, 6 from a subsequent or "primary" case or else from a coincident "normal" while 2 were later reported to have developed measles beyond that period. There were very few "mild" cases - 8 in all, and of these 7 were primary

TABLE 1.

GLASGOW - MEASLES.

Total number of Contact Cases injected			345
Doubtful negative history of measles. . .	89		
Known positive history of measles	11		
Negatives who died in observation period	12	112	
Total of definitely known susceptibles		233	
Result of injection -			
(a) No attack	185		
(b) Attenuated attacks - Primary	28		
Secondary. . . .	6		
Tertiary	3		
(c) Mild attacks - Primary	7		
Secondary. . . .	1		
(d) Normal attacks -	4		
Control Cases		32	
No attack. . . .	9		
Measles	23		

and 1 secondary. Out of the seven four had had only 1.7 c.c. serum instead of the usual 5 c.c. so that the number is even less than that given if the standard dose is considered. Four patients developed normal measles after serum injection but as these showed rashes soon after the injection it is apparent that the dose was given much too late to have any preventive effect. As controls there were 32 cases who did not receive an injection of serum and of these no fewer than 23 contracted measles. These results are summarised in Table 1.

Most of the factors governing the result of injection, such as type of attack of the donor, age of the serum, day of exposure on which serum was given, etc., were noted, but the evaluation of each is difficult since, even when all factors are exactly similar, varying results tend to occur.

DAY OF EXPOSURE.

Considering now the results obtained in the series of cross-infections these can be tabulated in various ways to let us estimate the influence of the several factors. First let us consider the effect of the day after exposure when injection was given.

RESULTS ACCORDING TO DAY OF EXPOSURE.

DAY.	TOTAL CONTACTS.	NO ATTACK.	ATTENUATED ATTACKS.			MILD ATTACKS.		NORMAL MEASLES.
			Prim.	Sec.	Tert.	Prim.	Sec.	
1.	-	-	-	-	-	-	-	-
2.	4	3	-	1	-	-	-	-
3.	7	6	-	-	-	-	-	1
4.	58	44	9	1	1	-	-	3
5.	52	42	7	2	-	-	1	-
6.	48	35	7	1	1	4	-	-
7.	29	25	2	-	-	2	-	-
8.	15	13	2	-	-	-	-	-
9.	4	3	1	-	-	-	-	-
10.	6	4	-	1	-	1	-	-
11.	-	-	-	-	-	-	-	-
12.	1	1	-	-	-	-	-	-
6-9.	9	9	-	-	-	-	-	-
Total.	233	185	28	6	2	7	1	4

The four cases in which there occurred a normal attack of measles after the injection of the serum were investigated with the following result:-

The one thought to have been injected on the third day was in Group 5. She was admitted on 7/11/31, got serum on 10/11/31, and showed the rash on 13/11/31. She therefore got the serum only three days before the rash occurred.

Of the three injected on the fourth day one in Group 15 was known to be in the invasion period when injected - the object being to see if any local effect was produced.

The other two occurred in the same group - Group 34. Here again one was suspicious and injected for the same reason as in the preceding one - but the second seemed normal though the temperature rose on the next day and the measles rash came on the fifth day.

Thus of the four cases with a normal measles rash
one showed the rash three days after serum
one showed the rash one day after serum
one showed the rash two days after serum
one showed the rash five days after serum.

It is only reasonable to conclude that they all had been previously infected and were incubating or were being invaded by the disease when the injections were given.

The average day of exposure on which the rash appears is shown by the control cases to be 17.4 days. These four cases therefore must have been injected not on the third and fourth days but on the 14th., 16th., 15th. and 12th. days respectively.

A table even with this correction would not illustrate clearly the real results. Correction must, of course, be made for the second exposure of a case, since, if this second exposure did not occur, the contact would have remained protected. This means that the primary cases alone should be the estimate of the protection afforded by the serum.

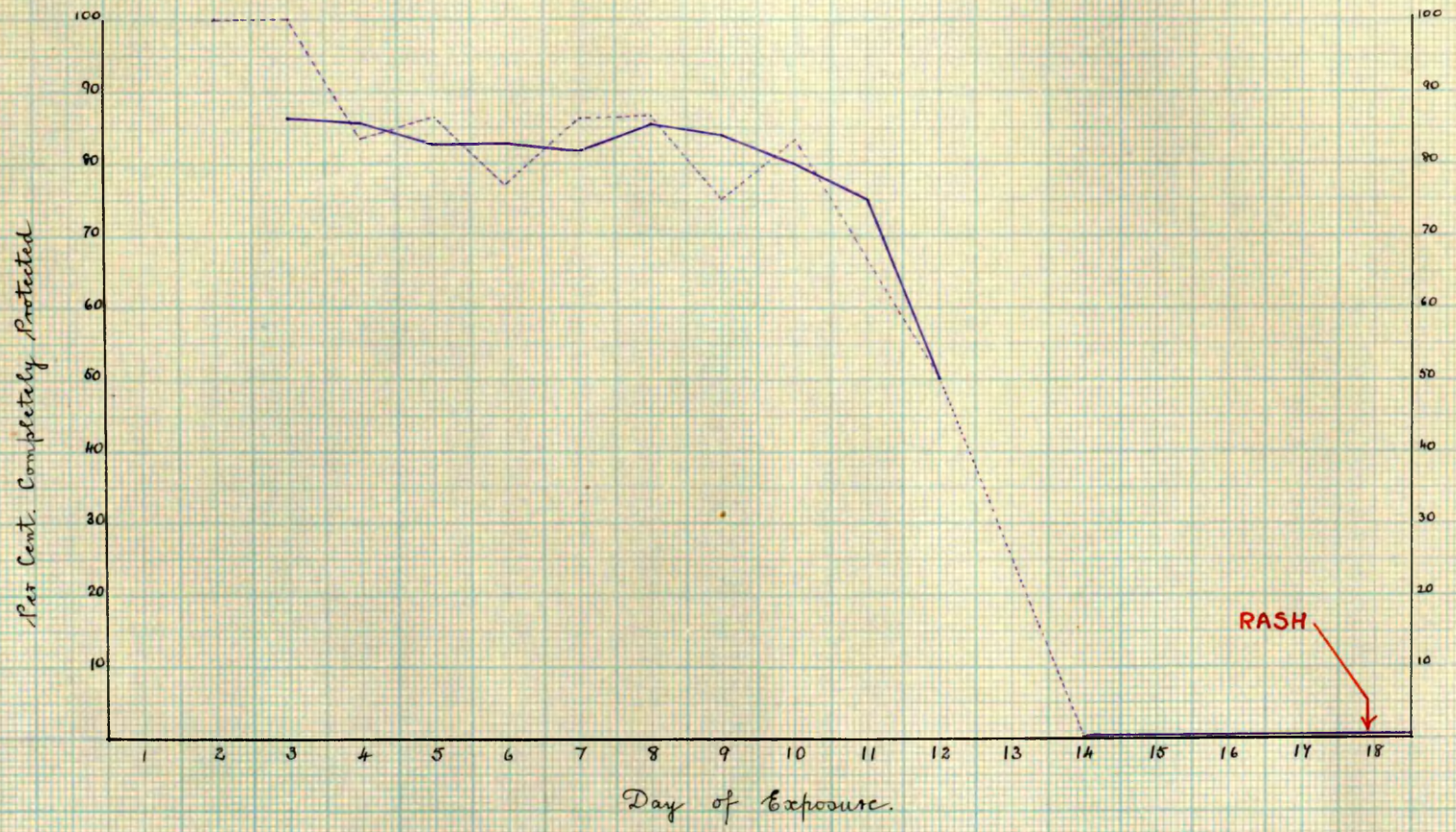
Now there is always some error creeping in with the clean-cut division into days, and in order to compensate for slight variations in estimating the days of exposure, an average of three days is probably more accurate for the central day than the single figure of the day concerned. Table II. overleaf is constructed on this principle.

TABLE 2.

GLASGOW - MEASLES

DAY OF EXPOSURE TO MEASLES.

Day	Total Contacts	No Attack	Primary Att.	Mild	Measles	Per Cent. Protected	Per Cent. Average of Three Days
1	-	-	-	-	-	-	-
2	4	4	-	-	-	100	-
3	6	6	-	-	-	100	86.15
4	55	46	9	-	-	83.63	85.8
5	52	45	7	-	-	86.54	82.6
6	48	37	7	4	-	77.08	82.9
7	29	25	2	2	-	86.21	81.5
8	15	13	2	-	-	86.66	85.4
9	4	3	1	-	-	75	84
10	6	5	-	1	-	83.34	80
11	-	-	-	-	-	-	75
12	2	1	-	-	1	50	50
13	-	-	-	-	-	-	-
14	1	-	-	-	1	0	0
15	1	-	-	-	1	0	0
16	1	-	-	-	1	0	
6-9	9	9	-	-	-	100	
Total	233	194	28	7	4	83.26	



Graph illustrating Table 2.

Day
Average of Three

From the figures presented there we can see that, presuming that the other factors are constant, there is evidently no marked change in the efficacy of the injections given up to the eighth day after exposure, i.e., taking the day of the rash as the fourth day. The numbers protected on the ninth and tenth days are rather small on which to base such a claim for them. Immediately after the tenth day, however, there is a very rapid falling off in the potency, and by the fourteenth day there is no protection whatever. These figures indicate fairly clearly that even a small dose of 5 c.c. is of value in the prophylaxis of measles.

AGE OF SERUM.

Another of the factors influencing the results is the age of the injected serum. It is known that there is a limit to the keeping properties of the immune bodies in the various therapeutic sera which have been in use for such diseases as diphtheria, scarlet fever, tetanus, etc., and there must be some time when the human convalescent serum loses its potency. There has been very little work done anywhere with regard to this aspect of the subject which I consider a very important one, for on it depends the advisability of collecting and storing serum when it is available against the time when it might be of use at the beginning of the next outbreak. The results obtained in the present series are as follows:-

RESULTS ACCORDING TO THE AGE OF THE SERUM INJECTED.

AGE IN DAYS.	Total Cases.	No Attack.	Attenuated attacks.			Mild attacks.		Normal Measles.
			Prim.	Sec.	Tert.	Prim.	Sec.	
- 25	11	11	-	-	-	-	-	-
- 30	29	23	1	2	1	1	-	1
- 35	47	36	7	-	-	4	-	-
- 40	32	25	6	-	-	-	1	-
- 45	9	8	-	-	-	-	-	1
- 50	5	5	-	-	-	-	-	-
- 55	8	3	4	-	1	-	-	-
- 60	10	5	2	1	-	-	-	2
- 65	4	3	1	-	-	-	-	-
- 70	4	4	-	-	-	-	-	-

AGE IN DAYS.	Total Cases.	No Attack.	Attenuated Attacks. Prim.	Sec.	Tert.	Mild Attacks. Prim.	Sec.	Normal Measles.
- 75	5	3	2	-	-	-	-	-
- 80	8	8	-	-	-	-	-	-
- 85	8	8	-	-	-	-	-	-
- 90	19	16	2	1	-	-	-	-
- 95	13	12	1	-	-	-	-	-
-100	13	8	2	2	-	1	-	-
-110	4	4	-	-	-	-	-	-
-120	2	2	-	-	-	-	-	-
-130	-	-	-	-	-	-	-	-
-140	2	1	-	-	-	1	-	-
Total.	233	185	28	6	2	7	1	4

In the same way as when considering the effect of the day of exposure in influencing the results correction must be made for the secondary cases. The normal attacks have been left in since they do not cause any great change in the figures although they would lower the discrepancies. Their removal might suggest juggling with the numbers to prove some perfect plan.

Table III. on the following page shows the percentages for each group of five days in the age and the averages of three such groups. It shows that within the limits covered, i.e., using serum up to 140 days old, there is practically no difference in the results attributable to the age of the serum.

AGE OF RECIPIENT.

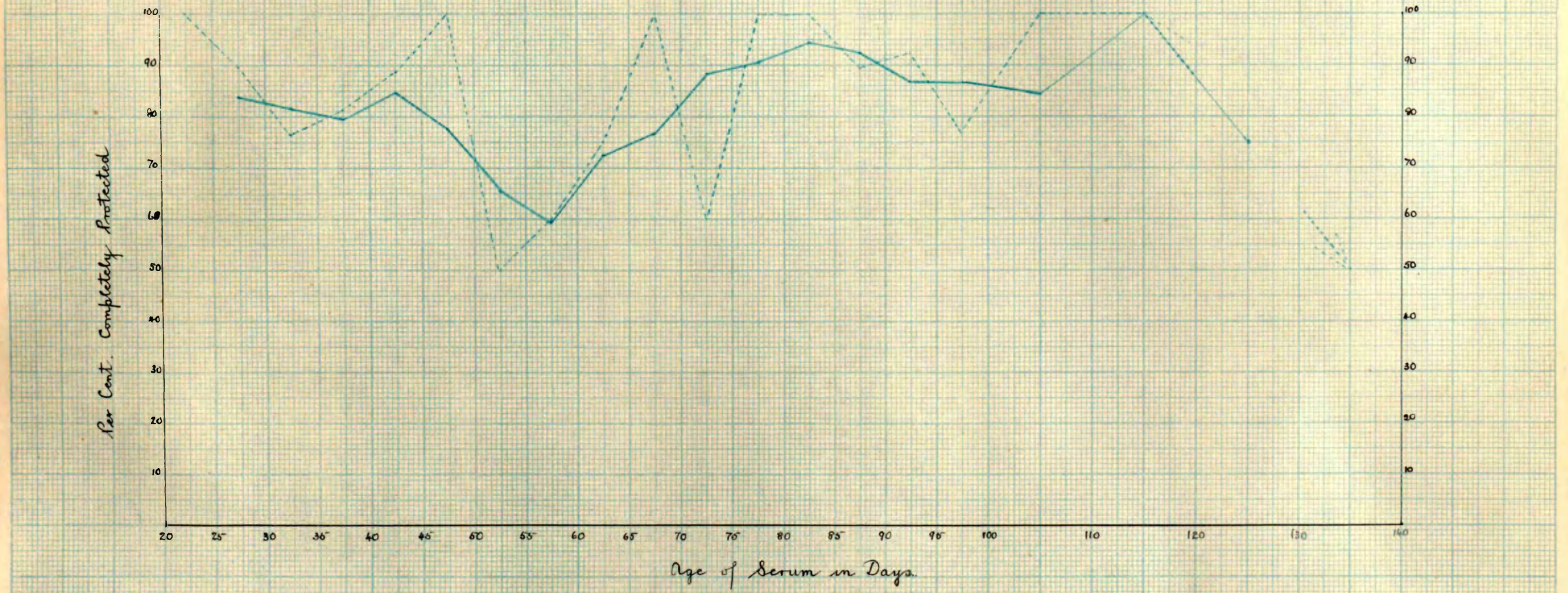
The next factor to be considered is the age of the injected child. Omitting the cases with a normal attack which we have seen was due to the late injection of the serum we get the following:-

TABLE 3.

GLASGOW - MEASLES

EFFECT OF AGE OF SERUM.

Age in Days	Total Cases	No Attack	Primary Att.	Mild	Measles	Per Cent Protected	Per Cent. Average of Three Groups
-25	11	11	-	-	-	100	-
-30	29	26	1	1	1	89.6	83.9
-35	47	36	7	4	-	76.6	81.5
-40	32	26	6	-	-	81.2	79.6
-45	9	8	-	-	1	88.9	84.8
-50	5	5	-	-	-	100	77.3
-55	8	4	4	-	-	50	65.2
-60	10	6	2	-	2	60	59.1
-65	4	3	1	-	-	75	72.2
-70	4	4	-	-	-	100	76.9
-75	5	3	2	-	-	60	88.2
-80	8	8	-	-	-	100	90.5
-85	8	8	-	-	-	100	94.3
-90	19	17	2	-	-	89.5	92.5
-95	13	12	1	-	-	92.3	86.6
-100	13	10	2	1	-	76.9	86.6
-110	4	4	-	-	-	100	84.2
-120	2	2	-	-	-	100	100
-130	-	-	-	-	-	-	75
-140	2	1	-	1	-	50	-
Total	333	194	28	7	4	83.26	



Graph illustrating Table 3.

Age
Average of Three

AGE OF THE CHILD IN YEARS.

YEAR.		AGE OF THE CHILD IN MONTHS.												Total.
		0	1	2	3	4	5	6	7	8	9	10	11	
0	F	-	-	-	11	15	12	10	3	5	3m	6	6	72
	A	-	-	-	-	-	1	1	-	-	m	1	-	4
1	F	7s	3	2	5t	1	2	4	3	2s	4	2	-	38
	A	4	-	1	1	-	1	3	3	1	-	-	-	14
2	F	10	2	4	-	2	-	7s	1	s	-	1	2	31
	A	1	1m	1m	1m	-	m	-	1	-	m	-	-	10
3	F	4s	1	s	2	-	1	-	-	1	-	1	-	12
	A	3	1	-	-	-	-	1	-	-	-	-	-	5
4	F	7	1	-	-	-	-	4t	1	-	-	1	-	15
	A	-	-	-	-	-	-	-	-	-	-	-	-	-

Years.	5	6	7	8	9	10	11	12	13	14	15	16	17	
F	5	2	2	5	2	1	3	3	1	-	1	-	1	26
A	1	-	m	-	-	-	-	-	-	-	-	-	-	2

F = Complete protection.
A = Attenuated measles, including (s)secondary, (t)tertiary and (m)mild attacks.

In the above table we have 229 cases and of these 201 were under the age of five years. Over the age of five years it can be seen that the effect of the injections was beneficial - under that age the results are very interesting indeed. In the case of this factor, as in the others, only the primary cases of measles are considered, this being the more fair estimate of the protective power of the injections.

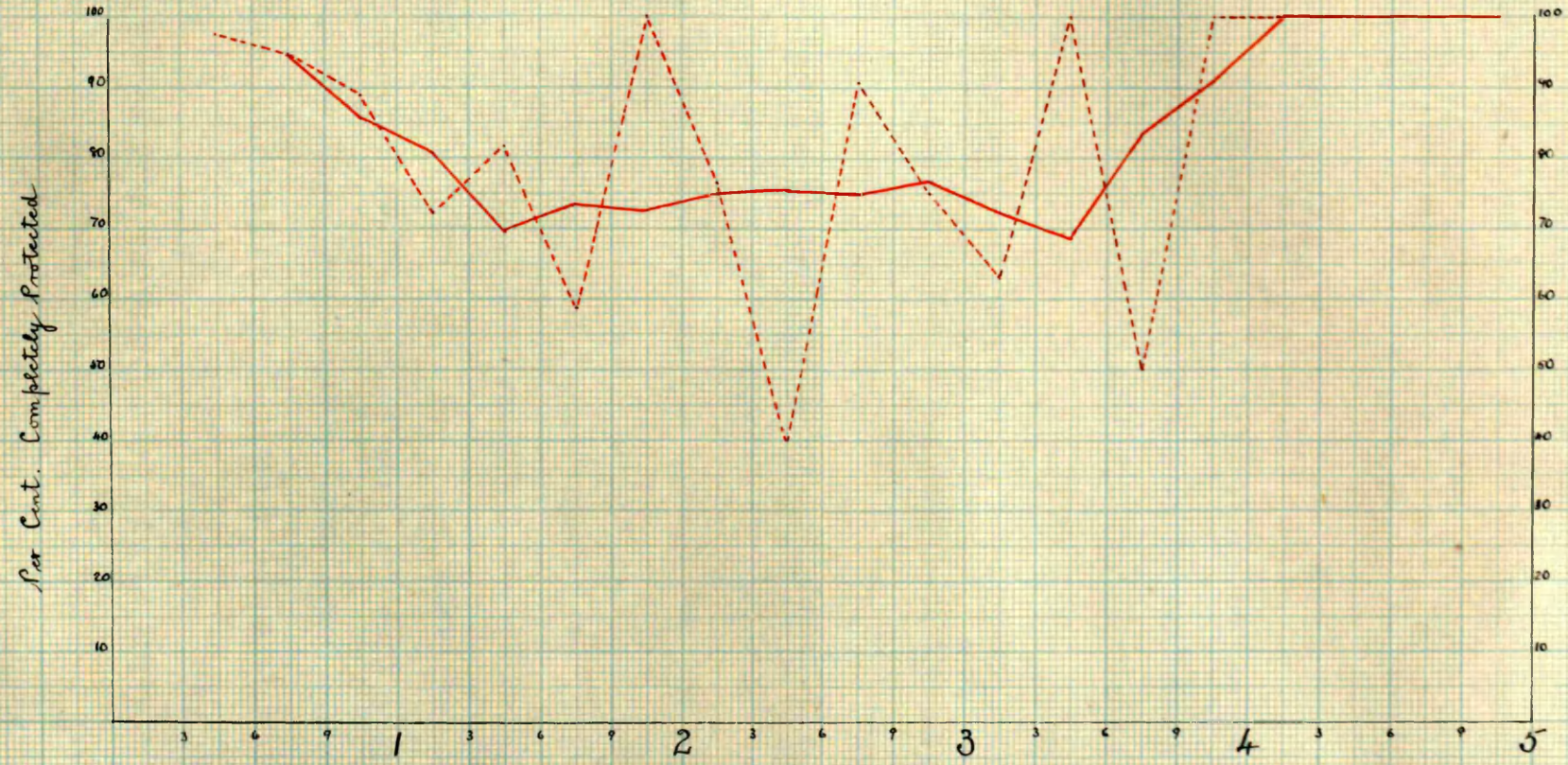
On the following page there is to be found Table IV. showing the figures on this basis indicating the effect of the age of the child on the results of the injections. There is a definite relationship between the effect produced and the age of the child. In the first year of life the protection, complete at first, falls, and in the middle of the second year is relatively low, remaining so until the beginning of the fourth year, after which the results improve. These figures indicate that the danger period is the second, third and the first half of the fourth years of life, the figures for these periods being under the general average of the complete series. These results

TABLE 4.

GLASGOW - MEASLES

EFFECT OF AGE OF PATIENT INJECTED.

Age of Patient		Total Cases	No Attack	Per Cent. Protected	Per Cent. Average of Three groups
	- 2 mos	-	-	-	-
	3 - 5	39	38	97.43	-
	6 - 8	19	18	94.74	94.74
	9 -11	18	16	88.89	85.45
One year	0 - 2	18	13	72.22	80.85
	3 - 5	11	9	81.82	69.56
	6 - 8	17	10	58.82	73.53
	9 -11	6	6	100	72.73
Two years	0 - 2	21	16	76.19	75
	3 - 5	5	2	40	75.68
	6 - 8	11	10	90.91	75
	9 -11	4	3	75	76.92
Three years	0 - 2	11	7	63.63	73.22
	3 - 5	3	3	100	68.75
	6 - 8	2	1	50	83.33
	9 -11	1	1	100	90.91
Four years	0 - 2	8	8	100	100
	3 - 5	-	-	-	100
	6 - 8	6	6	100	100
	9 -11	1	1	100	-
	Total	201	168	83.58	



Graph illustrating Table 4.

Age
Average of Three

are in keeping with the known epidemiological facts that the first five years of life are those most susceptible. The injection of convalescent serum into susceptible contacts of these years results in some failures, the graph for which shows a striking resemblance to the curve of the natural incidence of the disease.

QUALITY OF SERUM.

Another factor of importance in the determination of protection is the quality of the serum concerned but since the other factors influence the result the evaluation of this is not easy. On the following page there is illustrated in a graphic form all the doses withdrawn from each individual donor, each square representing 5 c.c. The number in the square shows the instance of cross-infection in which the dose was used, and the type of attack, if any, resulting. Incidentally it illustrates the varying success in withdrawal of blood and shows that the process became more successful towards the end when the early difficulties had been guarded against.

This compilation shows that while as a whole the sera of the donors during the investigation were fairly potent there were undoubtedly some poor ones. For instance, in one case of cross-infection twelve contact patients were injected and only three remained free from attack. The serum used was from the same donor injected in varying doses - but the effect produced was poor in comparison with that obtained under less favourable circumstances with another serum. It is quite possible that if another donor had been chosen more favourable results might have been obtained, since it was found from the records kept of each donor that this particular one had had a less severe attack of measles than the usual.

DOSAGE.

The amount of serum injected must have some effect in

The next page shows graphically the donor, the amount, the use and the result of every 5 c.c. dose collected. The same symbols are used as before.


indicates a test dose retained in store.


indicates complete protection.

indicates a very attenuated case (doubtful case)


indicates a primary attenuated measles.


indicates a primary mild attack.

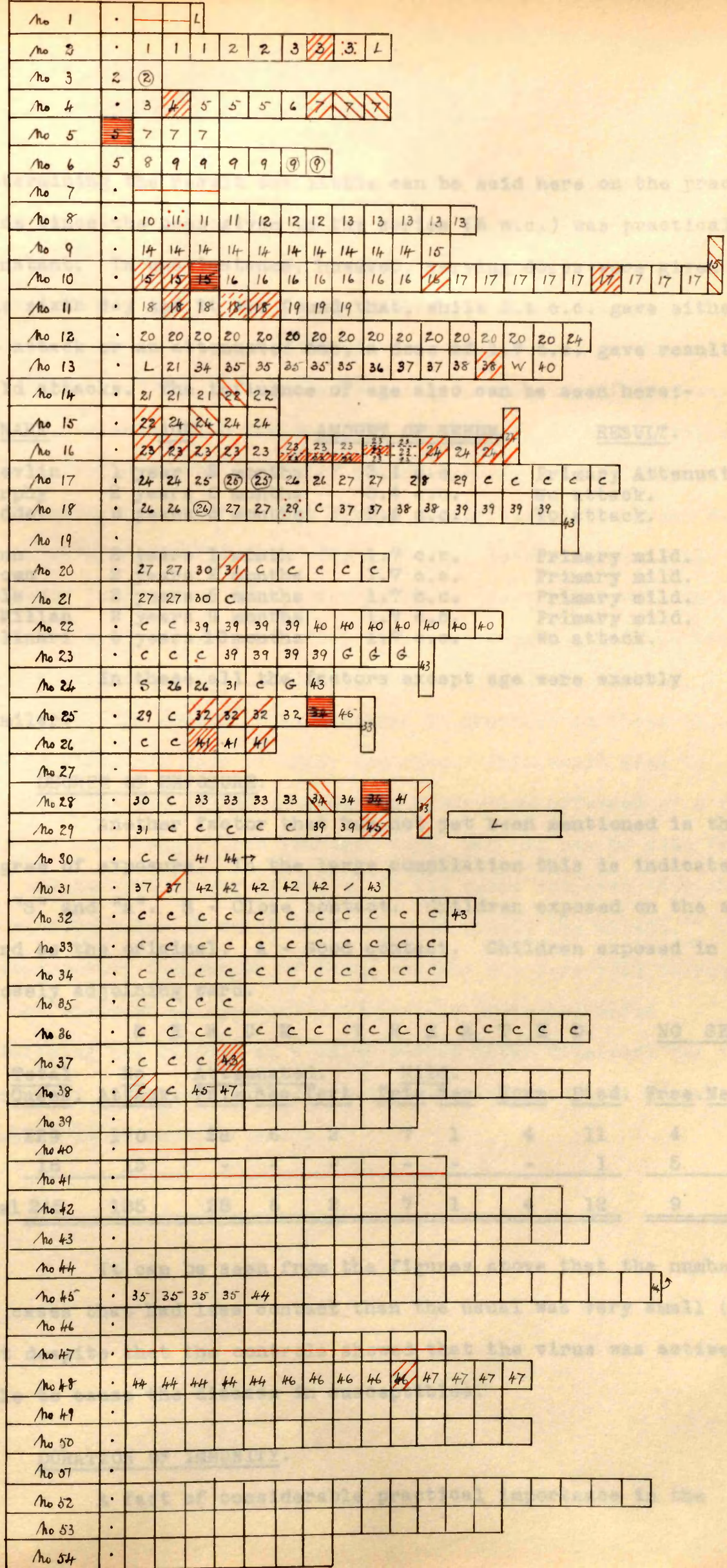

indicates a secondary attenuated measles.


indicates attenuated attack on later occasion.


indicates a normal attack of measles.


indicates a rejected dose.


indicates a dose still in store.



determining the result but little can be said here on the practical side since the dose given in the series (5 c.c.) was practically constant. In one instance, however, varying doses were given on the sixth day and it was found that, while 3.4 c.c. gave either no attack or an attenuated one, a dose of 1.7 c.c. gave resulting mild attacks. The influence of age also can be seen here:-

NAME.	AGE.	AMOUNT OF SERUM.	RESULT.
Shevlin	1 year 2 months	3.4 c.c.	Primary Attenuated.
Murphy	2 years 6 months	3.4 c.c.	No attack.
Cadder	6 years 5 months	3.4 c.c.	No attack.
Lynn	2 years 1 month	1.7 c.c.	Primary mild.
Brown	2 years 2 months	1.7 c.c.	Primary mild.
Bole	2 years 5 months	1.7 c.c.	Primary mild.
McMillan	2 years 9 months	1.7 c.c.	Primary mild.
Molinari	3 years 10 months	1.7 c.c.	No attack.

In these all the factors except age were exactly similar.

DEGREE OF EXPOSURE.

Another factor that has not yet been mentioned is the degree of exposure. In the large compilation this is indicated by "S" and "A". S - Close contact. Children exposed on the same ward as the original. A - Good contact. Children exposed in closely adjoining ward.

		SERUM TREATED.							NO SERUM.	
	Total Cases.	No Attack.	Attenuated. Prim.	Sec.	Tert.	Mild. Prim.	Sec.	Norm.	Died.	Free.	Measles.
S	229	170	28	6	2	7	1	4	11	4	20
A	16	15	-	-	-	-	-	-	1	5	3
Total	245	185	28	6	2	7	1	4	12	9	23

It can be seen from the figures above that the number of cases that had less contact than the usual was very small (16) but despite that the controls showed that the virus was active and able to cause the disease in susceptibles.

DURATION OF IMMUNITY.

A fact of considerable practical importance in the

utilisation of the power of convalescent measles serum is the duration of the passive immunity conferred by an injection. The duration varied in many of the cases; it probably varies with the amount injected. In the series under consideration, using the standard dose of 5 c.c. modified cases occurred after the usual incubation period, indicating that the protection afforded was not always complete. The numbers of primary cases do not increase in proportion to the length of exposure showing that other influences are at work. The age of the patient had a great deal to do with this variation. The number of secondary cases is probably larger than that recorded since there may have been some who developed the disease after dismissal from hospital as free from a primary attack. Judging, however, from the figures available, the number of secondaries is greatest in those injected in the first six days of their exposure. This would seem to suggest that the period of complete protection afforded by 5 c.c. is not much longer than fourteen days, but, as can be seen from the tertiaries, it may extend up to six weeks and even then the protective power is still sufficient to modify the attack. Unfortunately the number of those parents who were told to report in the event of an apparently completely protected child developing the disease at a later period after dismissal was very small and the important deduction of the length of the immunity remains as obscure as before.

DETAILS OF THE CASES OCCURRING AFTER SERUM INJECTIONS.

PRIMARY ATTENUATED ATTACKS.

Case.		Fever.	Catarrh.	Koplik's.	Prod.rash.	Rash.
3	Hughes	20	17	0	16	20
7	Brown	19	19	0	-	20
15	McLeish	13	-	16	-	17
16	Emery	25	0	0	-	22
17	Williams	18	0	0	-	18
18	McGie	10	0	0	-	12
	Gallacher	10	0	0	-	?13
	Mills	10	12	0	-	12
23	Buchanan	17	17	?	-	19
	Johnstone	14	15	0	-	15
	McCabe	13	13	0	-	13
	Bell	16	15	?	-	16
	Shevlin	10	9	?	-	13
24	Routledge	22	22	0	-	22
	Kelly	16	0	?	17	19
	Louden	14	0	0	-	15
31	Stewart	18	19	0	-	19
32	Clarke	14	0	0	-	19
	Sheerin	17	0	0	-	21
	Neilly	23	0	0	-	?22
33	Hanlan	21	21	?	-	22
	Murray	0	0	0	-	22
37	Smith	0	0	0	-	25
	Forsyth	0	0	0	-	22
38	Whicher	0	0	0	-	11
41	Kelly	16	0	0	-	14
43	Carstairs	14	14	?	-	14
46	English	0	22	?	-	22

SECONDARY ATTENUATED ATTACKS.

4	Johnstone	27/13	25/11	0	-	27/13
7	Healy	29/15	29/15	0	-	30/16
	Jordan	28/14	30/16	0	-	31/17
15	Reid	23/13	24/14	0	-	24/14
22	Quail	29/17	31/19	?	-	31/19
33	McCaffrey	26/19	26/19	?	-	27/20

TERTIARY ATTENUATED ATTACKS.

15	Collins	45	-	-	-	45
29	Russell	0	39	0	-	39

PRIMARY MILD ATTACKS.

22	Thomson	12	?	0	-	16
23	Lynn	13	12	?	-	14
	McMillan	9	9	?	-	14
	Brown	13	8	?	-	14
	Bole	14	12	?	-	15
41	Moley	8	10	?	-	11
45	McDuff	19	-23	?	-	24

SECONDARY MILD ATTACKS.

24	Wright	26/11	?	0	-	31/16

INCOMPLETE PROTECTION.

On the following pages there are some of the details of thecases that were not completely protected by the injection of the serum. They are put under the different headings adopted in all the tables and from them we will be able to come to a general description of the typical case in each class. The numbers under the different signs on the preceding page are the days on which that particular sign was first noted.

PRIMARY ATTENUATED ATTACKS.

There were twenty-eight patients scattered throughout the epidemic in this category.

Fever. This varied from 10 days to 25 days with the average onset on 16.1 days. It should be noted that there were five cases who did not in the least deviate from the normal range of temperatures. The others as a rule showed transient rises of one or two four-hourly readings.

Catarrh. This sign was totally absent in 15 out of the 28 cases. When it is remembered that the slightest sign of suffusion was noted it is evident that this sign was greatly influenced by the injection. Average was 16.5 days.

Koplik's spots. In only one case was it reported that Koplik's spots appeared and since I personally did not see the case at the time (and found the reporter's knowledge of them very poor) I do not think any stress should be laid on this single case. In other seven there was no note made about them but in the twenty remaining there was not one spot seen.

Prodromal rash. This was only noted in two cases. It was rather like the attenuated rash generally but is noted here as occurring before the more usual rash appeared. It really merged into the later rash and did not differ much from it.

Rash. The time of appearance varied from 11 days to 25 days, the average being 17.8 days. This eruption varied but slightly generally being present on the face and chest especially the upper part above the nipples. It was also frequently on the trunk but its appearance on the limbs though not rare was uncommon. In character it was suggestive of the disease in that it was blotchy looking but closer inspection revealed that it was more punctuate and less macular than the normal eruption. The colour was not as bright being more like the staining of the normal fading rash. It was rather papular and fairly characteristic - being more easily known by sight than by any description that could be given.

As can be seen from the preceding page the different signs varied somewhat in their appearance in the individual case, the averages being ascertained as follows:-

Primary Attenuated.	Fever.	Catarrh.	Koplik.	P.Rash.	Rash.
Number showing sign.	23	13	? 1	2	28
Total days.	370	215	16	33	499
Average (in days).	16.1	16.5	16	16.5	17.8

SECONDARY ATTENUATED ATTACKS.

Six cases come under this heading and there is less variation in the times the signs appeared.

Fever. The time varied from 23 to 29 days after the original exposure and from 13 to 19 days after the second. In no case was this sign absent - differing from the primaries.

Catarrh. This ranged from 24 to 30 days from the first exposure and from 11 to 19 days from the second case.

Koplik's spots. In four their absence was noted - in the other two there was no report.

Rash. This appeared 24 to 31 days and 13 to 20 days afterwards.

Secondary Attenuated.	Fever.	Catarrh.	Koplik.	Rash.
Number showing sign.	6	6	0	6
Total days.	162/91	165/94	0	170/99
Average (in days).	27/15.2	27.5/15.7	0	28.3/16.5

Secondary cases seem to show the signs sooner after the second exposure than the primary cases after the original exposure.

TERTIARY ATTENUATED ATTACKS.

Only two cases reported details and these do not allow any comparison. Some more are bound to have taken measles after the injection but unfortunately no other report has been received.

PRIMARY MILD ATTACKS.

Seven cases took mild attacks on the first exposure.

Here even with the modifications not quite as marked there were no Koplik spots reported. In one there was no catarrh. One case showed a long period but the other six had signs at a shorter interval than above.

Primary Mild Attacks.	Fever.	Catarrh.	Koplik.	Rash.
Number showing sign.	7	6	0	7
Total days.	88	74	0	108
Average (in days).	12.6	12.3	0	15.4
ONE SECONDARY MILD ATTACK.				
	26/11	?	0	31/16

DETAILS OF THE CONTROL CASES DEVELOPING MEASLES.

Case.	Name.	Fever.	Catarrh.	Koplik.	P.Rash.	Rash.
1.	Jenkinson.	16	14	15	15	17
	McLeod.	14	17	18	17	18
	Rennie.	?	29/16	?	30/17	31/18
	Ross.	13	15	?	15	17
2.	Taylor.	15	15	15	15	17
3.	Connelly.	?	?	?	?	14
4.	Ferrier.	?	18	?	-	20
	Brown.	16	15	17	-	18
	McIlvenny.	12	15	15	15	18
	McLauchlan.	16	18	18	18	20
7.	Dunn.	13	14	16	17	18
	Cameron.	17	17	18	-	20
	Wilson.	11	10	?	13	15
11.	Petrie.	?	?	?	-	17
15.	Stirling.	11	14	-	-	14
	Blair.	15	-18	18	-	18
17.	Kennedy.	?	18	?	-	21
24.	Naismith.	14	15	15	-	15
29.	Smith.	17	17	?	-	20
31.	McMillan.	12	16	16	-	16
34.	McEwan.	0	18	?	-	19
38.	McAllister.	?	0	?	-	13

Omitting then the case of Rennie who took on second exposure

Fifteen cases with fever totalling 212 days Average 14.13 days.
Eighteen with catarrh totalling 284 days Average 15.78 days.
Eleven with Koplik's totalling 181 days Average 16.45 days.
Eight with prodromal rash totalling 125 days Average 15.62 days.
Twenty-one with the Rash totalling 365 days Average 17.38 days.

Comparing the times of the appearances of the different signs of the infection there does not seem any justification for

saying that the effect of serum is shown by lengthening of the interval from infection to invasion. It is worth noting, however, that there seems in the modified cases to be less uniformity in the times:-

	Modified Attack.	Extent.	Normal Attack.	Extent.
Range of Fever,	10 - 25	(16)	11 - 17	(7)
Range of Catarrh,	12 - 22	(11)	10 - 18	(9)
Range of Koplik's,	0		15 - 18	(4)
Range of Rash,	11 - 25	(15)	13 - 21	(9)

It is not, however, in the time of appearance of the signs but in the character of them that there is an enormous difference. There is no comparison in the comfort of the patients in the two groups that can be indicated by mere figures. The view of one in each lot is more eloquent of the benefits of serum than a long dissertation.

The standard dose of 5 c.c. used throughout the work was very successful and need not be increased except in special cases which should include delicate children of 2 or 3 years recovering from a serious attack of any of the exanthemata especially whooping-cough, diphtheria and scarlet fever. The earlier the dose is given after exposure the smaller it requires to be but this variation in dosing should not be carried too far for there is no mathematical precision in the results owing to so many variable factors. As has been demonstrated in this work even where all the factors are exactly similar, varying results occur due to some influence beyond our present knowledge.

Examination of the literature shows that many investigators advocate larger doses for children over five years, increasing according to the age. Table IV. indicates, however, that after a decrease in the age periods 1 - 2y., 2 - 3y., 3 - 3½y. the natural resistance of the patient increases with age and the writer therefore thinks it unnecessary to inject more serum after these very susceptible periods have been passed.

O U T L I N E

for

F U T U R E U T I L I S A T I O N

of

C O N V A L E S C E N T S E R U M.

FUTURE UTILISATION.

It is universally acknowledged that among the infectious diseases measles constitutes the greatest menace to child life. It is a typical disease and it has for long been considered a simple inevitable evil that must be faced by everyone at some time in his life, but unfortunately it is not as innocent as the majority of people used to think. On the contrary it causes six to eight times the number of deaths from scarlet fever and unlike this latter disease it does not seem to be decreasing in virulence.

I have been fortunate in having the figures for measles in the City of Glasgow for the last eleven years and have reduced them from actual quantities to relative proportions. Sufficient it is to stat that the tables following cover a total of 118,265 patients. Such a large number over the period mentioned would constitute a representative population affected by measles and any deductions reached from such data as they afford would be fairly accurate in general application.

The first of these - Table V. - shows the relative mortality in the various age groups: under 6 months, 6 months to 1 year, etc. in the eleven years prior to the current one, the figures for the present year including only those up to the end of May. It will be noticed immediately that, year by year, there is a very striking relationship between the different age groups, the variations on each side of the average being but slight. The percentages practically coincide with those quoted at the beginning of the work from Chalmers (Glasgow 1908), Rolleston (London 1912) and Halliday (Glasgow 1926). Here the deaths under five years form 97.32% and those in the second year 46.72%. These three other observers give corresponding figures of 95.06, 97.7 and 95.88 - and 45.65, 47.3 and 47.31 respectively.

It is perfectly obvious that the field for the utilisation of convalescent serum is in these groups particularly the second year. Now a glance at Table VI. shows that this particular group shares with the first year of life the highest case-death rate - the percentages in them being 13.83 and 16.94 respectively.

RELATIVE MORTALITY.

Per Cent in each Age Group.

Year	-6m	-1y	-2y	-3y	-4y	-5y	-10y	-15y	15y+
1921	2.73	18.18	47.27		22.73		9.09	-	-
1922	2.56	24.49	44.56		25.38		2.80	-	.31
1923	2.68	23.39	49.03		22.14		3.03	.36	.36
1924	3.49	24.80	49.42		20.54		1.36	.39	-
1925	.85	27.12	49.15		19.49		3.39	-	-
1926	3.98	24.82	47.07		21.78		1.87	.23	.23
1927	1.95	25.08	45.93		25.08		1.63	-	.33
1928	3.99	27.39	48.40		18.08		1.33	.27	.53
1929	3.75	23.75	53.75	7.50	5.00	2.50	3.75	-	-
1930	4.13	35.71	43.81	10.53	3.38	.75	1.13	.37	.37
1931	2.89	28.37	43.27	14.18	6.01	2.40	2.88	-	-
1932 May	2.26	29.94	49.72	6.78	6.78	1.13	2.82	-	.57
				11.18	23.73 5.33	1.70			
Average	2.98	25.80	46.72		21.82		2.47	.15	.26

TABLE 5.

CASE MORTALITY

Per Cent in each Age Group.

Year	-6m	-1y	-2y	-3y	-4y	-5y	-10y	-15y	15y+	Total
1922	27.31		20.32		4.54		.5	-	1.82	6.82
1923	20.45		17.71		2.98		.47	1.33	1.61	5.43
1924	22.49		21.07		3.13		.35	1.17	-	6.20
1925	8.27		7.8		1.04		.13	-	-	1.81
1926	12.68		10.20		1.47		.12	.41	.6	2.65
1927	15.04		13.14		2.32		.13	-	1.05	3.42
1928	16.86		13.56		1.71		.13	1.04	1.75	3.72
1929	5.09	6.78	6.63	.95	.52	.30	.09	-	-	1.24
1930	7.8	14.91	7.78	1.84	.64	.13	.06	.77	.69	2.14
1931	8.83	14.18	9.95	3.39	1.23	.59	.17	-	-	2.71
1932 May	5.13	16.4	13.56	2.03	1.98	.36	.27	-	1.35	3.67
	7.24	18.96 13.75		2.32	2.67 1.04	.36				
Average	16.94		13.83		2.23		.22	.45	.89	3.83

TABLE 6.

It will be more convenient to have these figures in a form where the relative values can be seen at a glance. Thus:-

Age Group.	Cases.	Deaths.	% Relative Mortality.	Case Death-rate.
Up to 1 year.	7,744	1,335	28.78	16.94
1 - 2 years.	15,224	2,158	46.72	13.83
2 - 5 years.	44,258	1,012	21.82	2.23
5 - 10 years.	48,137	115	2.47	.22
10 - 15 years.	1,553	7	.15	.45
Over 15 years.	1,349	12	.26	.89
TOTALS.	118,265	4,639	100.20	3.83

From the above figures for these years there can be seen the number of notified cases of measles in each age group. Now these figures are not strictly accurate before the school age since cases are not notifiable, so, while those for school age are more or less right, the pre-school group is probably much larger and the case death rate less. Out of the total of 118,265 cases in these years there were 1,553 between the ages of 10 and 15 years while there were 1,349 over 15 years of age. Thus in the period of eleven and a half years there were 1,349 possible donors. Of course, of these, there must have been some who were not acceptable owing to the presence of tuberculosis, positive Wassermann or Kahn tests while the presence of some complicating disease may have been sufficient to exclude others. If the proportion of these rejected donors is more or less a constant (5% to 10% in this investigation) there may have been about 1,200 patients suitable. If they had each given 100 c.c. blood (50 c.c. serum) the total number of 5 c.c. doses would have been 12,000. Considering that the total number of cases of measles under review was 118,265 it is quite evident that the supply for general use would have been very inadequate. Even enlisting the cases between 10 and 15 years there would only be an additional 15,000 doses - a quantity still insufficient. Furthermore these possible injections would have only given a passive

immunity lasting for a few weeks when the danger of an attack would have returned. These figures clearly show that however desirable the wholesale prevention of measles might be it is at present impossible of attainment by means of convalescent serum. To attempt this impossible task would be to throw away the opportunity of utilising the available supplies to the best advantage. Convalescent serum is very valuable owing to its scarcity as well as to its power in influencing favourably the course of the disease.

During the last epidemic period it was clearly shown that administratively the procedure of protective inoculation of convalescent serum was of great value in controlling possible outbreaks of measles in hospitals and country homes devoted to the treatment of young children.

Another possible practical use of serum in the control of measles is suggested by the following table. The figures have been placed at my disposal by Dr.W.A.Horne of the Northern Division of the City of Glasgow Public Health Department and refer to the previous measles epidemic in 1929-1930.

Measles in the Northern Division: 1929-1930.

	AGE GROUPS.				
	-6m.	-1y.	-2y.	-3y.	Total.
Total number of cases of measles in age groups, ...	45	236	547	969	1797
Total number of deaths from measles in age groups, ...	7	40	32	15	94
Number of cases taking from previous case in house, ...	15	94	194	333	636
Number of deaths in these secondary cases, ...	1	7	11	3	22

This table suggests that in the course of a measles epidemic the best use of convalescent serum, outside institutions, would be to immunise those susceptible children who can be considered certain victims of the disease due to the occurrence of a previous

case of measles in the household. The figures show that about one third of cases under three years could be reached in this manner and that the measles mortality would be reduced though there would always remain some children whose exposure was unknown.

Thus in the period shown there were 22 deaths under three years which might have been saved by 636 suitable injections, or 19 deaths under two years which might have been avoided by 303 injections. This amount of work would probably enable the measles mortality to be reduced by one-fifth besides saving much ill-health in those who survive. The question arises whether convalescent serum should be used in this field or whether after investigation parental serum might not meet the occasion and so free the limited supply of the former for institutional use.

Any scheme for the utilisation of convalescent serum must provide for the collection of the raw material. It is not only the collection but the treatment of the blood in the various stages on the way to serum or plasma that is difficult, and it would be indeed dangerous to leave to any inexperienced collector. In the preparation of the serum on the large scale that would be necessary these essentially important steps should be allocated to a special worker competent to deal with such material. There must be perfect reliablity in the sterility of the finished product since fatal accidents have been reported elsewhere owing to contamination of the serum injected. The only way to lessen the risks entailed in the collection and storing of the serum would be to set aside one of the Fever Hospitals in the City as the destination of all adult measles cases. This, of necessity, would interfere to a certain extent with the normal duties of the staff but the efficient production of a standard serum would be of great benefit in the long run. There ought also to be efficient cold storage accommodation to keep the serum in as good a condition as possible,

for, though it has not yet been determined the exact time chilled serum will retain its potency, the experience of the last outbreak indicates there is no appreciable change in strength at the end of four and a half months. Some serum has been stored against future use and it is hoped from the results of the injections of this serum to find out if it retains its potency. If so it will be available at the beginning of an outbreak occurring one or even two years after its withdrawal. On the determination of this point depends to a large extent the utility of the whole procedure for as has been demonstrated earlier in this work the donors did not become plentiful until the height of the epidemic was reached. There had been a demand for the serum long before it was available and doubtless there were many children who succumbed to the disease who might have resisted the attack if they had had the help of the serum. Another point that might easily arise in the future organisation of the supply is the question of remuneration of the donors. During the investigation concluded no such question arose but in the event of the withdrawal of larger quantities that point would have to be considered.

The limited quantity of convalescent serum which will be available at any time demands that only the best use should be made of it. This entails a study of its action such as has been done here during the investigation.

Measles is one of the diseases which seem to be unavoidable. The infectivity is so very intense and the contacts so numerous that the disease must be encountered by everyone some time and the problem is reduced to rendering it less dangerous. This can be done in either of two ways. The first is to postpone the onset till the years when the mortality and morbidity are very low; the second is to render the disease attenuated and so obtain an early active immunity. Each of these methods has its place.

Postponement involves the complete protection of the child from measles attacks during the early years which, as we have seen, are the dangerous ones. This can be done by convalescent serum in families where contact with measles occurs only once during an epidemic period. Such is the case in better class areas where the source of infection is an older child. If a dose of the serum is given as soon as possible after exposure there is little likelihood of the younger child contracting the disease. A dose of 5 c.c. should give complete protection in the great majority of cases. This small dose is quite sufficient and should allow a large number of susceptibles to benefit from the available serum.

The children who should have first claim on the supply are those in fever hospitals suffering from infectious diseases and in this group the injections can be given on the day the case of measles is discovered. Similarly those in general institutions for children such as Child Welfare Homes, Creches, are also suitable subjects for complete protection from an administrative as well as from a personal point of view.

These groups can be reached in the early days of exposure but there is another group that demands attention. This consists of those sickly children who are at home and who have been exposed to measles in another of the same family. It is matter for regret that such cases - who are those in most need of protection - are at present beyond the scope of our help. The amount of serum available during the last outbreak was insufficient for the needs of the two institutional groups mentioned but provided that the supply can be increased in the future there is no doubt but that these last children might be protected.

In contradistinction to complete protection attenuation should be the aim, this being the most important of the uses to which convalescent serum can be put. It is not in all cases that

attenuation should be the goal but the advantages in its favour are many. Besides being economical in serum the immunity produced is more or less permanent and the fact that the child does not feel in the least ill is a great consideration. (There were no complications in any of the cases in the series who had injections of the serum and the literature also indicates that this is the common experience.) With such advantages it is regrettable that so many children must of necessity be left to bear the full brunt of an attack of measles.

An attempt might be made to use the serum not to prevent but to attenuate measles in such groups of healthy children as can be found in industrial schools, orphan homes, etc., where the exposed are under daily supervision. It might also be applicable to healthy children at home when in contact with measles in the house provided that those thus injected are over the age of five years - this to ensure that no risk would be run with those in the dangerous years.

Attenuation can be brought about by either making the dose smaller or by giving the dose later in the incubation period. Of these two the more economical in serum is the former but the latter might be more easily performed in practice when the dose in each phial is the standard 5 c.c. From the experience of the work done it is not easy to foretell which cases will take attenuated attacks and which will escape entirely. In the event of a small dose producing complete protection where it was not specially desired, the patient should be exposed to a second acute case at the end of the normal incubation period when in all probability an attenuated attack would ensue. This method of making sure that there would be attenuation is more likely to be carried out without protests, a state of affairs unlikely to result from the continental suggestion of injecting active measles blood into the protected patient. This latter procedure is fraught with a certain amount

of danger for the blood must be fresh, it must have a negative Wassermann reaction and should undergo other tests before it is passed as fit for injection into humans.

There is a large field in which measles convalescent serum can be used in the campaign against the disease but it is doubtful if any permanent benefit will result to the recipients unless a definite though modified attack ensues. In assessing the dose most suitable to a particular child the factors to be considered are the day of exposure and the age of the child. Perhaps in the light of further knowledge there will be some modification due to the age of the serum but at present this is not easily ascertained. The other factors do not have any great influence on the effectiveness of the serum, provided, of course, the donor has had a good and unmistakable attack of measles.

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