THE TUBERCULIN SKIN REACTION (VON PIRQUET'S).

By J. W. BRIDE, M.B., B.S. LORD, M.B., CH.B. VICT.,
Senior Resident Medical Officer, Manchester Children's Hospital, Pendlebury.

I am indebted to the kindness of Dr. Hutton and Dr. Heywood for permission to publish an account of our experience in their wards in the Manchester Children's Hospital, with the von Pirquet skin reaction during the months of October, 1909, to March, 1910.

The test was applied in 92 cases, which I have tabulated below. The procedure we adopted was to make three injections—one on the forearm, saponically prepared, two above, parallel, and one below. The upper two were inoculated with 25 per cent. tuberculin solution obtained from Messrs. Martindale. The lower was used as a control. The appearance of a ring of hyperemia or red papules in twenty-four hours was regarded as positive. In the table below the cases styled "non-tuberculous" were chiefly chorea or enuresis, in which no signs of tuberculosis were discoverable clinically. The table contains the clinical diagnoses of the diseases in which the test was applied.

<table>
<thead>
<tr>
<th>Test for Tuberculin Reaction</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Undoubted pulmonary tuberculosis</td>
<td>18</td>
<td>4</td>
<td>22</td>
<td>68.1</td>
</tr>
<tr>
<td>2. Doubtful pulmonary tuberculosis</td>
<td>10</td>
<td>1</td>
<td>11</td>
<td>90.9</td>
</tr>
<tr>
<td>3. Bronchitis</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>57.1</td>
</tr>
<tr>
<td>4. Pneumonia</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>50.0</td>
</tr>
<tr>
<td>5. Bronchopneumonia</td>
<td>1</td>
<td>5</td>
<td>6</td>
<td>16.6</td>
</tr>
<tr>
<td>6. Pleurisy</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>57.0</td>
</tr>
<tr>
<td>7. Encephalitis</td>
<td>—</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>8. Abdominal tuberculosis</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>60.0</td>
</tr>
<tr>
<td>9. Doubtful enteric fever</td>
<td>2</td>
<td>2</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>10. Renal tuberculosis</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>50.0</td>
</tr>
<tr>
<td>11. Tuberculous meningitis</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>33.0</td>
</tr>
<tr>
<td>12. Cerebral tumour</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>100.0</td>
</tr>
<tr>
<td>13. Non-tuberculous cases</td>
<td>—</td>
<td>13</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>44</td>
<td>92</td>
<td>52.1</td>
</tr>
</tbody>
</table>

1. In the Twenty-two Cases of Undoubted Pulmonary Tuberculosis. In the 15 positive cases all presented definite signs of phthisis; 11 gave definite family history of tuberculosis; in only 4 was there pyrexia, the rest were quiescent. (b) In the 4 negative cases, all presented definite signs of phthisis. In one there had been an attack of pneumonia seven weeks previously; another, with definite family history and definite signs of pulmonary tuberculosis, had traces of a recent attack of chicken-pox upon him; the other 2 gave a marked family history of tuberculosis, no history of pneumonia, and both had marked physical signs.

2. In the Eleven Cases of Doubtful Pulmonary Tuberculosis. (a) In the 10 positive cases, 6 gave definite family history of tuberculosis, 5 of previous bronchitis or pneumonia, and 6 a history of measies. There was no pyrexia, the signs were very vague, and the history of loss of flesh and night sweats was variable. The majority of these improved under treatment. In the disease it was thought that the disease might have been freshly lighted up by the application of the tuberculin; but on the whole the test was an aid to diagnosis, and led to earlier and more definite lines of treatment than might otherwise have been adopted. (b) In the 1 negative case there were definite signs and symptoms of phthisis; no pyrexia was present. The patient was discharged cured.

3. In the Seven Cases of Bronchitis. (a) In the 4 positive cases, the clinical diagnosis in 3 was bronchitis (pulmonary tuberculosis); there was a definite history of measies in 3; no family history of phthisis. All presented signs so vague that a definite diagnosis could not be made except from the history of chronic cough, expectoration, and loss of flesh. In the fourth case there was loss of flesh, and no expectoration, and there was a very vivid reaction, and it seemed as if the tuberculin might have lighted up the disease there. Post-mortem sections were developed at both apices, and the case did not clear up on discharge. (b) In the 3 negative cases, 2 there was definite history of phthisis, in all of measies, and there were only signs of chronic bronchitis and cough. These were treated for this and discharged cured.

4. In the Three Cases of Bronchopneumonia. (a) In the 2 positive cases, in 1 the clinical diagnosis was tuberculous pneumonia; there was a definite history of phthisis. In the other chronic bronchitis had existed for a year; no family history of tuberculosis. The case improved but still displayed signs of discharge. (b) In the 2 negative cases, both were definite cases of pneumonia, and they both cleared up absolutely and were discharged cured.

5. In the Six Cases of Bronchopneumonia. (a) In the 1 positive case there was a definite history of phthisis and history of bronchitis and the chronic bronchitis had existed for a year before admission, and the diagnosis of phthisis seemed established. (b) In the 5 negative cases there was family history of phthisis; there were no measles in 2 cases. All seemed definite cases of bronchopneumonia. The signs cleared up, and in all the voice to the skin reaction was negative.

It is not necessary to summarize the other cases. In literature we found the test of help in diagnosing the case of the effusion, which we were able to verify in some cases by microscopical examination of the fluid, and by culture methods. The same help was obtained in the cases of encephalitis. In the diagnosis of suspicious cases of enteric fever we got great help from the test. In the cases of meningitis it is difficult to understand why the test was negative in 4 of the 6, as all had equally satisfactory statistics. From our experience it is not established that the test is quite without risk to the patient, as mentioned above. Up to the present, however, it has been most helpful in diagnosis, and appears to us not entailing any serious risk to the patient.

SOME POINTS RELATING TO THERAPEUTIC IMMUNIZATION.*

By J. COURTENAY MACWATTERS, M.R.C.S., L.R.C.P.,
Honorary Medical Officer, Almondbury Hospital.

Therapeutic immunization is a method of treatment in cases of bacterial infection whereby the aid of proved scientific phenomena is brought to Nature in establishing a rising tide of immunity, and thus enabling the human organism to react successfully to the infection, in precisely the same manner as is accomplished by Nature in those cases where spontaneous cure results. We here remind you that opsonin renders the bacteria vulnerable to the phagocytes, that without its presence in a germ laden tissue phagocytosis cannot take place, and that from the early experiments of Wright and Douglas it is evident that opsonin acts on the bacteria and not on the phagocytes.

In vaccine therapy we are dealing with a method that is capable of giving the most gratifying results—at least beyond the dreams of the most sanguine—yes, unless foolishly applied it may lead to disappointment, and receive much undeserved condemnation. Where this has occurred I have almost invariably found that the fault lay with the would-be immunizer rather than with the method. It is useless to inject vaccines into a patient, in

* Read before the Bath and Bristol Branch of the British Medical Association.
even in the most suitable doses, if the flow of highly opsonized lymph through the diseased tissues is not arrested. I am equally a failure in using a vaccine prepared from other than the variety of organism causing the disease; or again, it is useless to expect one vaccine to effect a cure in a multiple infection; yet there have been failures of the method. It is my belief that cure is prac-
tically certain in any uncomplicated case of localized bacterial infection if one can succeed in three things—
neutralizing the offending organisms, preparing a vaccine from it and administering it in suitable doses, and
determining the flow through the attacked tissues of the resulting highly opsonized lymph. I have mentioned
localizing the organisms, only, for so much has not been done in systemic infections to warrant my
speaking dogmatically regarding the treatment of these by
vaccines. Much light is being thrown upon the treatment of some infections by Morgan, Freeman, and other workers
at St. Mary's Hospital Inoculation Department and else-
where, and I have obtained most encouraging results in
whooping-cough, phthisis, rheumatism, and in some cases
of pneumonia and diabetes.

Those who have read Metchnikoff's lectures on the
Comparative Pathology of Inflammation will remember his
generalization that everywhere in the vertebrate and invertebrate organism the tissues are responded to by a determination of phago-
cytes to the seat of infection, and that this migration of phagocytes is the only antibacterial agency, and that
this is the cause of the local reaction. Wrigth, Douglas, Bulloch, and others have since then shown that
phagocytes, when unsailed by the opsonic power of the blood as to such action. So that to-day we must regard the processes
of inflammation as anything but immunization, on the
one hand by the transference of phagocytes and on the
other by the transference of antibacterial fluids from the
blood to the invaded tissues. In other words, Nature
takes care in a local bacterial invasion by producing a
migration of leucocytes into the infected tissues accom-
panied by a levelling up of the amount of opsonin in the
invading tissues to that in the circulating blood; and it therefore follows that if the opsonic content of the blood
is deficient we shall fail to obtain a destruction of the
invading bacteria. Herein lies an explanation of the failure of Metchnikoff's original theory in those cases of
inflammation where phagocytic migration is unattended
by cure.

Spontaneous cure in localized bacterial infection is being
practised both of the local invasion by phagocytes, and opsonized lymph, from the circulating blood to the infected tissues; when spontaneous cure fails we can give aid on the one hand by raising the anti-
body content of the blood, and on the other by assisting
the flow of these substances through the infected tissues.

With these points in view I would draw your attention
to the advisability of relying on the use of antiseptic
applications to the attacked tissues, for it is very doubtful
if they act against bacteria in vivo; and their application
to tissues whose superficial layers are invaded by bacteria
is of very doubtful value. By such applications we
paralyse and destroy the chief line of natural attack—the
phagocytes, whose action is aided by the presence of
opsonin, which even the mildest of antiseptics will
destroy. The aim of local treatment should be to promote a
migration of leucocytes to the part, and to ensure the
bacteria present being kept in a seductively attractive
condition by stimulating a good flow of opsonized lymph
through the involved tissues. Hostile conditions must be made favourable for the egress of
antibacterial agencies from the blood, by raising the
hydrostatic pressure in the capillaries of the infected part,
and obtaining the coagulability and viscosity of the blood.
A way must also be made for the entrance of
these elements into the focus of infection by evacuation,
preferably combined with the local application of a
caustic. Hot, ether, benzoin, or even dry hot sandbags, when applicable, will determine a
flow of blood to the part, and consequent egress of phago-
cytes. The leucocytes may be increased in number six or
seven times in five grains tablets. The hydrostatic
pressure in the capillaries may be increased by Bier and
Kappa's method of constriction or vacuum cupping.

There is a low thickening of the blood, due to the
bacteriotoxic elements of the blood being arrested by
cogulation, thus choking the tissues, and preventing both
leucocytes and opsonized lymph from reaching the infected;
causing death. The viscosity of the blood
must be diminished; this is best accomplished by adminis-
trating citric acid as such, in doses of 1 drachm three
times a day; or as the juice of lemons, about four or five a
day being necessary.

To effect an entrance of bacterial elements into the
focus of infection evacuation, a ray and electro-radiant heat applications, cura
tage, and massage, show the regular sequence of
"negative phase," "positive phase," and "phase of
increased resistance" identical with that produced by
antiseptics. From the isolation of from the
invasion of the whole organism causing whooping-cough,
is the whole
invertebrate system, the organism is isolated, and others have since
read the lectures;

antibacterial effect is obtained in a case of systemic
infection. Therefore, we see that the organism has a natural method of producing immunization with-
less distress to the patient, with greater accuracy, and,
when properly applied, producing better results than other
methods. I have been speaking only of localized bacterial
infections; in those cases where there is necrotic tissue,
or a barrier of much cicatricial tissue preventing access to
the lymph, surgical interference must of course be
sought.

When in any case of localized bacterial infection it is
considered advisable to employ vaccines, it is in the first
place necessary to discover what organism may be the
exciting cause of the local infection. If only one organism
is isolated it is almost certainly the case, and the
vaccine may be straightway prepared; but where two
or more are present serious consideration is required to
determine whether one or all are responsible for the
patient's condition.

In deciding which are the offending organisms in a
case of multiple infection, the estimation of the opsonic index
of each organism to which an abnormal index is obtained should
be administered. Failing this, it is well to employ a vaccine
prepared from those bacteria which clinical experience has
shown to be the most pathogenic. In the case of open infection it is comparatively easy to obtain the
offending organisms, and in cases of closed infection the
organism may be at times recovered from the urine. For
this purpose repeated giving of vaccines is of frequent help. Vaccines of each organism, even
of tuberculous organisms. Speaking broadly, deep skin suppara-
tions—bolts and carbuncles, for example—are, as a rule,
due to Staphylococcus aureus; superficial lesions, such as
eczema, acne, etc., to the Staphylococcus albus. Ulcerous
conditions, including onychia, are due to streptococcus.
Inpeth is usually due either to a streptococcus, when
the lesion appears at first as a fluid vesicle and later as a
scab, or to a Staphylococcus, usually the aureus, whereas
these is scab formation from the first. Chronic sinuses,
including those arising from a tuberculous lesion, are a
favourable habitat for streptococci, which may be found
alone, or in conjunction with staphylococci, or a
coliorganism. A white, sudden, eroded appearance
round an ulcer or mouth of a sinus is usually associated
with the Bacillus pseudo-diphtheriae, and this organism
is frequently present in, and is sometimes the cause of
chrooboia.

In bronchitis the usual organisms present are the
pneumococcus, Pfeiffer's bacilli of influenza, Micro-
coccus catarrhalis, and the staphylococcus. In
In pyorrhea alveolaris I have invariably found a
streptococcus present in every case, and frequently
pneumococci or Micrococcus catarrhalis.

One who has had much experience with vaccine
therapy knows how much more prevalent is infection by
the tubercle bacillus than is generally imagined. If sus-
tected in any case, confirmation or the reverse may readily be obtained by the estimation of a few tuberculo-
opsonic indices.

In the estimation of dosage it is often most diffi-
cult to decide; on it depends whether we get a max-
imum immunizatory response with a minimum toxic ef
fect or not. If the patient has symptoms of toxemia—
high temperature and rapid pulse—or is anemic, in other
words, has a low resisting power, particularly if his
opsonic index is markedly reduced to, say, 0.6 or 0.5, the
dose of vaccine should be much smaller than that which
suffices for a more robust organism, and obviously—a
small man should, other things being equal, have a
smaller dose than a big man.

The opsonic index, taken before and two or three days
after inoculation, is a most important guide. In many
cases this is not a necessity, but if a case does not im-
prove, the dosage will usually be found at fault, and may
be increased or diminished, according to the information
afforded by the indices. If, for instance, in a case of
boils, a dose of vaccine is followed by increased pus-
tulation, discharge, and pain, with the appearance of fresh
crops of boils, and possibly a marked rise in the patient's
temperature, with in a case of typhoid fever, increased
fever, increased frequency of urination, pain, and irrita-
tion of the mucous membrane, there has undoubtedly been a
marked "negative phase," and it will probably be some-
delay before the rise in temperature will set in. In
such cases the dose has probably been too large, and must
be correspondingly diminished when the next dose is due;
this will be as soon as any improvement that has accrued
begins to wane. On the other hand, when the index begins
to fall after the rise that should follow the "negative
phase." When a dose is followed by immediate im-
provment, and this improvement lasts but a day or so, being
followed by regression, it is likely to an excess, and that
the dose was slightly too small, and it may with advantage
be increased. The ideal immunizatory response usually
follows a clinical "negative phase" lasting about twelve
hours.

With Staphylococcus aureus, albus, and citreus, and in
the case of superficial lesions such as eczema, acne
pustulos, impetigo, and sycoas, a dose of 50 to 100
millions at intervals of six to eight days is suitable. In
boils and carbuncles, however, to get the best results,
200 to 250 millions may be given with advantage, followed
in three or four days by a dose of 400 to 500 millions, after
which the lesion usually heals rapidly and incipient
boils abort. Staphylococcal invasion of small skin
abrasions associated with lymphangitis and enlargement of
the corresponding lymph glands usually yield to
100 to 200 millions of the aureus variety, repeated, if necessary, in three or four days.

Streptococci are very toxic, and, as a rule, a dose of
5 to 10 millions is sufficient, to be repeated in eight to ten
days. In the case of cervical or pharyngeal suppura-
tion—of tonsils, gingivitis, etc.—20 to 25 millions, or even more, being usual. As regards gonococci, in cases of gonococcal
infections—for instance, of joints, or the pelvic organs of
the female, and in cases of "latent" or chronic gonorrhea in
the male—treatment by doses of 5 to 25 millions every
six to ten days will often be followed by marked relief.
In dealing with a suspected joint, the estimations of a
series of lesions indices before and after vaccination
produced by massage of the joint will settle the
diagnosis. The coliform group are also toxic, and a
dose of 10 to 20 millions is sufficient. The Bacillus
globiceps furnishes a good vaccine, and I have seen
satisfactory results with doses of 25 millions every eight
to ten days.

Tetanus, in this vaccine is undoubtedly the most
toxic, and therefore requires far more careful handling
than the others; a dose of one ten-thousandth of a milli-
gram is frequently far too large, so that till the effect of
two doses on the patient is known, it is wise to be satis-
fied with the dose of 0.1 micro-gram. I have known
one fifty-thousandth of a milligram seriously to
upset an adult case of tuberculosis of the bladder. The
dosage in the tetanus vaccine should be repeated in from eight to
twenty-one days.

The frequency of staphylococcal infection in diabetes is
well known, and I would submit that the glycosuria may
be the result, and not the cause, of the lowered resistance
ton these organisms. In one case at present under my
care I have on three occasions found copious glycosuria
clear up after the administration of an auto-staphylococcal
vaccine as soon as the opsonic index was lowered. As a
rule, however, I have found that sugar has been absent from his urine for the past four months, during which his index has been between 0.4 and 0.5. I have had under observation three other cases of glycosuria, each of which has improved definitely while under treat-
ment on these lines: all have gained weight, and there has been a more marked diminution in the outcome, and, of course
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THE CLASSIFICATION OF THE SYMPTOMS OF LEAD POISONING.*

By W. Dowling Prendergast, M.D., M.Ch., M.A.O., D.P.H.

Armand Gautier has enumerated seventy occupations in which the workman is subject by his occupation to lead poisoning. We also consider the fruits of this industry in the materials for our common and everyday use, all impregnated with a salt of lead. From our earliest age we come in contact with the poison. I have in my hand an ordinary child's toy tea set, which in a child of 4 years under my care produced lead poisoning; the child sucked the paint off it. I had another case of a child of 12 months, who was in the habit of sucking the leather covering of its perambulator: the leather on analysis was found to be impregnated with a salt of lead.

Sir Thomas Oliver, in his Goulstonian Lectures, cites the case of an old gentleman whose symptoms were of a puzzling nature. He consulted a London physician, who elicited that he was an inveterate snuff taker; the snuff was found to contain lead: when it was discontinued, the patient soon recovered. He quotes another case in which the symptoms were obscure; he noticed that the patient for her age had very black glossy hair, and found that she was accustomcd to dye it with a wash which contained a large amount of lead.

A more remarkable series of cases occurred affecting the French navy in 1876, whilst serving abroad. In the first instance the symptoms were attributed to malaria; so grave was the outbreak that the French Government appointed a committee, which found that the outbreak was due to the large amount of lead used in the paint for the internal decoration of the warships. Since that time only zinc oxide paint is used. The use of tin mine foods is prohibited as far as possible, and the distillation of drinking water is no longer conducted by lead pipes. The health of the men has since then improved considerably.

In another case I will cite I saw the patient the day before he died; he was convulsed, and showed to me unmistakable signs of lead poisoning. I will quote his wife's evidence at the inquest:

Dr. A.'s locum tenens called on January 3rd, and told her that her husband was suffering from typhoid. He was treated for typhoid from that day to his death. The witness added that Dr. A. came the following Sunday, and confirmed the diagnosis of typhoid. Afterward, the sanitary inspector came and steps were taken to remove him to the Bradwell Sanatorium, but there was no bed there for him. Deceased gradually grew worse, and the following Tuesday he became insensible, and jumped out of bed. He was convulsed from the Tuesday night until his death on Wednesday.

The deceased's organs were analysed for me by Professor Bedson of Durham, with the following result:

Bottle 1. Containing kidneys and spleen:
Total weight of contents ... 13 oz.
Total lead present ... 0.859 grain

Bottle 2. Containing brain:
Total weight of contents ... 3 lb.
Total lead present ... 0.176 grain

* Read before the North Staffordshire Division of the British Medical Association.