The conclusion to be drawn from these cases of late and negative reaction to v. Pirquet's test is that the vigour of the reaction varies directly with the vigour of the patient and inversely with the amount of tuberculous infection. Where the general vigour is only slightly impaired a rapid and intense reaction is obtained. The most intense reactions I obtained were among the cases of osseous and joint tuberculosis, and also of pleural effusion. But where the vigour of the patient is low and the disease is widespread or complicated, the reaction is late in appearance and feeble or is absent altogether. With regard to the same point in the ophthalmic-reaction there is some difference of opinion. That will be discussed later. But in v. Pirquet's reaction the whole evidence strongly points to the conclusion just reached.

Comparison of the Conjunctival and Skin Reactions.

In 78 cases the Calmette and v. Pirquet reactions were tried in the same patient. The v. Pirquet test was performed as already described. In the Calmette test the dried tuberculin was used in 0.5 per cent. solution in distilled water. The solution was only employed freshly made up. The results were as follows:

	Positive.	Negative.
V. Pirquet	31	47
-Calmette	21	57

I should say that these cases are not new, but have already been included in the v. Pirquet series. Out of the 78 cases, the v. Pirquet test was positive in 31; it was negative in 47. In these 47 negatives the Calmette reaction was also negative in every case. It was positive in 21 of the cases in which v. Pirquet was positive, but it failed to react in the remaining 10 cases in which v. Pirquet was positive. That is to say, out of a total of 78 cases, the Calmette test either coincided with the v. Pirquet or contradicted it negatively. It did not contradict positively in a single case—that is, it never gave a positive reaction where the v. Pirquet was negative. A closer analysis of those 10 cases may be useful.

Name.	Condition.
G. B. ...	Tuberculous ankle.
D. W. ...	Tuberculous spine.
J. W. ...	Simple pleural effusion.
W. B. ...	" "
F. G. ...	" "
A. S. ...	Chronic bronchopneumonia.
C. W. ...	Tuberculous peritonitis.
R. S. ...	" "
H. C. ...	Tuberculous hip-joint (mixed infection).
J. A. ...	Tuberculous meningitis.

(V. Pirquet's reaction was positive and Calmette's reaction negative in all these cases.)

These conditions may be said to include all degrees of severity of tuberculous infection, so that in this list the v. Pirquet test is superior to the Calmette over the whole range of tuberculous conditions. The superior delicacy of the skin reaction is not partial or in one direction. It is total and in all directions. In these 78 cases it undoubtedly failed in some cases of widespread tuberculosis; it may have failed also in some incipient cases. But in each of these extreme directions it gave some reactions where the conjunctival test did not; and in neither of these groups did the Calmette test succeed where the other failed.

At the last meeting of the British Medical Association Calmette held that the conjunctival reaction was more useful than the skin reaction, because of the failure of the former to detect healed or quiescent tubercles.⁴ That is really an admission of the greater delicacy of the v. Pirquet test. Moreover, it is a difficult matter to say when a tubercle is healed. So long as the blood reacts to the skin test the tuberculous focus is potentially active. In the adult the limitation of the focus is more thorough; but in the child the activation of a buried tuberculous lymphatic gland may in a few weeks cause a general dissemination of tubercles, so that in children the power of the v. Pirquet test to detect latent or quiescent tuberculosis gives it an important advantage.

It must be noted that in the above cases a weak solution

of tuberculin (0.5 per cent.) was used for the eye test. Again, the subjects were all children, and though the solution could always be dropped on to the eye, it was often much diluted by a flood of tears. But these difficulties are inherent: stronger solutions in the eye are sometimes unsafe, and children will not cease to cry. Dealing with the skin much stronger solutions are used and can there be brought more effectively into contact with the local circulation. In a comparison of these two forms of tuberculin reaction, their essential similarity must be admitted. Both are vascular reactions depending on the close contact of toxins with the capillary circulation. But their practical application is different. With the skin it is safe to sensitize the local circulation by some form of scarification or abrasion. With the conjunctiva it has from the first been recognized as dangerous to employ the test where any degree of inflammation is already present. We aim at producing an abraded cutis. We deliberately avoid an injured conjunctiva. In that contrast lies the cause of the superior delicacy of the v. Pirquet test.

But it is needful to point out that the superficial circulation is much less accessible in the skin than in the eye. Therefore a proper technique in preparation of a vascular surface on the skin is highly important. Neglect of that may turn the balance in favour of the eye reaction, and may throw away the advantage in delicacy and safety which the v. Pirquet test undoubtedly possesses.

One final point is worth mentioning. It is much disputed whether severe conjunctival reaction means an active tuberculous process or the reverse. Wolff-Eisner holds the former view.⁵ Calmette, in his statement that the severity of the reaction corresponds with the number of antibodies present in the blood, inclines to the latter view.⁴ The evidence seems to be conflicting; but in the v. Pirquet test it has already been shown that the severity of the reaction varies inversely with the severity of the disease. In the skin the conditions almost approximate to those of an exact experiment by a definite abrasion. In the conjunctiva, the local vascularity, and therefore the local sensitiveness, must vary much even within the range of health. That fact probably explains the discrepant results obtained.

In conclusion, I would cordially express my thanks to the members of the staff of the East London Hospital for Children for their permission to use the abundant material of the hospital for the purpose of this investigation.

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¹ *Deut. med. Woch.*, May 23rd, 1907. ² Report upon 1,000 Tuberculin Tests in Young Children, *Trans. Amer. Ped. Soc.*, vol. xx, 1909. ³ *Ibid.* ⁴ *BRITISH MEDICAL JOURNAL*, August 28th, 1909. ⁵ *Berl. klin. Woch.* 1908, vol. xiv, p. 365.

A CASE OF DISSEMINATED TUBERCULOSIS TREATED WITH MARMOREK'S SERUM.

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THE results of treatment by Marmorek's serum in the following case seem to me sufficiently striking to render its publication desirable.

The patient was a schoolboy, of Spanish nationality, aged 15. He was first seen on December 14th of last year, when he was suffering from severe haematuria of more than six months' duration. His temperature was 103° F., and the abdomen was distended. There was an operation scar in the right kidney region. The case rapidly assumed a typical typhoid condition, with evening temperature about 104° F. and slight morning remissions. The following is a summary of the symptoms at this time:

The pulse was very rapid and feeble, the abdomen distended, with thickening in the right kidney region; pale yellow diarrhoea with much mucus and some blood; profuse haematuria but no pyuria; rapid emaciation. Widal's reaction was repeatedly negative, and so was the Ehrlich-Diazo test. The blood counts showed distinct paucity of leucocytes.

We were a little baffled at this stage by misleading information to the effect that the operation scar was due to a successful nephrolithotomy, but we now obtained a more veracious account from France which made it obvious that the case was tuberculous. We ascertained that the right kidney had been removed in the previous June for tuberculosis, and the bladder and prostate were found cystoscopically to be tuberculous.

Within the next few days crepitations gradually developed all over both lungs, and there was constant short, dry cough, but no expectoration. Intestinal matting occurred throughout the abdomen, especially in the flanks. A distinct squint developed in the left eye, but no choroidal tubercles were discovered. The ophthalmoscopic examination was not very complete owing to the patient's deplorable condition at this time. He became delirious, with constant twitchings of the face and eyes, and emitted loud meningeal cries.

About this time the patient was seen by several eminent medical men, including specialists, from London and Paris, and I think I may fairly say the consensus of opinion was that the boy could not live more than three or four weeks; at any rate, I expressed that opinion emphatically to the relatives. He had been given sodium cacodylate and 8000 mg. T.R. injections without apparent effect.

On January 17th, 1909, after the patient had been acutely ill for a month, Dr. Marmorek arrived from Paris, and in spite of the fact that the lad was almost moribund, with every evidence of generalized miliary tuberculosis, he took a positively cheerful view of the case, and advised injection each day of 5 c.cm. of his new serum, which is made from what he calls the primitive tubercle bacillus obtained from the growing margin of a culture. With this he immunizes a horse for about eight months, and thence obtains his serum. Injections were made subcutaneously in the thighs in the usual way through a bead of lysol for twelve consecutive days, at the end of which some abatement of the acute symptoms was observed. Dr. Marmorek then visited the patient again and advised 10 c.cm. of serum per rectum, but this produced no good result, and this, indeed, has been my experience of giving any serum by the rectum.

Hypodermic injections were therefore resumed, and twenty-eight doses of 5 c.cm. were given during the ensuing seven weeks, during which time the patient slowly but surely improved. He gained weight and strength, intestinal matting subsided, diarrhoea ceased, squint disappeared, and the urine showed no blood except under the microscope. Crepitations and rhonchi gradually subsided, and though a pleuritic effusion of slightly turbid fluid appeared on the left side, this absorbed rapidly after tapping.

By April the patient was able to return to Paris, looking the picture of health and having regained his normal weight. Dr. Marmorek has sent most favourable reports since. The only apparent abnormality now is the presence of a little albuminuria, and this is diminishing. The last report, received during October, was that the patient was very well and putting on weight.

The chief features of interest were:

1. Repeatedly negative Widal's when every symptom was consistent with typhoid. I may say that in my experience Widal's test is actually more reliable than clinical evidence. This was very noticeable in the Bristol typhoid epidemic some years ago.

2. There seemed no doubt that Marmorek's serum—of which this patient had forty injections, or nearly half a pint altogether, in less than three months—was responsible for the improvement. The clinical signs pointed to tuberculous lesions of the intestines, peritoneum, bladder, lungs, and meninges, and I suppose the invasion was of the miliary type, in which case, by all the rules of medicine, surgery, and midwifery, the patient ought to have died.

3. Temperature reactions, commencing about three hours after injections, are prominent in the charts.

4. Of course it is impossible to say that the lad will not ultimately become a chronic phthisic, but his improvement being so steady and consistent is most encouraging.

I have not entered into minutiae of symptoms and treatment, and I am aware the case is open to certain criticisms, inasmuch as no tubercle bacilli were actually demonstrated in the urine or elsewhere, and there was no sputum at any time to examine. I have merely published the crude facts as they appeared to me, and I think they justify a more extended use of this antituberculous serum.

4. The pneumococcus was seen in the swabs in a few cases, but in small numbers, and it was not isolated.

5. The bacillus of Friedländer was isolated from a few of the cases.

The organisms which appeared to me to be the causal factors in the majority of the cases were the *Micrococcus catarrhalis* and the *Micrococcus paratetrigenus*. The *Micrococcus catarrhalis* is already well known, having been described in a paper by Drs. Dunn and M. H. Gordon on The Bacteriology of an Epidemic Simulating Influenza.² It is described at length in an article by Neisser and Kolle in Wassermann's *Pathogenen Microorganismen*.³

Characters.—It is a rather large coccus, occurring in pairs, or sometimes in dense masses, in the sputum or in swabs taken from the noses and throats of patients suffering from common colds, "influenza," bronchitis, and pneumonia. It can be seen in masses in pharyngeal cells, and occasionally in leucocytes. It is negative to Gram's stain, and resembles the gonococcus, though I think it is usually rounder and less bean-shaped.

Cultures.—It grows readily on nasagar, blood agar, and on ordinary agar (especially if made with 2 per cent. of Witte's peptone). On these media colonies appear in twelve to eighteen hours at 37° C. They are at first translucent, but rapidly become yellowish-white, rounded, and raised above the surface of the medium. The colonies are very viscid, and adhere firmly to the medium, so that it is easy to touch them without removing any of the growth. This may account for the difficulty of subculture which the writer and others formerly experienced. If one is careful to remove a visible portion of

growth from a colony, the subcultures grow readily and are vigorous.

On gelatine growth takes place more slowly, and the gelatine is not liquefied. It grows in broth, and does not produce acid in broth containing 1 per cent. of glucose, lactose, maltose, saccharose, or mannite.

THE SCIENCE COMMITTEE OF THE British Medical Association.

REPORT CXVII.

FURTHER RESEARCHES INTO THE BACTERIOLOGY AND VACCINE THERAPY OF COMMON COLDS.

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In a former paper¹ I drew attention to the occurrence of a diphtheroid bacillus for which the name *Bacillus septus* was suggested. This germ was associated with the *Micrococcus catarrhalis*, and occurred in 20 out of 21 cases examined during the winter 1905-6.

During the winters of 1907-8 and 1908-9 further researches have been carried out on similar lines, with results which may be summarized as follows:

1. The prevailing organisms—that is, those which were present in greatest numbers and grew most readily—were the *Micrococcus catarrhalis* and the *Micrococcus paratetrigenus*.

2. The *Bacillus septus* was present in a number of the cases, but did not grow readily, and was difficult to isolate. This is in marked contrast to its behaviour in 1905-6, when it grew with great ease on ordinary media.

3. The bacillus of Pfeiffer was present in small numbers in a few of the cases, but it was not possible to isolate it.

Fig. 1.—Photomicrograph of a forty-eight hours' culture of *Micrococcus catarrhalis* × 1,000 diameters.

Fig. 4.—Culture of *Micrococcus paratetrigenus*.