me, and I made separate diagrams which were afterwards compared with those of Dr. Batty Shaw. Out of 19 cases there was substantial agreement in 17 cases, and minor differences in 2, which were afterwards adjusted. In some cases the extent of rales had increased, in some retrogressed, and in others remained stationary, while in still others there had been increase of rales in one lung and diminution in another. In such cases a balance had to be struck between the two, and the case adjudged as worse, stationary, or better accordingly.

Physical signs were, therefore, taken as the main criterion, and alteration and increase of weight, amount of exercise, and general condition correlated secondarily.

Choice of Cases.

In agreement with one of the safest recognized methods of giving tuberculin, it was adopted as a *sine qua non* that all the cases should be afebrile when up and about all day, and that rise of temperature maintained for more than a day or two should disqualify the patient from being one of the series.

Another point now cropped up, which was that many cases are adjudged suffering from pulmonary tuberculosis on slight and often equivocal signs at one apex, or on no signs at all, and on some haemoptysis which may very possibly have not been haemoptysis at all, but have been concealed epistaxis or bleeding from gums, teeth, or posterior naso-pharynx. Therefore, as the second *sine qua non* it was resolved to take only those patients into the scheme who had expectorated sputum in which tubercle bacilli had been found.

The third point was the distribution of the cases between the two methods of treatment, and where a number of cases presented all grades of involvement of the lungs from very slight to extensive (1 apex to 5 lobes), and where some showed fibrosis and some not, it would be almost impossible to apportion the cases fairly between the two treatments so as to be free from any suspicion of bias. To obviate this, the patients were chosen by lot. In this way two series of nine were chosen, but, because of rise of temperature or because they left the hospital, three soon fell out from the names not treated by tuberculin. To replenish these, the next four patients fulfilling the conditions of afebrile tuberculosis drew lots, one to have tuberculin treatment, and three not. The final result was that ten patients were treated with new tuberculin (T.R.) and nine were not, the one out of the latter ten cases being set aside, as she left the hospital before the expiration of three months.

Method of Giving Tuberculin (T.R.).

As before mentioned, tuberculin was only given to afebrile cases.

Dosage.—Treatment was commenced with a very small dose, increased every second day at first, and afterwards at intervals of four days.

General Scheme.—The dose given was as follows in milligrams every second day: 0.00001, 0.00003, 0.00005, 0.00007, 0.0001, 0.00015, 0.0002, 0.0003, 0.0005, 0.0007, 0.001, 0.0015, 0.002, 0.003, 0.005, 0.007, 0.01, 0.015, 0.02, 0.03, 0.05, 0.07, 0.1.

Every Fourth Day.—0.15, 0.2, 0.3, 0.5, 0.7. The last—0.7 mg.—was the maximum dose reached.

The injection, however, was conditioned by the occurrence of reactions. If the temperature rose to 99° F. or above with all but the smallest doses (where the temperature was possibly not due to the injection of tuberculin) the patient was put to bed until it became normal, and no further dose was given for five to ten days (five with small doses and up to ten with the larger), and then the last dose repeated. In the case of the smallest doses, the next dose was given after an interval of four or five days. If the temperature now remained normal, the original increase of dosage was gone on with. If another reaction occurred, the patient was again put to bed till the temperature was normal, and when it had kept normal for from two to seven days, the same or a smaller dose was given. If this produced a reaction a still smaller dose was given after an appropriate interval until one was found which produced no response. This dose was now repeated two or three times before increasing again.

Out of 10 cases, 2 gave no reaction till 0.7 mg. was injected. A third case reacted first with 0.1 mg., whilst the other cases reacted two to seven times with various doses.

A Typical Example.

CASE V.

First dose=0.00001 mg. This produced a reaction temperature 100° F. After eight days' interval 0.00003 mg. was given, and at two days' interval, 0.00005, 0.00007, 0.0001, 0.00015, 0.0002, 0.0003, 0.0005, 0.0007, 0.001, 0.002, 0.003, 0.005, 0.007, 0.01, 0.015, and 0.02 mg. After this last the temperature rose to 99°; five days' interval, and then 0.02, 0.03, 0.05, 0.07, and 0.1 mg. were given at two days' interval, then at four days' interval, 0.15, 0.2, 0.3, 0.5, and 0.7 mg.

At the end of three months all the 19 cases were again examined in the way described and note also made of their weight and amount of exercise taken.

SUMMARY OF RESULTS.

1. Physical Signs:

(a) Tuberculin-treated patients. Out of 10: Improved 1, worse 4, *in statu quo* 5.

(b) Non-tuberculin-treated patients. Out of 9: Improved 4, worse 3, *in statu quo* 2.

2. Increase of Weight:

(a) Tuberculinized patients (10 cases). Gained 10–20 lb. 4, gained less than 10 lb. 4, *in statu quo* 2.

(b) Non-tuberculinized patients (9 cases). Gained over 20 lb. 2, gained 10–20 lb. 3, gained less than 10 lb. 4.

In (a): Average per cent. of increase of weight, 6.3 per cent.

In (b): Average per cent. of increase of weight, 10.3 per cent.

3. Exercise—capacity of walking, maximum amount per diem:

(a) Tuberculin patients (10 cases). Two miles and over, 3; 1–2 miles, 5; less than 1 mile, 2.

(b) Non-tuberculin patients (9 cases). Two miles and over, 6; 1–2 miles, 3; less than 1 mile, 0.

4. **General Condition.**—This is a difficult criterion, but, generally speaking, in (a) only 5 out of 10 were in thoroughly good condition; in (b) 8 out of 9 were in thoroughly good condition.

The net result of these observations is to show that the administration of new tuberculin by one of the more popular approved methods is not followed by greater improvement in the *physical signs*, nor by greater increase in weight, nor by more greatly increased capacity for physical work, nor by a greater improvement in the general condition, as compared with the results of ordinary hospital methods.

The observations on the signs do not support the idea that new tuberculin in any way lessens the activity of the local lesion. It is possible that the less favourable influence on weight, the less capacity for work, and the falling off of the general condition are due to the disabilities imposed on the patient by being treated with tuberculin, as they so often were kept in bed to help restore the temperature to normal.

ORGANIC ACID RATIO OF URINE AFTER TUBERCULIN.

By ARTHUR H. GREGSON, M.B., B.Ch., VICT.,
BLACKBURN.

A GIRL, born in 1892, had suffered from lupus vulgaris of the left cheek from 1895 to 1905. Roentgen rays were tried, but did not benefit. Curetting was successful in 1905, but afterwards the glands of the neck and beneath the jaw on both sides enlarged.

She consulted me, and on December 4th, 1909, received an injection of $\frac{1}{10000}$ mg. T.R. This was repeated weekly in increasing dose until, on February 1st, 1910, $\frac{1}{100}$ mg. T.B.E. was given; after this the temperature rose to 103° F., the patient became delirious, and suffered from severe abdominal pain and tenderness. The temperature was intermittent for months; various methods were tried to reduce it, including administering on May 3rd and 22nd of $\frac{1}{10000}$ mg. T.R. of human origin, as before, but without benefit.

About the middle of July $\frac{1}{8000}$ mg. of bacillary emulsion of bovine origin was administered; the temperature fell to normal and pains decreased.

It seemed as though the failure were associated with the human origin and the success with the bovine origin, and it was determined to repeat the experience.

On August 2nd, 1910, the patient weighed 7 st. 8½ lb., and $\frac{1}{8000}$ mg. T.B.E. was administered. It was increased to $\frac{1}{2500}$ mg. on the 13th and to $\frac{1}{1000}$ mg. on August 23rd and September 1st, after which the temperature became erratic. The question of over-dosage had to be considered, but on September 6th the girl weighed 8 st., a gain at the rate of 1 lb. a week; the idea of the wrong variety of tuberculin was therefore adhered to, and $\frac{1}{3000}$ c.cm. original bovine tuberculin was administered on September 13th.

The temperature fell suddenly on the eighth day. Increasing doses were given on September 23rd, October 6th, October 19th, and reached $\frac{1}{3000}$ c.cm. concentrated bovine tuberculin on October 26th.

The patient felt considerably better, and it was determined to attempt an investigation into the acidity of the urine under the action of the different varieties. No constant effect was found upon the total free acidity, and this was then divided into the mineral and organic portions, and the following results obtained for the ratio of organic to total acidity:

Increased Organic Acidity after Human Tuberculin on January 4th.

Before.	Injection.	After.
0.26	$\frac{1}{2000}$ c.cm. T. Koch	1.04 (2 days); 2.2 (5 days); 2.5 (6 days).

Decreased Organic Acidity after Bovine Variety on January 17th, 26th, and February 6th.

Before.	Injection.	After.
1.7	$\frac{1}{1000}$ c.cm. P.T.	1.6 (3 days); 1.5 (6 days).
2.5	$\frac{1}{750}$ c.cm. P.T.	1.1 (5 days).
1.0	$\frac{1}{500}$ c.cm. P.T.	0.56 (2 days); 0.4 (9 days).

An injection of $\frac{1}{1500}$ c.cm. T.K. on December 19th had sent the temperature to 100°, but no rise was noticed after that on January 4th, whilst after the bovine tuberculin on February 26th the temperature rose again to 100°, so this is some evidence that the difference in result is not dependent upon the weaker nature of the bovine variety.

As the effect of only one "human" injection had been tested the following confirmatory observations were made, and the effect upon the lime, magnesium, and phosphorus noted at the same time:

E. H.

February 12.				Feb. 15.	Feb. 20.	Feb. 28.
Lime in 24 hours	...	0.122 gram	Injection $\frac{1}{750}$ c.cm. T.K.	Grams. 0.288	Grams. 0.378	Grams. 0.254
Lime in 100 c.cm.	...	0.0135 "		0.026	0.031	0.026
Mg in 24 hours	...	0.536 "		0.277	0.708	0.431
Mg in 100 c.cm.	...	0.049 "		0.025	0.059	0.044
Ratio of organic to total acid	...	1.37		1.65	1.44	2.1
Ratio of phosphorus to total acid	...	0.2		1.2	0.7	0.5
Ratio of phosphorus to lime...	...	1.75		2.9	2.35	2.35

A. R.

				Oct. 27.	Nov. 1.
Lime in 24 hours	...	0.688 gram	Inject $\frac{1}{500}$ c.cm. T.K.	Grams. 0.790	Grams. 0.292
Lime in 100 c.cm.	...	0.055 "		0.046	0.03
Mg in 24 hours	...	0.979 "		0.884	—
Mg in 100 c.cm.	...	0.034 "		0.026	—
Ratio of organic to total acid	...	0.03		1.59	1.15
Ratio of phosphorus to total acid	...	0.02		0.3	0.26
Ratio of phosphorus to lime	...	11		0.8	1.5

These and four other experiments therefore confirm the increase of the organic acid ratio after administering human tuberculin, and show that it is not due to the lime and magnesium being reduced.

The methods used were as follows:

Total Acid.—Neutralization with decinormal NaOH after adding 1 per cent. neutral potassium oxalate, using phenolphthalein as indicator.

Ammonia.—After neutralization of 20 c.cm. as above, add 8 c.cm. freshly neutralized 40 per cent. formalin and continue the addition of decinormal NaOH.

Ethereal SO₄.—Difference between precipitation of urine by barium nitrate with and without previous oxidation by conc. HNO₃.

Mineral Acidity.—Add 5 c.cm. decinormal NaOH, ignite, oxidize, boil with excess of acid, neutralize, and estimate alkali lost. Deduct the ammonia and ethereal SO₄.

Organic Acidity = Total acidity — mineral acidity.

I have been unable to trace any similar experiment. If the prevailing opinion be correct, that there is no fundamental difference between the various tuberculins, we may as well settle the relative activities and cease to encumber ourselves with so many specimens. If incorrect, we ought to find their differences and discover the indications for each.

A YEAR'S EXPERIENCE OF DIORADIN IN SURGICAL TUBERCULOSIS.

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ALMOST a year ago I read a paper before this Section of the Academy, giving the results of treatment by dioradin of 15 cases of tuberculosis. Since then I have been more or less continuously engaged in the further treatment of these and other cases by the same means, and I desire to record the results I have obtained during fifteen months' trial of this remedy in cases of surgical tuberculosis, and the conclusions at which I have arrived as to the value of this method of treatment.

I shall first consider the cases which I reported a year ago; they were 15 in number, but to-night I shall only speak of 14 of these, as one of them was a case of pulmonary tuberculosis, and the number of this class of case has been too small to be worth recording the results at present. These 14 cases were divided into two classes according to whether they were complicated by sepsis or not.

Of the 5 uncomplicated cases each had received one course of injections, and one was apparently cured, and the other 4 were greatly improved, and they showed an average gain in weight of 8.3 lb. Four of these have since received a second course of injections, with the result that there are now 4 apparently cured, and 1 greatly improved, and the average gain in weight is 10.5 lb.

Of the 9 cases in the second class, that is, cases complicated by sepsis, there was 1 apparent cure, 2 greatly improved, 4 improved, and 2 not improved, with an average gain in weight of 2 lb. Four of these cases were given a second course of injections, and a fifth was given both a second and a third course, with the result that there were 3 more apparent cures and 1 greatly improved. The fifth, which was a case of tuberculous and septic hip which had been excised, improved further after a second course of injections, but about a month later developed acute nephritis and died. The average gain in weight of these 5 patients was 5.4 lb. As regards the other 4 of this group who did not receive a second course of injections, 1 was a case of multiple foci which left the hospital cured after the first course (No. v previous paper¹). The second, a septic hip in which there was always much doubt as to the presence of tuberculous disease, left hospital unimproved after the first course of injections (No. viii, previous paper). The third was a case of tuberculous cystitis with almost certainly a similar affection of both kidneys as well; he also left hospital unimproved after the one course of injections and died shortly afterwards (No. xii previous paper). And the fourth was a case

* Read before the Surgical Section of the Royal Academy of Medicine in Ireland, November 29th, 1912.