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EXPERIMENTAL MEASLES.*

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INTRODUCTION.

THE search for the cause of an infectious disease like measles becomes greatly simplified when we learn how to secure the unknown "virus" in relatively pure form unmixed with common microbes. Various methods may now be applied to the investigation of the virus. The transmission of measles from mother to fetus would seem to point to the presence of the cause of the disease in the blood. In the 20 cases of fetal measles collected by Ballantyne¹ it seemed that the infection of mother and fetus must have been simultaneous because the eruption in both corresponded in character. In order to learn something further as to the presence in the blood of the cause of measles, inoculations of human beings would seem to be necessary because, so far as we now know, this disease is probably not communicable to animals. Grünbaum's² experiments with measles in the chimpanzee appear to have given negative results.

In the present article I propose to review briefly the results of the inoculation of measles as they appear in the literature, and then to record two experiments of my own from which I believe certain conclusions may be drawn.

REVIEW OF THE LITERATURE.

The first attempt at inoculation of measles of which we have any record was made by Francis Home, in Edinburgh, in 1758. Although he nowhere in his writings makes any acknowledgement thereof it has been regarded as probable that he received the inspiration to make this attempt from the following suggestive statement by Alexander Monro (secundus):³

*Received for publication January 10, 1905.

¹*Arch. of Pediat.*, 1893, 10, p. 301; also *Manual of Antenatal Pathology and Hygiene*, 1902, p. 196.

²*Brit. Med. Jour.*, April, 9, 1904, 1, p. 817.

³*De venis lymphaticis valvulosis et de earum in primis origine*, 1757.

How successful inoculation of smallpox has turned out is known to all, but I regard it as altogether certain that inoculation of measles will be much more useful and successful. For it is well-known how liable this disease is to infest the lungs, and how great destruction it causes there. This seems in the first place to be due in large part to the contagion which flies about in the air, and is drawn into the lung cells in breathing, and persistently clings to them, and causes a cough there, or in other words, excites an attempt by nature to drive off the noxious matter. If measles were really to be induced by inoculation artificially produced, it is very likely that the lungs would be more free from inflammation, and in general the disease would attack the skin only. If this should turn out so what a great profit and utility it would bring to mankind! The experiment can bring about no inconvenience or loss. It is probable that inoculation can be performed, if only the pustules and spots of matter can be rubbed on cotton, and if this (either fresh or put on glass carefully covered and preserved) be applied to a little wound, exactly in the same way as variolous matter.

What Home himself appears to have hoped to accomplish by this experiment, as well as the methods he employed, may be given best in his own words:¹

Considering how destructive this disease is, in some seasons; considering how many die, even in the mildest epidemical constitution; 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 as the Turks have taught us to mitigate the smallpox. I suspected strongly that the cough, often so harassing in the mildest kind, was produced by receiving the infection mostly by the lungs; and I hoped that this symptom would abate considerably, if I could find a method of communicating the infection by the skin alone.

But there was no matter to be had from the measles. A woollen glove taken from the arm of a measly patient would not answer my purpose, as a part of the infection might be drawn in by the lungs. I could not find a sufficient quantity of scaly matter, after the measles were dried to serve my purpose. I then applied directly to the magazine of all epidemic diseases, the blood.

As the measly matter behaved to be but a small portion of the whole mass, I chose to make use of the blood when it contained the morbid matter in the highest state of acrimony. In that situation the blood seemed to me to be, the next day after the turn of the measles, when their matter by juxtaposition and stagnation becoming more acrid, as we know happens in all eruptive cases, was again absorbed into the mass of the blood, and was the cause of the inflammations which happened then and afterwards. I chose to take it from the most feverish patients.

I was not contented with that alone, but thought that I should get the blood more fully saturated with what I wanted, if it was taken from the cutaneous veins amongst the measles, than if I took it from a large vein, where there was a much greater proportion of blood from the more internal

¹ *Medical Facts and Experiments*, Edinburgh, 1759.

parts, than from the skin. I therefore ordered a very superficial incision to be made amongst the thickest of the measles, and the blood which came slowly away was received upon some cotton.

What I had most to fear was a deficiency of morbillious matter; and therefore, it was plain, that the sooner it was applied, and the more close it was kept, the better chance it had to succeed. An incision in each arm, as is made in the smallpox, was giving it a greater opportunity to take place. I thought it a very material point to allow the wounds to bleed for a quarter of an hour before the cotton was put in, that the fresh blood might not wash off, or too much dilute the morbillious matter. I have always let it remain three days in the wound. I have kept exactly to all these circumstances, finding that the observance of them was attended with success.

Under an uncertainty whether I was able to produce this disease, I made a trial and found it succeeded. This success encouraged me to proceed towards completing the discovery. From the prejudices of mankind, I found it difficult to get the blood as I wanted it, and much more difficult to find subjects for inoculation. I shall circumstantially narrate the experiments which are already made, and which appear to me amongst the most material that ever were made for the good of mankind, in this part of the world; for the inoculation of the smallpox was already established in Turkey before it was brought here. Even there it was probably the effect of chance, and not the result of reason. This improvement of our art has been long wished for by many, but never yet, so far as I know, been put in practice.

According to his own records Home attempted to inoculate measles in 15 different persons, and he concludes that in most instances he succeeded in producing the disease in a mild and modified form. In his "Principia Medicinae" (1770) he summarizes the matter in the following statement:

"Morbilli per insitionem, ope sanguinis infecti, communicantur, uti a me usu confirmatum est. Die sexto plerumque febricula sese monstrat, mitissima tussicula, sine insomnio et inflammationis symptomatibus, concomitante; et neque febre hectica, neque tusse, neque oculis inflammatis succedentibus."

Home's inoculations have been accepted as successful by many contemporary and later writers and his name has been handed down even into the text-books of the present as the one who first succeeded in inoculating measles. Perhaps the following letter by J. Cook, in the *Gentleman's Magazine and Historical Chronicle* for 1767, conveys a fairly accurate idea of how the question presented itself to some at least of that period:

The measles, though not so fatal as the smallpox, is yet attended in the natural way with many dangerous symptoms, and often produces very troublesome effects. I would therefore beg leave to recommend to the public the

practice of inoculation in this distemper as well as in the other, and am confident that by this method many may be preserved from that malignant sort which often proves mortal, and is always dangerous.

Dr. Francis Home was the first who attempted this practice at Edinburgh about nine years ago, since which, many physicians in that country have followed his example, though I do not find it is much encouraged in England, though in smallpox it is now become universal.

The method is easy, may be performed with safety by a careful nurse, and is not attended with the remotest danger.

Dip a little bit of cotton or lint, on the watery humour that stands in the eyes of persons ill of the measles about the time of the crisis, make a slight scratch in the arm, above the elbow, of the person to be inoculated, put the watery pledget upon the incision and cover it with a bit of sticking plaster to keep it on; and this without further trouble will produce the measles in a gentle and favorable degree, which, during the whole course, will want no other care than that of keeping the patient moderately warm, nor any attendance but that of watching the fever, and encouraging the crisis, which, in a few days will carry off the infection, and complete the cure. This epidemic disease should be communicated to those young subjects who have not yet had it, when it makes its first appearance in any neighborhood, by which the dangerous symptoms that often attend it will be effectually prevented.

We see that a different source of material for inoculation has been selected, namely, "the watery humour that stands in the eye" in measles, but I have looked in vain for other evidence than the mere statement contained in the letter that this method actually produced the disease "in a gentle and favorable degree."

One year later E. Spry¹ writes:

The method of procedure in inoculating for measles does not differ from that which, as we have before described, is to be followed in the case of smallpox. I think there is only one thing which in this case deserves notice as being peculiar, viz., that the linen threads which are used for introducing the contagion ought to be impregnated with blood, for matter is rarely found, drawn from the pustules of the measles near the tip or a little way from it.

In this method of treatment, not yet so common as the earlier one all the symptoms are found to be less serious—a fact of which I am quite certain, not from one observation, but from the study of many cases.

But unfortunately Spry was also content with merely making the bare statement quoted, so that we have no actual facts to aid us in forming an independent opinion as to the nature of the disease he claims to have produced.

Home's inoculations were regarded as highly successful by Buchner, Nils Rosén von Rosenstein,² Holst³ and others and the

¹ *De variolis ac morbillis iisque inoculandis*, 1768.

² *Kinderkrankheiten*, 1798, p. 352.

³ *Med. Chir. Ztg.* 1811, p. 205.

practical use of the method, or some modification thereof, was urged. According to Themmen desquamated skin, blood, tears, nasal discharge, and saliva were recommended by various writers for inoculation, the application to be made to each arm, the skin either being left intact or cut.

Judging from the following quotation Erasmus Darwin¹ was either not familiar or not favorably impressed with Home's work:

. . . it is probable that inoculation might disarm the measles as much as the small pox, by preventing the catarrh, and frequent pulmonary inflammation, which attends this disease; both of which are probably the consequence of the immediate application of the contagious miasmata to these membranes. Some attempts have been made, but a difficulty seems to arise in giving the disease; the blood, I conjecture, would not infect, nor the tears; perhaps the mucous discharge from the nostrils might succeed; or a drop of warm water put on the eruptions, and scraped off again with the edge of a lancet; or if moistened with a little warm water? Further experiments of this kind would be worthy the public attention.

Robert Thomas² says that notwithstanding Home's success, "inoculation for the measles is seldom or never practiced. The few who have been induced to attempt it, have not, I believe, made quite so favorable a report of it; on the contrary, it has been said to produce an aggravated disease." And Ronalds³ writes that Home's plan "has been adopted since his time upon a small scale apparently without furnishing the desired results, but it certainly appears worthy of a more extended trial."

The first and practically the only serious criticism of Home's experiments and his interpretation of the results was made by Thomassen a Thuessink⁴ and his pupil C. J. Themmen⁵ in Holland. Themmen in particular calls attention to the possible danger of unrestricted inoculation of measles if the inoculation really transfers the disease; indeed Girtanner is said to have warned against inoculation because it was sometimes followed by serious pulmonary and other affections. The conveyance of measles by the blood they consider as remarkable, to say the

¹ *Zoonomia*, 1796, 2, p. 243.

² *The Modern Practice of Physic*, third Am. from fourth Eng. ed., 1815, p. 223.

³ *Lond. Med. and Surg. Jour.*, 1816, 36, p. 13.

⁴ *Ueber die Masern*, 1831, p. 231.

⁵ *Dissertatio Medica Inauguralis Historiam Epidemiae Morbillosae, Groningae, Anno 1816, Observatae, Exhibens*, 1817.

least, in view of the fact that Hoffmann had found that in small pox the blood was not infectious.

Themmen also doubts that measles really was transferred by Home's inoculations because the symptoms appeared so early as on the sixth day, whereas Van den Bosch had observed that measles which came in the natural way broke out on the 14th day after exposure—subsequently established as the rule chiefly by the observations of Panum¹ in the Faroe Islands. Inasmuch as the inoculations were made at the time when the disease was endemic, he considers it likely that the disease had been acquired in the natural way previous to inoculation. This opinion was greatly strengthened by the wholly negative results of Themmen's own experiments. He placed blood of measles patients, taken at the height of the exanthem upon small wounds on the arms of two children; cotton saturated with the tears of a measles patient upon a ruptured vesicle on the arm of an infant; in another case a similar experiment was made with cotton soaked in the perspiration of a patient thickly covered with the eruption of measles; and in the fifth experiment he placed cotton soaked in the tears of a patient with measles upon the intact skin of each arm of a girl. "Though all these things were performed cautiously and in accordance with the precepts of the authorities, yet we saw no effects therefrom, and these five children, although they had not previously been attacked with measles, remained entirely free from this disease," says Themmen, who acknowledges, however, that the children were apparently not very susceptible to measles because they all lived in houses in which measles was prevalent and yet remained free from the disease.

But the Dutch authors are not content with this open attack upon Home's experiments. Thomassen a Thuessink indicates that there may be reason to doubt that the experiments were ever made. He says that "many doubt that these inoculations really were made by Home in the year 1758, as old physicians who then lived with Home, in Edinburgh, like Professor Black, Cullen,²

¹ VIRCHOW'S *Archiv*, 1847, 1, p. 492. (In this classical article it is established that measles is most contagious in the period of early efflorescence and that 14 days elapse between exposure and appearance of eruption).

²Cullen makes no mention of inoculation of measles in the early editions of his *First Lines of the Practice of Physic*. But Themmen (*loc. cit.*) quotes Cullen (*Anfangsgr. der*

Duncan, and Gregory told me that they knew nothing of the experiments." Thomassen a Thuessink visited Edinburgh in 1784 and 1785, walked the hospitals with Home himself, and he says that he "often did not see the results which Home indicated to us." Themmen finds it rather peculiar, too, that Home "who praised the usefulness of this inoculation so highly, afterwards undertook no further experiments in this matter."

Very unlike so many others who have made experimental inoculations with measles, Home left behind him full records of his experiments. Inasmuch as the doubts expressed by the Dutch investigators as to their genuineness have not been and probably will not be more fully substantiated than indicated in the foregoing, it may not be without interest to try to determine the possible value of Home's experiments upon the basis of the facts given in his own records. These facts are summarized in Table I.

Examination of this table cannot but lead to the conclusion that probably not a single one of the 15 cases inoculated by Home had measles as a result of the inoculation. In support of this view I may point out that in no single case is the period between inoculation and the appearance of the rash given as more than 10 days, but generally as less, and even so short as seven days, whereas we now know definitely that the period between exposure and eruption in measles is 13 to 14 days.

If any of Home's cases really had measles, which seems quite doubtful indeed from his descriptions, then we are without information as to what steps he had taken to exclude infection by natural routes before making his inoculations. Lack of confidence in his diagnosis only increases when we read that case 10, which is described as a typical case of measles from inoculation, "took measles again" a few weeks later. On the whole there seems to be no escape from the conclusion that Home's claim to have produced measles by inoculation is without foundation.

In the meantime other experiments had been made. Thus Pansonia of Istria is mentioned by Themmen and Thomassen a

Pract. Arzneyk, Leipz., [1789] 2, p. 94) as having "declared in his lectures that the effects of inoculation were dubious, since, out of 12 infants, only one was afflicted with measles when inoculation was performed, and concerning this one it was by no means evident at the time, whether the measles which came upon him were really to be ascribed to inoculation, or rather to contagion received somewhere else."

TABLE I.
HOME'S FIFTEEN CASES OF INOCULATION OF MEASLES.

No.	Nature of Material Inoculated	Age of Person Inoculated	Date of Inoculation	Date of Appearance and Nature of Symptoms	Date of Appearance and Character of Eruption	Remarks
1	"Blood taken from a measly child two days before."	7 months.	March 21.	March 27: Hot, sneezing, eyes watery, no cough.	March 29: Three pustules on face and one on back. March 30: "About a dozen out." April 1: "A few more measles." April 2: "A few more out on face."	This subject had "a scabby head," running behind the ears, and an eruption over its body" before it was inoculated. Sisters. Measles 2 years previously. Took measles again Aug. 20. No natural measles at this time. Placed in nose of three persons (two, nasal discharge; one, blood)—no result.
2	Same as in 1, but kept ten days loosely in pocket book.	8 years.	March 27.	"The sixth day this child sneezed much, but never was hot or struck out."		
3	Blood one day old.	6 years.	April 20.	April 27: Hot, restless, sneezing. April 28: "A great quantity of water comes out of her eyes."	April 30: "Has had the measles out since yesterday." May 2: Measles gone.	
4	Same as in 3.	3 years.	April 20.	April 27: Hot, sneezing.	April 30: "Some measles out." May 2: "Measles pretty large."	
5	Same blood as in 3 and 4, but 14 days old. Carefully kept in a glass.	8 years.	May 3.	May 10: Uneasy. May 11: Running at eyes, sneezing.	May 12: Some spots present. May 13: "About two dozen out." May 15: All measles gone.	
6	Same as in 5.	8 months.	May 3.	May 10: Hot, sneezing, running at eyes, coughing. No symptoms.	May 13: "Three dozen measles appeared."	
7	Same as in 5, kept five weeks.	8 years.				
8	Blood seven days old.	13 years.	June 3.	June 9: Hot, sneezing, and a little cough.	No eruption.	
9	Same as in 8, but ten days older.	5 years.	June 14.	June 18: Shivering, headache, sneezing.	June 21: "Measles beginning to appear." June 22: More measles June 23: "Still out." June 24: "Almost all gone."	
10	Mixture of blood taken May 27 and June 27.	18 months.	July 6.	July 9: Feverish. July 14: Coughing, sneezing.	July 14: "Had many spots out this morning but almost all gone in again." July 15: "A great many spots out, but especially on sides and thighs, where they almost touch one another." July 17: Spots disappearing.	
11	Blood two days old from 10, Aug. 27.	8 months.	Aug. 29.	Sept. 7: Hot, restless for some nights.	Sept. 7: Some spots seen yesterday. Sept. 8: "About a dozen and a half of spots." Sept. 9: Spots almost gone.	
12	Same blood as in 11.	18 months.	Aug. 30.	Sept. 7: Hot, coughing, sneezing.	Sept. 8: "About three dozen spots to be seen."	
13, 14, and 15	Cotton with nasal discharge of measly patient on fourth day of eruption and cotton with blood.					

Thuessink as having made inoculations, but the latter remarks that there is no authoritative report of this work. Willan¹ inoculated three children with the fluid of miliary vesicles in measles but without success. And Chapman² in Philadelphia in 1801 tried in vain to inoculate measles by means of blood, tears, "the mucus of the nostrils and bronchia, the eruptive matter in the cuticle, properly moistened." On this account Dewes thought that the contagious nature of measles could be fairly disputed.

James Stewart³ mentions the following experiment: "On the authority of the late Colonel Green, it is confidently stated that his relative, Dr. Green, of Greenwich, R. I., inoculated in the year 1799, three young persons in his circle, with blood taken from the eruptive surface of a patient laboring under an aggravated form of measles; and that these cases of inoculation were entirely successful, so that the distinctive characters were recognized by all who saw them."

Mr. Wachsels's experiment on Richard Brookes, a lad of 18, reported by Willan (*loc. cit.*) is stated by Hugh Thompson and others to have been successful, but this is, to say the very least, exceedingly doubtful. The boy was inoculated January 6, 1810, with cowpox and with fluid taken from measly vesicles. The cowpock was fully developed on the 15th. On the 22d, coughing, sneezing, and running at the eyes set in with chills followed by measly eruption on the 28th—22 days after inoculation. In the light of our present knowledge the measles in this case must be ascribed to a natural infection received about eight days after the inoculation.

In 1822 Speranza of Mantua caused inoculation of measles to be made with results regarded by him as eminently successful and so accepted without reserve by several subsequent writers. Speranza describes these inoculations as follows:⁴

. . . we invited to perform the operation Dr. Frigori, staff physician of the Workhouse and Convalescent Hospital, where measles was always prev-

¹ *On Cutaneous Diseases*, 1809, 1, p. 106, footnote.

² MS. lectures cited by DEWES, *A Treatise on the Physical and Medical Treatment of Children*, 11th ed., 1858, p. 439.

³ *A Practical Treatise on the Diseases of Children*, 1844, p. 416.

⁴ *Storia del morbillo epidemico della provincia di Mantova, nell' anno 1822. Arguinto un giu'duzio med.—legale sopra imputazione d'Infanticidio*. Parma, 1824.

alent among the children. A slight incision was made with the lancet upon a group of the more inflamed disease-spots, and with the point of the instrument charged with the bloody matter several incisions were made on the arm of a healthy person, the wounds being covered at once with a bandage. This operation was performed, with the greatest care and under our observation, upon six boys of different ages. The boys complained, a few days afterwards, of not feeling well; about the fifth or sixth days there appeared very slight traces of cold in the head, with cough and watery eyes, which remained after the appearance of a few exanthematic spots; there was very slight febrile irritation, in some cases a mild diarrhea, and by the ninth or the tenth day after the inoculation the measles had run its course without leaving any trace of secondary malady. Dr. Frigori, not content with this result, to which he had given close and daily observation, tried the experiment upon himself;¹ the outcome was the same, but still milder, the morbid phenomena being merely a passing catarrhal affection, involving the frontal sinuses, and the pituitary membrane rather than the trachea and bronchi. A similar inoculation performed by Dr. Negri upon two boys had the result, as did our own experiments upon four other individuals, carried out in the same way. We were not equally fortunate when following the practice of Home, of Horst, and of Ronalds; that is in saturating a little cotton with the blood from an incision upon a group of exanthematic spots, and applying it to the arm before any puncture had been made. This was attempted in two cases, but the experiment did not fulfil our wishes; no catarrhal phenomena and no exanthematic spots appeared.

Speranza also states that—

In the year 1806, during the prevalence of an epidemic of measles in Parma, Dr. Rasori, staff physician of the Hospital, inoculated one of his nephews with the disease by introducing with a needle, bloody matter taken from the exanthematic sores of an infected person. The formation of papillae at the point of inoculation, with slight traces of catarrhal irritation, and immunity from the epidemic then general, were the result of this salutary operation.

From the description given by Speranza of the symptoms in the inoculated persons it would seem very doubtful, indeed, if any of them really had measles. And if the symptoms described be accepted as those of “a mild and morbillious affection,” how may natural infection be excluded when we are told that measles was always prevalent among the children in the hospital and when the incubation period is given as five to six days? Under these circumstances I cannot see how it is possible to read any value into Speranza’s experiments.

¹Several writers, e. g. EBERLE (*Treatise on the Practice of Medicine*, 1830), THOMAS in ZIEMSEN’S *Cyclopedia*, and others speak of this experiment as having been made on Speranza himself.

Several older writers (Good,¹ Jörg,² and others) mention that inoculation sometimes produced attacks of measles quite as severe as the natural disease.

In 1834, Albers³ without success inoculated four persons using Home's method in two, and the method of vaccination in two, the blood being taken on the second day of the eruption. From this he concludes that the blood does not contain the contagion of measles. He quotes Alexander Monro, Bourgois and Spray (Spry?) as having made unsuccessful inoculations with saliva, tears, and cutaneous scales, but no references are given.

The largest series of inoculations of measles is that of Katona (1842) in Hungary who during an epidemic made 1122 inoculations with positive results in 93 per cent. and without any evil effects. His report is very brief and without any details.⁴ He inoculated as in vaccination by means of a needle dipped into fluid mixed with blood obtained by opening the little vesicles when the rash was at its height. Slight and evanescent local changes developed and on the seventh day fever appeared with the usual early symptoms of measles followed by eruption on the ninth, or at the latest on the 10th day. The symptoms were milder than usual. In two instances the rash did not develop until the 13th day. The epidemic then raging was severe according to Katona.

Here again we have the abnormally short incubation period encountered so commonly in the reports of inoculation of measles, beginning with Home, and Katona gives us absolutely no hint as to the measures used, if any were used, to determine that the disease actually was inoculated and not perchance acquired in the natural way. It is to be noted that the inoculations were made *during an epidemic* of measles so that the opportunity for natural infection was present. So far as I know we have no means by which to determine whether the percentage of inoculated that took measles was larger than the percentage that fell sick among the uninoculated. We do not know whether the communities

¹ *The Study of Medicine*, VIII, 4th Am. edition, 1826, 8, p. 34.

² *Handb. d. Kinderkrankh.*, 1836, p. 895.

³ *Jour. d. Chir. u. Augenh.*, 1834, 21, p. 541.

⁴ *Osterreichische med. Wchnschr.*, 1842, p. 1.

concerned at this time contained a large number of susceptible persons by virtue of having long been free from measles. Hence Katona's imposing number of inoculations can have little or no real significance in this discussion.

Bell and Stokes¹ quote with silent approval the following statement from Chapman:² "Not unlikely, in the instance of alleged success by inoculation (of measles), the individuals had been previously exposed to the infection of the disease, and to this mode may its production be properly ascribed; the coincidence being mistaken for the effect, one of the most common sources of vitiation in our medical inductions."

In 1850 McGirr³ of Chicago made a series of inoculations with measles upon children in an orphan asylum in which the disease was then present. "Early in December the first case of measles was brought into the female asylum. I proceeded to inoculate from this case when the eruption was at its height. Blood was drawn from a vivid exanthematous patch on the diseased child's arm, and inserted into the arms of . . . three children. . . . On the fourth, sixth, and seventh days, after the inoculation, the measles appeared, pursuing a regular and typical course."

Encouraged by this result McGirr continued his inoculations, and he states that "the cases of all those inoculated, commencing from the fourth to the ninth day after inoculating, proceeded regularly with the ordinary symptoms of simple measles to convalescence which was speedy and complete. . . ." Compared with those not inoculated the inoculated cases were much milder, and McGirr concludes that if there is no advantage in inoculation the result of this comparison would be a strange anomaly. Be this as it may, the fact that McGirr's experiments were made in an asylum infected with measles robs them wholly of weight. The incubation periods given by McGirr indicate too, that the infection in most cases was received before inoculation.

The reports of F. Mayr⁴—a name well known in the history

¹ *Lectures on the Theory and Practice of Physic*, 1848, 4th ed., p. 881.

² *Lectures on the More Important Eruptive Fevers, Hemorrhages and Dropsies, and on Gout and Rheumatism*, 1844, p. 118.

³ *Northwest. Med. and Surg. Jour.*, 1850-51, 7, p. 434.

⁴ *Ztschr. d. k. k. Gesellsch. d. Aerzte zu Wien*, 1852, 1, p. 6.

of pediatrics—concerning the epidemics of measles in Vienna during 1845–51 show him to have been a keen and critical observer. Although he gives only very few details of his experiments there is nevertheless good reason for regarding his results as reliable. Mayr “vaccinated” successfully six times using for inoculation the material obtained from scratching the center of a rubeolous spot. It cannot be said, therefore, that he used blood only as he himself claims, but rather blood, tissue juice, and epidermal débris mixed. In three experiments he used fresh nasal mucus which was placed upon the membrane of the nose. In two of the cases measles appeared in regular time, the eruption coming out on the 14th day. In all these instances the attacks were typical though mild, and the patients remained free from subsequent attacks. Mayr emphasizes that inoculation transfers the whole process from one individual to another and consequently offers no conspicuous advantages nor protection against complications or sequelae. There were in his cases no changes at the point of inoculation and he concludes that so long as it is not possible to localize the process as in vaccination inoculation of measles has no practical importance.

Since this time—1850—inoculation of measles has received little notice. Bufalini¹ in a report on an epidemic of measles in Siena in 1869 states that 15 years previously he tried inoculation in six cases. “Four of these had the eruption while in the other two there was no result.” In one of the failures epidermal scales were used, and the “maximum effect” is said to have been obtained with the combined methods of Home and Speranza. On account of the absence of details Bufalini’s experiments add nothing to our knowledge of the cause of measles.

Various writers speak of experiments with measles by Locatelli, Rossi (Rasori?), Frigeri (Frigori?), Horst (Holst?), Percival, Giotanna (Girtanner?), Vaidy, Fellegen (Tellegen?), and others, but I have not found any definite references to any articles on the subject by these persons. Undoubtedly some of the names were misspelled and have been so handed on from writer to writer.

¹*Rev. sci. d. R. acad. di Fisiocritici*, 1869, 1, p. 111. Also Abstract by Ullersberger in *Jahrb. f. Kinderkr.*, 1871, 56, p. 282.

Reese¹ recommends inoculation in measles as the best means to prevent serious results and sequelae, but he gives no new facts and no original observations.

Hugh Thompson² in Glasgow accepts the inoculations of Home, Wachsels, Speranza, and Katona as successful. He regards the practicability and the safety of inoculation in measles, as well as its production of a much milder attack than the spontaneous, as definitely established, and recommends that the method employed be superficial scarification followed by the application of the fluid from blisters on the skin of measles patients. In two instances however, in which Thompson practiced this method his inoculations failed.

From this review we learn that, almost without exception the recorded experiments in the inoculation of measles, for which positive results have been claimed, are without real significance. The claims that the experiments of Home, of Wachsels, of Speranza, of Katona, of McGirr, of Bufalini gave definitely positive results do not stand close scrutiny in the light of the evidence at hand: In many instances the rubeolous nature of the sickness, sometimes very mild, following the inoculation and regarded by the experimenters as measles, is not at all securely established, and in practically all cases the possibility of natural infection has not been excluded. These experiments, practically all of which were undertaken with the idea of producing a modified form of the disease, consequently permit no conclusion as to the infectiousness of the blood or other substances in measles. If we accept Mayr's results as they are given by him it may be concluded that in measles, nasal mucus and cutaneous scrapings (containing blood, epithelial debris, and tissue juices) may contain the cause of measles at or near the height of the eruption.

It already has been pointed out that in congenital measles the indications point to the simultaneous infection of mother and fetus.

In the following experiments I have tried to determine whether or not in measles at the height of the attack the blood contains the cause of the disease.

¹ *Trans. Med. Assn. Alabama*, 1880, 33, p. 396.

² *Glasgow Med. Jour.*, 1890, 33, p. 428.

PERSONAL EXPERIMENTS.

In these experiments special care has been taken to exclude natural infection.

1. The blood injected was taken from a boy of nine who in the later stages of desquamation after an uncomplicated attack of scarlet fever developed a rather mild but typical attack of measles. The first symptoms of measles appeared after he had been free from fever for about two weeks. There was headache, coryza, cough, running of the eyes, and mild febrile symptoms. Three days later a papular eruption was noted and on the fourth day a typical rubeolous rash was present, that soon began to fade and was followed by typical branny desquamation.

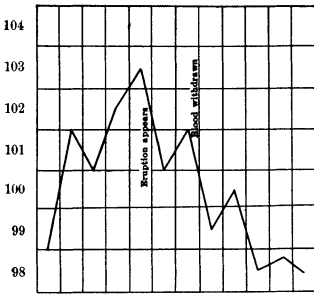


CHART I.—Temperature curve of patient furnishing blood for Experiment 1.

On the fourth day (see Chart I) four c.c. of blood were withdrawn from the vein at the right elbow after carefully scrubbing the skin with soap and water followed with alcohol. Two flasks with ascites broth 50 c.c. (peptone broth two parts, ascitic fluid heated to 55° C. for 54 minutes one part) were inoculated¹ at once with one and three c.c. of blood respectively and placed in the incubator at 37° C. for 24 hours. At the end of this time both flasks appeared sterile, the corpuscles having settled, the supernatant fluid being clear. Subcultures made at this time upon ascites agar, glycerin agar, and Loeffler's serum and kept under aerobic and anaerobic conditions remained sterile; and the contents of the flask of ascites-broth containing one c.c. of blood remained permanently sterile.

Four c.c. of the flask of 50 c.c. of ascites-broth mixed with three c.c. of blood and kept in the incubator at 37° C for 24 hours were injected under the skin of the chest of a healthy medical student 24 years old, just finishing desquamation after an uncomplicated attack of scarlet fever, and who readily gave his consent to the

¹ In both experiments a few drops of blood were allowed to run out before inoculating the ascites-broth which was done without the needle of the syringe touching the culture fluid.

experiment. This man was not in the same hospital as the boy furnishing the blood for injection, but had been for 26 days in a different institution, at that time as well as before and afterwards entirely free from measles.¹ So far as could be learned, and careful inquiry was made, the man injected had not had any disease at all resembling measles except scarlet fever. At no time did any local symptoms appear at the site of the injection. On the 13th day after injection the temperature was 101° F; the next morning it rose to 103 (see Chart II). At nine the following morning he was given a warm bath and immediately afterwards a

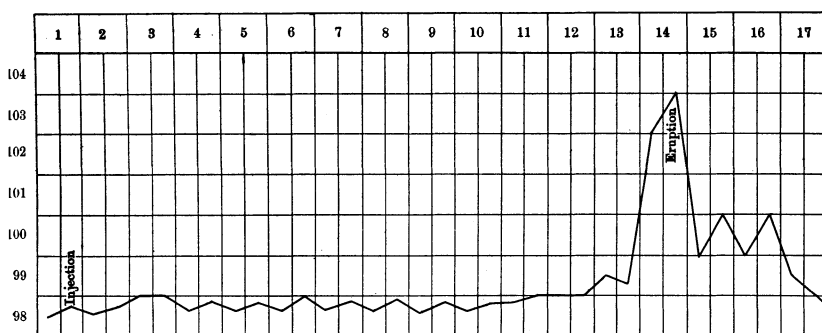


CHART 2.—Temperature curve in Experiment 1.

red, papular, blotchy eruption broke out on the forehead and spread quite rapidly to the face, neck and chest. Dr. James B. Herrick who saw him at this time felt no hesitancy in making the diagnosis of measles. By two o'clock an unmistakably typical full-blown, rubeolous rash was present over the greater part of the body. The temperature remained above normal for two days, when it fell to normal about the same time that the eruption began to fade. An uneventful recovery promptly followed without any complications whatsoever, the desquamation being branny. There was during the entire illness freedom from respiratory symptoms of all kinds. Even during the pre-eruptive period there were no special local symptoms (*morbilli sine catarrho*). The patient's

¹ In both experiments the injections were made by me. At the time the injections were made I had not seen any cases of measles within 24 hours. When in the measles ward the usual precautions were used and of course similar precautions were followed when visiting the subjects of the experiments—clean long gowns, caps, clean hands, etc. Freshly autoclaved syringes were used for the injections.

subjective condition was not much changed if at all at any time during his illness. The appetite continued unimpaired.

2. In this case the blood was furnished by a well-developed

Irish servant girl, 21 years old, who passed through an uncomplicated attack of typical measles (Chart III).

About 30 hours after the earliest appearance of the rash, which still was coming out upon the extremities, 10 c.c. of blood were withdrawn from a vein at the elbow and distributed equally among four flasks each containing 50 c.c. of broth and 25 c.c. of ascites fluid. These flasks all remained perfectly sterile so far as

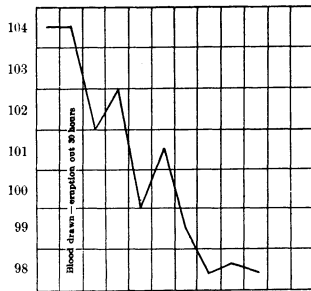


CHART 3.—Part of temperature curve of patient furnishing blood for Experiment 2.

bacteria demonstrable by the usual methods are concerned.

After 24 hours at 37° C. five c.c. of the mixture of blood in ascites-broth were injected subcutaneously in the back of M., aged 28, who had not had measles so far as he knew and consented to the experiment. This patient was also recovering from a mild attack of scarlet fever and had been at the time of inoculation for 24 days the sole occupant of the isolation

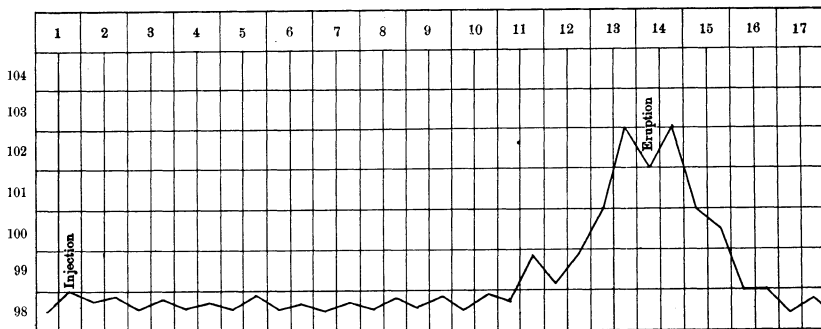


CHART 4.—Temperature curve in Experiment 2.

room of a general hospital in which at that time there were no other cases of measles. There were no local changes at the site of the injection. The temperature and general condition remained

normal until the evening of the 11th day when the temperature rose to 99.8° F. and the next day a mild conjunctivitis already suspected a day or so previously became definitely apparent. On the 13th day there was some cough, the tonsils were bright and red, and there was an increased amount of mucus in the throat. In the afternoon the temperature which was rising, reached 103° F. (Chart IV). During the next night a typical rubeolous eruption came out, the first spots being noticed on the nose and then on the forehead, face, scalp, chest, back and abdomen. The rash consisted of pink macules and papules which disappeared readily on pressure, being largest and brightest red over the face. The forehead was quite uniformly red. The patient was not seriously ill; there was some loss of appetite, but he slept well during the night, having been somewhat restless the preceding night. Recovery was prompt.

Cultures of the blood on the 13th day (one c.c. of blood in each of three flasks each containing 50 c.c. of broth and 25 c.c. of ascites fluid) remained permanently sterile.

CONCLUSIONS.

The results of these two experiments permit the conclusion that the virus of measles is present in the blood of patients with typical measles sometime at least during the first 30 hours of the eruption; furthermore that the virus retains its virulence for at least 24 hours when such blood is inoculated into ascites-broth and kept at 37° C. This demonstration shows that it is not difficult to obtain the virus of measles unmixed with other microbes and in such form that it may be studied by various methods.