

three days, while in the others the serum became positive within thirty-six hours.

These observations show that no dependence can be placed on a negative Wassermann reaction in individuals who have ingested considerable amounts of alcohol within twenty-four hours of the making of the test, and therefore a careful inquiry should always be made regarding the recent use of alcohol before collecting blood for the complement-fixation reaction.

INFLUENCE OF BACTERIA ON THE TEST

The serum for the Wassermann test should be collected under aseptic precautions, especially if it is to be kept for any length of time before it is tested, as I^o have been able to show that certain strains of staphylococci and streptococci, when growing in normal serum, are capable of producing substances in the serum which may give rise to a positive result with the complement-fixation test for syphilis. These non-specific results do not occur in normal serums which are sterile, even though the serums be kept at room temperature for as long a period as a month, and while such false reactions are probably very rare in actual practice, the fact that they can occur as the result of bacterial activity is of enough importance to justify the use of aseptic methods in the collection of blood for the Wassermann test. This reaction is quantitative as well as qualitative, and it is only by the most careful attention to every technical detail that reliable results can be obtained.

For this reason the test should be made only in properly equipped laboratories by those who have received special instruction and who devote a large part of their time to this work. Under such conditions results will be satisfactory, but the interpretation of the test must always remain with the clinician. The laboratory report deals only with the result of the test, and it rests with the clinician to correlate this result with the clinical condition present.

VACCINATION AND LOCAL ANAPHYLAXIS

JOSEPH H. BARACH, M.D.
PITTSBURGH, PA.

During the recent small-pox epidemic in Western Pennsylvania, and particularly in Pittsburgh, which through the effective administration of the Department of Health was quickly circumscribed and subdued, the physicians of our vicinity had an unusual opportunity to observe large numbers of vaccinations. It has been estimated that in Pittsburgh about one-third of the population was vaccinated.

The ordinary vaccination with cow-pox creates little interest in the mind of the practicing physician, and the results are not carefully observed. There is one phase of this topic, however, which is very interesting, and while mention of it is made in the recesses of the English literature, I think that it is not presuming too much to say that it is not generally recognized, and that its explanation is almost unknown. A patient is vaccinated and after a slight redness or perhaps a small raised papule lasting one to three days the entire effect of the inoculation seems to have subsided, and the case is considered as one which did not take. On revaccination, say about two weeks later, we do get a "take," and we are surprised to find that the previous

vaccination, apparently unsuccessful, now becomes active and goes through the same evolution as the revaccination. The lesion of the first vaccination usually does not develop as fully in any of its stages as that of the revaccination.

This observation was made long ago; we have no positive data on the frequency with which it occurs. Even if we could collect data on the frequency of its occurrence we should have to eliminate many other sources of error, such as technic of vaccination, dose and potency of virus, condition of skin, etc. After eliminating all external sources of error, we might then consider sensitiveness of the organism to the virus. Ordinarily this irregularity does not occur frequently enough in the experience of the average practitioner to make its impression on him, and if it has happened in his work he passed it by as an accident. On questioning physicians, I find, however, that the good observer can usually recall one or two such instances, and he admits that he thought it noteworthy at the time but had almost forgotten it since. In the general run of work, including the above-named sources of error, the frequency with which it occurs may be judged by the accompanying table. These figures include my own observations and those of my colleagues with whom I have discussed this subject.

	Ages	Vaccinated	Revaccinated	Local Anaphylaxis
Inst. C. H. . . .	5-15	40	14	2 children.
Inst. N. H. . . .	10-20	70	10	2 children.
Dr. D.	Adults	125	?	1 adult.
Dr. F. B.	All	75	?	1 adult.
Dr. R. J.	All	172	5	1 child.
Dr. F. S.	All	125	25	0
Dr. W. W.	All	200	50	7 or 8
Dr. S. L.	All	500	?	3
Dr. H. J.	All	65	15	1 child.

Judging by this table, its occurrence is not very exceptional. It seems more frequent in the cases not previously vaccinated.

CASES EXEMPLIFYING FORMS OF THIS REACTION

CASE 1.—D. P. Primary vaccination on left arm; slight local reaction, at ten days disappearance of all traces. Revaccination on tenth day on same arm, 3 inches from previous site; reaction marked. On fourteenth day, area of the first vaccination inflamed. Course of lesion about ten days, simultaneous with revaccination. Resulting scab smaller and fell off earlier.

CASE 2.—Reported to me by Dr. R. R. Jones. Primary vaccination no "take;" complete healing. Successful revaccination fourteen days later. Three days later reaction of primary vaccination, running its course in eighteen days. Course of revaccination more protracted, the scab still adhering at the end of thirty days.

A very important feature in this case is that the first vaccination was on the right leg and the revaccination on the left leg. The possibility of auto-inoculation is eliminated.

CASE 3.—Dr. S. First vaccination twenty years ago "took." Second vaccination nine years ago did not take. Third vaccination was made two months ago. Three days after inoculation there were evidences of a "take." Several days later the old scar of the vaccination of twenty years ago became red, inflamed, slightly elevated, and very itchy. This continued for about five days and subsided. The vaccination ran a usual course.

CASE 4.—Dr. B. Vaccinated in childhood successfully. Revaccinated at age of 20 successfully. Revaccinated again at age of 22 unsuccessfully. Shortly afterward (exact time not known) exposed to small-pox. Last vaccination scar became extremely sensitive and itchy for several days.

NATURE AND CAUSE OF VACCINATIONS

Extensive and painstaking studies of vaccination had been made by Bohn. Later, in 1903, von Pirquet pre-

O. Craig, C. F.: The Relation of Certain Bacteria to Non-Specific Reactions with the Complement-Fixation Test for Lues, Jour. Exper. Med., 1911, xiii, 521.

sented his "Zur Theorie des Vakzination."¹ Prior to that time it was assumed that the symptoms of vaccination were due to absorption of bacteria or their toxins. Von Pirquet saw that the body reacts with the micro-organism only through the agency of the antibodies and presented the subject from his point of view, that of allergy. Inoculation with a strange protein, vaccine virus in this instance, causes the production of antibodies as protectors to the organism. These develop progressively, reaching their height in a variable period of time. At the end of that period, we then have the normal organism plus antibodies. The antibodies were created for the purpose of immunity; we may, therefore, say that the organism is in a state of altered immunity. This state of altered immunity von Pirquet termed "allergy." We may also say that the organism has become sensitized toward that particular protein, or has become hypersusceptible or anaphylactic toward it.

Let us suppose that after the organism has become sensitized to this strange protein by a full development of antibodies, another inoculation is made. The antibodies rush immediately to this point of inoculation and proceed to destroy the protein for which they are antidotal. The destruction of the protein substance by the antibodies is, let us say, a molecular disintegration. In this molecular disintegration certain by-products are let loose; these prove to be poisonous and manifest their presence by "the anaphylactic reaction," accompanied by local and at times constitutional manifestations. Von Pirquet showed that, after cow-pox vaccination, the incubation period of future vaccinations became shorter and the reaction milder, because of the development of antibodies from the primary inoculation. In the state of allergy if the antibodies are developed to such an extent that the incubation period is shortened, the resulting reaction is designated as "accelerated reaction." If the antibodies are developed to a much greater extent, so that the organism reacts immediately, the reaction is called "immediate reaction." So long as there is a sufficient "amount" of the antibodies to react immediately against the strange protein, we have immunity. Thus, by inoculation with virus at certain intervals, we can keep up antibody formation and maintain immunity.

POSSIBLE EXPLANATIONS FOR THIS PHENOMENON OTHER THAN LOCAL ANAPHYLAXIS

Auto-Inoculation.—From the observations of von Pirquet and others, and from my own observations in many cases, it is known that auto-inoculation probably never or almost never occurs. If that could happen there are so many chances for its occurrence in a large proportion of the vaccinations that it would have become a recognized factor long ago.

Superinfection.—Finger's theory of superinfection cannot be unequivocally applied here. Finger, as quoted by Noguchi,² believes that in syphilis a trauma of the skin creates a spot of weakened resistance, and that the virus from a focus of activity wanders to the area of weakened resistance, creating a local area of reaction. The undoubted cases in which long-healed vaccine scars become active on reinoculation speak strongly against superinfection.

Neisser's Umstimmung.—According to Neisser, and recently Noguchi,² in syphilis and perhaps in other diseases, the skin itself may at times be abnormally sensi-

tive to trauma, so that the site of a control area reacts simultaneously with the inoculation area. In the luetin reaction Noguchi believes that this *Umstimmung* reaction occurs exceptionally, if ever, and that his luetin vaccination is a manifestation of allergy.

Torpid Form.—Noguchi, in his work on the cutaneous reaction in syphilis, describes a torpid form of the reaction. "In rare instances the injection sites fade away to almost invisible points within three or four days, so that they may be passed over as negative reactions. But sometimes these spots suddenly light up again after ten days or even longer and progress to small pustular formations." This reaction von Pirquet, in his studies of vaccination, describes as the dormant form (*schlafende Keime*).

Moro's Bilateral Reaction.—Moro,³ in his work on the cutaneous tuberculin reaction known by his name, observed that, in certain cases studied for control purposes, after rubbing one arm with tuberculin ointment and a similar spot on the opposite arm with pure lanolin, he obtained characteristic reactions on both arms. He explained this phenomenon as being due probably to the tuberculin reaching those parts of the cord which preside over the area of skin affected by the inoculation, and assumed that the reaction was due to a reflex nervous influence on the vasomotors.⁴

The above-mentioned forms of local reaction and the explanations offered are all deserving of thoughtful consideration in this connection.

SIMILAR LOCAL REACTIONS

Those who have worked with tuberculin reactions are familiar with cases in which the first conjunctival instillation with tuberculin proves negative. Following this, when a cutaneous or subcutaneous injection is administered, we get a local reaction at the site of the injection, and we find that the conjunctiva also becomes inflamed. A similar reaction is observed when first one eye and then the other is used; at the second instillation we get a reaction in both eyes. It is also known that the conjunctiva of healthy persons can be sensitized to tuberculin, so that after primary negative results, reinoculation will show positive reactions.^{5,6} These tuberculin reactions, it is almost universally conceded, are due to sensitization by the first inoculation and the second inoculation precipitates an anaphylactic reaction.

SUMMARY

All considered, in the light of our present knowledge of the subject, based on the evidences adduced, the best explanation for the lighting up of the first apparently unsuccessful vaccination, when the revaccination does "take," is that of local anaphylaxis.

The first inoculation results in the production of antibodies against the strange virus substance; it sensitizes the organism. At the second inoculation the virus, wherever deposited, is attacked by the antibodies, and in this attack certain "by-products" are let loose. These "by-products" act as poisons and produce the anaphylactic reaction. In this case the reaction is limited to local manifestations. In other instances when the dose is large, or when the protein and antibody are diffused throughout the organism, the anaphylactic reaction is constitutional.

4502 Fifth Avenue.

1. Von Pirquet: *Vakzination und Vakzinale Allergie*, Leipzig, Franz Deutick, 1907.

2. Noguchi: *A Cutaneous Reaction in Syphilis*, Jour. Exper. Med., 1911, xiv, 557.

3. Moro: *München. med. Wehnschr.*, 1908, iv, 2025.

4. Patterson: *Arch. Int. Med.*, 1909, iii, 301.

5. Rosenau and Anderson: *THE JOURNAL A. M. A.*, March 21, 1908, p. 961.

6. Vaughan: *THE JOURNAL A. M. A.*, Jan. 2, 1909, p. 34.