

The Liability of the Insane to Tubercular Infection as demonstrated by an Examination of the Tuberculo-opsonic Index. By C. J. SHAW, M.B., Ch.B., Assistant Medical Officer Perth District Asylum, Murthly. Awarded the Bronze Medal of the Medico-Psychological Association.

Introduction.

DEATH-RATE statistics of persons dying in large institutions are often inexact, as their accuracy depends to a very large extent on the personal factor of their compiler. Unfortunately, the statistics of the death-rate from tubercular disease, particularly phthisis, occurring in asylums leave no room for doubt that the insane, as a class, are particularly liable to contract tubercular disease. The English Lunacy Commissioners in their report for 1902 say: "The proclivity of the insane, whether confined in asylums or not, to tubercular disease, especially pulmonary, has long been recognised." In all asylums, according to Clouston, who was amongst the first to draw attention to the fact, consumption is between three and four times more common than in the general population at the same ages.

There is, however, great difference of opinion as to whether this high tubercular death-rate is due to the fact that the insane are herded together in asylums, or whether the insane, as a class, have an abnormally low resistive power to the invasion of the tubercle bacillus. Clouston says that four-fifths of the insane dying of phthisis contract the disease after admission to asylums. Another observer has stated that not more than 7·5 *per cent.* of cases admitted into asylums are phthisical, and in 10 *per cent.* a family tendency exists. In English asylums about 15·5 *per cent.* of deaths are officially assigned to phthisis, and in at least 20 *per cent.* signs of tubercular deposit in the lungs may be traced. The average duration of residence of those dying from this cause in Scottish asylums is 3·66 years. It is therefore probable that in many cases phthisis is contracted after admission to the asylum.

Clouston further states that out of ninety-seven cases of general paralysis who died, twenty-seven were phthisical. Mickle has stated that of all the general paralytics examined

post-mortem, 26 per cent. exhibited caseation or cavities, 12 per cent. arrested phthisis, and 65 per cent. pleuritic adhesions. In the last report of the General Board of Commissioners in Lunacy for Scotland, the percentage of deaths from phthisis in all Scottish asylums is given as 14.6. The percentage of deaths due to general paralysis for the same year was 14.8. If one takes into consideration the fact that many cases of general paralysis really die of tubercular disease, although returned as dying of general paralysis, the death-rate from tubercle must be higher than that above stated.

As during recent years, with improved hygienic conditions in asylums, the death-rate from phthisis has diminished among the insane, it is possible that at one time confinement in an asylum did act as a factor in swelling the tubercular death-rate. On the other hand, it cannot be denied that many cases of phthisis admitted into asylums make most excellent recoveries, and the environments of the modern asylum do not suggest that tubercle should be an endemic disease. In this asylum, among patients drawn largely from a rural population, of the last hundred deaths, seventeen were due to tubercular disease. Quite a number of phthisical patients are admitted, however, who are ultimately discharged recovered with no apparent signs of active tubercular disease.

It is reasonable to suppose that, if the insane contract phthisis through residence in asylums, the resistive power of those who have been long resident should be considerably below that of those more recently admitted, always provided that the patients so examined show no symptoms of active tubercular disease. On the other hand, if the insane, as a class, be more liable to phthisis than the sane, their average resistive power should be below that of the sane healthy population.

The recent researches of Wright and others on the opsonic power of human blood-serum to the tubercle bacillus and other organisms have opened up a field of inquiry which, although at present little explored, has already, they contend, yielded certain results, in so far that it is now possible to calculate the resistive power of the individual, not only to tubercle but also to other organisms. As Wright found that in cases of staphylococcal and tubercular infection with an entire absence of clinical symptoms there was a diminished phagocytic power

to those organisms as compared with that of healthy individuals, and as this power could be increased by injections of the corresponding vaccine, he concluded that the lowered phagocytic power permitted infection to occur, and that the resistance to infection by any organism could be estimated by calculating the opsonic power of the blood-serum. The results of observations recorded by Bulloch and others agree with those obtained by Wright and support his conclusion.

It occurred to me that in the study of the opsonic index of the insane resident in the asylum we have a means of determining the question as to whether the insane contract tubercle as a result of residence in asylums or as a result of a lowered resistive power to infection by the tubercle bacillus. With this object in view I made observations on the opsonic index of six members of the staff, who were, so far as could be ascertained, absolutely free from tubercular disease. I also made observations on thirty cases of persons suffering from various forms of mental disease, commencing with those most recently admitted, and extending my observations to those who had resided in the asylum for so long a period as eleven years. All these cases were, at the time of observation, free from active tubercular disease, but five showed evidences of having, at some time, suffered from tubercular infection. One of them had cicatrices in the neck. Four had flattening of the chest, with diminished movement, some dulness on percussion, and increased vocal fremitus with prolonged expiration. Two of these were cases of general paralysis. During their period of residence none of the thirty cases observed had ever required medical treatment for any serious ailment.

The opsonic index of the blood-serum was determined for five consecutive days, and the average index of each case calculated for that period. In all cases the serum was compared with my own, which was taken as unity. To ascertain if any further information could be gained from the opsonic indices, I injected the control cases and the insane patients with Koch's new tuberculin T. R. Four of the control cases, and twelve of the insane persons received an injection of $\frac{1}{1000}$ mgr. T. R., while two control and eighteen cases were injected with $\frac{1}{750}$ mgr. T. R. The opsonic indices were then observed for a further period and the results tabulated.

Technique employed.

Before reliable results can be obtained in estimating the opsonic power of the blood, considerable experience in the technique of the operation is necessary. I had been engaged at this work for three months before I considered my results sufficiently accurate for definite conclusions to be drawn from them. I have continuous records of many cases for so long as three weeks, but as I had records of only five consecutive observations in all cases prior to injection with tuberculin, I give the results for that period only.

The blood examined was taken at the same hour daily, and therefore as nearly as possible under the same conditions as to exercise and the digestive processes. Any change which these conditions may cause in the opsonic power of the blood, and which might lead to error in the results obtained, was thereby reduced. The blood, in all cases, was taken from the lobe of the ear, which was purified before being punctured. The first drop of blood was removed, and a sufficient quantity for the number of observations being made was drawn into a straight glass pipette with capillary ends. The pipette was not quite filled, and, to prevent heating the serum, the vacant end of the pipette was sealed in a flame. After centrifuging, the serum separated from the corpuscles. The unsealed end of the pipette was then broken off and the serum exposed. My own serum, which was the control observed in every case, was drawn from my finger. My leucocytes were also used during the observations. Blood was dropped directly from my finger, which was deeply punctured and bled freely, into a solution of 1 per cent. citrate of soda in .85 *per cent.* chloride of sodium solution. Two parts of this solution were put into a small tube set in a piece of cork, and the blood run into it, the whole being thoroughly mixed during the process. With a less dilution the blood tended to clot. This mixture was then centrifuged. The supernatant fluid was pipetted off and the corpuscles again washed with a solution of .85 *per cent.* sodium chloride. After centrifuging, this solution was drawn off with a pipette, and the corpuscles left in the tube. These were gently stirred and the leucocytes fairly distributed.

A suspension of tubercle bacilli was made in a 1 in 1000 sodium chloride solution. With a stronger solution this

organism tends to clump, and the results are then less accurate than with a more uniform suspension. The amount of tubercle powder necessary was moistened with the solution and pounded in an agate mortar. More solution was added, and when the suspension was complete the whole was filtered into a small sterilised test-tube. The suspension was renewed at very frequent intervals, though the contrast staining employed prevented any error of enumeration which might have resulted from the presence of contaminating organisms in the solution. The suspensions were made as nearly as possible of the same strength throughout, but as the same control serum was used in all cases, and the index calculated by the result obtained in the control case, no error resulted from a slight variation in the strength of the suspensions used from day to day.

Having obtained the blood-serum, leucocytes, and organismal suspension, equal quantities of these three were measured in a capillary tube, and thoroughly mixed in the cell of a hanging drop-slide. The mixture was then drawn into a capillary tube, the end of which was sealed in a flame, and the whole incubated for fifteen minutes at a temperature of 37° C. The end of the capillary tube was then snipped off, and the contents blown upon a slide. As uniform a film as possible was made, so that the leucocytes and the organisms not ingested were fairly distributed and not clumped at the edges of the film. Enumeration is prolonged by so doing, but the result obtained is more accurate, as it can at once be seen whether the organism is actually inside, or only lying on the top of the leucocyte. The slides were dried in the air and stained with Ziehl-Neelsen carbol-fuchsin stain by the usual method, decolourised with a 20 per cent. sulphuric acid solution, and counter-stained with a saturated watery solution of methylene blue.

The microscope used for enumeration was fitted with an oil-immersion lens and a movable stage. The cedar oil was applied directly to the film, no cover-glass being used. The centre of the slide was always the part examined, so that clumping of the leucocytes or organisms might not affect the results obtained.

To estimate the opsonic index the number of organisms ingested by a definite number of leucocytes was first calculated in the control film. The number so obtained was taken as representing unity for the series of observations made that day.

By the comparison of the number of tubercle bacilli ingested by the same number of leucocytes in the film of any case under observation, with the number found in the control film, the index of that case for that particular day was obtained. For example, if in the control film 80 leucocytes ingested 160 tubercle bacilli, while in the film of a case under examination 80 leucocytes only ingested 140 organisms, the tuberculo-opsonic index of that case for that observation would be $\cdot 87$. Only polymorphonuclear leucocytes were examined. The number of organisms ingested was enumerated in never less than fifty of these cells, and in the majority of the observations made eighty cells were examined. The same number of leucocytes was examined in each film on any one day. The same organismal suspension and my own leucocytes were used for each series of observations, the only variable factor being the blood-serum in each film, so that the relative opsonic power of each serum was ascertained. The opsonic power of the control serum was very constant, the number of organisms ingested showing little variation from day to day when the same organismal suspension was used. As the same methods of procedure were employed throughout these observations, the amount of spontaneous phagocytosis which might occur could not affect the results arrived at.

Opsonic Indices to the Tubercle Bacillus in the Control Cases prior to Injection with Tuberculin.

In six control cases the tuberculo-opsonic index was estimated for five consecutive days before injection. The average index obtained by these observations was 1.07, the average for each case being .98, .97, 1.32, 1.06, 1.01, 1.11, the variation therefore being between .97 and 1.32.

Urwick found the average tuberculo-opsonic index in twenty healthy persons to be 1.006, while Bulloch found the average index of eighty-four healthy persons to be .96, the variation ranging from .8 to 1.2. Lawson and Stewart obtained an average tuberculo-opsonic index of one in twenty-five healthy persons, with a variation between .9 and 1.2. In none of these records, however, is any indication given as to how often each case was examined before the average index was calculated. As I have found a considerable daily variation in the

opsonic indices of healthy persons, in my opinion a single observation cannot be relied upon to give a correct indication of the opsonic power of an individual. There is no indication given in these records either of the time when the observations were made. As it has been shown that in tubercular patients at least there is an increase in opsonic power after exercise, the observations ought to be made at the same hour daily, and as nearly as possible under the same conditions. Urwick states that there is little variation in the opsonic index of the same persons from day to day. I found a considerable variation in the indices registered in the control cases from day to day. One of them fell as low as '65 on one occasion. In cases of acute tubercular disease fluctuations in the opsonic index occur, some of the patients having indices which pass from subnormal to above normal on occasions, while others have a persistently high index. In none of the control cases examined was there any evidence of active or latent tubercular disease, but the control who showed on one occasion the low index of '65 had a tubercular family history. I found, however, that the average opsonic index of my control cases differed very little from week to week, and I have therefore based my results upon these averages. Considered in this manner the results of my observations on the control cases are very similar to those obtained by Lawson and Stewart in healthy country subjects.

The Tuberculo-opsonic Indices obtained in the Insane Cases prior to Injection with Tuberculin.

The thirty insane patients examined for five consecutive days gave an average index of '88. The variation was between '65 and 1'23. This result is below the indices obtained by Lawson and Stewart, as well as those recorded in the six control cases examined by myself. The daily variation in the indices of the insane patients was also greater than in the control persons, and the fluctuations were more marked, the rise and fall being abrupt.

The average indices of the five patients with evidences of old tubercular disease were 1'03, '96, '65, '84, '93, giving an average index of '88, the same as that found for all the thirty cases.

The difference between the index found in the six control cases—1·07—and that found in the insane patients examined—·88—is very striking. As the insane are admitted by all to be liable to tubercular infection this observation is strong evidence in favour of the view expressed by Wright and previously stated, that the opsonic power of the blood-serum can be used as a test of the liability to infection by particular organisms. That being so, it may be concluded that the insane, as a class, have a lowered resistive power to the tubercle bacillus as compared with the healthy sane population.

To estimate whether the length of residence in asylums has any bearing upon the liability of patients to contract tubercular infection, in the first table the patients examined are classified according to their length of residence.

TABLE I.—*Table classifying the Insane Patients according to their Length of Residence in the Asylum.*

Length of residence.	Number of cases.	Average opsonic index.
A. Under 6 months	8	·83
B. Over 6 months and under 1 year	5	·80
C. Over 1 year and under 2 years	3	·89
D. Over 2 years and under 3 years	3	·92
E. Over 3 years and under 4 years	4	·96
F. Over 4 years and under 5 years	4	·89
G. Over 6 years	3	·95

This table shows that the average opsonic index of the patients in the classes A and B is lower than that found in any of the other classes whose length of residence in the asylum had been greater. That this is not due to the fact that the number of patients included in these two classes is larger than that in any of the other classes is proved by the fact that the average tuberculo-opsonic indices of all the patients of less than one year's residence is ·82, while the average index for all the seventeen patients of longer residence is ·92. Length of residence in an asylum is therefore not a factor which of itself tends to lower the resistive power of the insane to tubercular infection but rather the reverse, as those patients who had resided for over one year in the asylum had an average

opsonic index of '92 as compared with the index of '82 in those of under one year's residence.

As the chronic insane are believed to be more prone to tubercular infection than the acute cases, the second table is drawn up so as to classify the patients according to their mental state.

TABLE II.—*Table classifying the Insane Patients according to their Mental State.*

	Number of cases.	Average opsonic index.
A. Cases with acute mental symptoms . . .	7	'87
B. Cases with subacute mental symptoms . . .	8	'86
C. Chronic cases (secondary dementia).	11	'93
D. Cases of general paralysis	4	'79

This table seems to me to point to the fact that the acutely insane have a much lower resistive power to tubercle than the chronic demented cases, and it is quite possible that these become infected with tubercular disease during the period of onset of the mental disease.

The acute cases were all recent admissions except one—a case of mania who had been resident for more than three years, but whose opsonic index was '95. With three exceptions these patients were adults. In all the demented cases the illness had commenced during adolescence.

All the general paralytic cases had been resident in the asylum for less than one year. Two of them showed evidences of having at some time suffered from tubercular disease, but I could detect no symptoms of active disease at the time these observations were made. The average opsonic index of the remaining two cases was very low, being only '78. General paralytics are as a class very liable to tubercular infection, and the low tuberculo-opsonic indices recorded in these four cases indicate that their liability to tubercular infection is due to their low resistive power.

Certain forms of mental disease are supposed to predispose

the patient to tubercular infection, and the type of mental disease which is believed to be most frequently associated with tubercular infection is adolescent insanity. The three most common forms of insanity met with in adolescent subjects are acute mania, katatonia and hebephrenia.

Table III classifies the acute cases according to their form of mental disease.

TABLE III.—*Table classifying the Insane Patients with Acute Mental Symptoms according to their Form of Mental Disease.*

Form of mental disease.	Number of cases.	Average tuberculo-opsonic index.
A. Adolescent insanity	3 cases (katatonia 1, hebephrenia 2)	·84
B. Melancholia . . .	2 cases (adults)	·88
C. Mania	" "	·91

The table shows that the tuberculo-opsonic index of the acutely insane adolescent patients is lower than that of the acutely insane adults. It is interesting to compare this index in the acutely insane adolescent cases with that obtained in the eleven chronic cases, in all of whom the mental disease had originated during adolescence. These eleven cases, in spite of their state of dementia, and in spite of their long residence in the asylum, had a tuberculo-opsonic index averaging '93. Such a finding does not suggest that a lengthened asylum residence predisposes to tubercular infection, but it points to the fact that the resistive power to tubercle is lowered by the onset of mental disease. It is also an interesting fact that the tuberculo-opsonic index in the melancholic cases is only '88 as against '91 in the two cases of acute mania, as it is an undeniable fact that adults suffering from maniacal excitement are much less prone to contract tubercular infection than adults suffering from melancholia.

Observations on the Control Cases after Injection with Tuberculin.

To estimate still further if there was any difference between the sane and insane persons in their reaction to tubercle, I

injected the six control cases, all members of the asylum staff, with Koch's new tuberculin, which will be subsequently referred to in this paper as T.R. So far the only record of such injections in healthy persons is that recorded by Lawson and Stewart, who injected four control cases; the dose of T.R. which they employed is not stated.

It is now generally believed that if a person be infected by any of the pathogenic organisms, an injection of a vaccine of the infecting organism is followed by an immediate fall in the opsonic power of the blood-serum of the person so injected. The amount and duration of this fall, commonly spoken of as the negative phase, depends, according to Wright, on the amount of the dose of vaccine administered, and if the dose injected be large enough a temperature reaction and constitutional symptoms may be produced. The negative phase is followed by a positive phase, as it is called, when the opsonic power of the blood-serum is increased. This positive phase may last a variable time, but ultimately the opsonic power falls back to the level at which it stood prior to injection.

In estimating the effect of the use of any drug or vaccine, it is always necessary to take into consideration the idiosyncrasy of the individual to the particular drug or vaccine used. With a vaccine injection the idiosyncrasy of the person injected may be taken to represent the liability to infection by that particular organism from which the vaccine is made.

So far no exact definition of the term "negative phase" has been made. After months of careful work and by noting the differences found in the opsonic power of the blood-serum of healthy persons to various organisms upon several successive days, I do not consider that a reliable idea of the amount of fall in the phagocytic power produced by the injection of a vaccine can be obtained by a single observation of the opsonic power made before injection, even though daily observations are made thereafter. In many instances I found, especially in the insane cases, that a slight rise of the opsonic power occurred within eighteen hours after the injection of the vaccine, which was followed by a very pronounced fall. I therefore define a negative phase as: "Any fall in the opsonic index to a particular organism occurring at any time within forty-eight hours after the injection of the vaccine made from that organism, the index being below the level noted at the time

of injection, and also below the level of the average opsonic index for at least five days preceding the injection." Any fall, however slight, occurring within forty-eight hours and falling below the two levels stated is described as a negative phase in the following observations :

The Opsonic Indices of the Control Cases after Injection with T.R.

Four of the control cases were injected with $\frac{1}{800}$ mgr. T.R. Two of them gave a distinct negative phase. The fall in the opsonic power was immediate, and lasted in the one case two, and in the other three days, reaching $\cdot 59$ and $\cdot 63$ respectively. The subsequent rise was rapid, reaching $1\cdot 57$ in the one and $1\cdot 74$ in the other, on the sixth day after injection. The average index of one of these cases prior to injection was $\cdot 98$ and of the other $1\cdot 32$. In the remaining two control cases injected with $\frac{1}{800}$ mgr. T. R. no negative phase followed injection.

In the healthy persons injected by Lawson and Stewart no negative phase occurred. As the results I obtained did not agree with the observations recorded by Lawson and Stewart I concluded that the dose of T. R. which I had used was too large. The remaining two control persons were, therefore, injected with $\frac{1}{750}$ mgr. T.R., and with this dose no negative phase occurred. The rise in the tuberculo-opsonic power occurring after injection in these two controls was immediate, the maximum being reached the day following injection. The average index of these two control cases prior to injection was high, being $1\cdot 01$ and $1\cdot 11$, and they rose to $1\cdot 25$ and $1\cdot 38$ respectively.

As all the control persons were in good health and free from tubercular infection it is probable that the large dose of T.R. used in the first four cases accounts for the occurrence of the two negative phases recorded. It is necessary, however, to state that one of the two control cases who presented a negative phase after injection had a tubercular family history. No rise of temperature or constitutional symptoms occurred as the result of injection in any of the cases.

The Opsonic Indices of the Insane Patients after Injection with T.R.

Twelve of the insane patients received an injection of $\frac{1}{100}$ mgr. T.R. Eleven of them, or 91 *per cent.*, gave a negative phase after injection. Four of the patients who gave a negative phase had, in the first instance, a slight rise in the tuberculo-opsonic index. This initial rise was followed by a decided fall which was complete in all the cases on the third day after injection. In the insane patients who gave a negative reaction it was noticed that the fall in the tuberculo-opsonic index was gradual and prolonged when compared with the same fall in the two control cases who gave a negative reaction, and in whom the fall in the curve of the tuberculo-opsonic index was abrupt. The onset of the positive phase in the insane patients was gradual and prolonged, the majority taking longer to attain their maximum than the two control cases who showed a similar reaction. The insane patients also at the height of their positive phases failed to reach such a high level of tuberculo-opsonic power as the two control cases who showed a negative reaction. In other words the positive reaction to the injection was much slower and less pronounced in the insane patients than in the control cases.

In two of the insane patients who presented signs of old tubercular disease, the negative reaction after injection was much less marked than in some of the other insane patients who presented no signs of old tuberculosis.

On comparing the results of the injection of tuberculin upon the opsonic indices of the acutely insane and chronic cases, I find that in the acute cases the negative phase produced was more marked than in the chronic cases and that the succeeding positive phase was more prolonged. The three most chronic cases who were injected with $\frac{1}{100}$ mgr. T.R. showed a much less marked and prolonged reaction than the acutely insane.

These observations would seem to indicate that the resistive power of the patients suffering from acute mental disease was less than that of the more chronic cases who had to some extent recovered their power of resisting tubercular infection, but in whom the mental disease had left irreparable brain damage. The views recently advanced, that many of the acute forms of insanity owe their cause to bacterial toxins may

explain this difference in reactive power, if it can be proved that a severe organismal infection by one organism lowers the resistive power of the human body to other organisms. If this should be so then the acutely insane have their resistive power so reduced as to render them liable to any form of infection, while the chronic cases, who have recovered from the acute toxæmia, although left with damaged brain cells, have, to some extent, regained their general resistive power; at all events this seems to apply to tubercular infection.

It may also be further deduced from these observations that prolonged residence in an asylum does not predispose the patient to tubercular infection, as the acutely insane, all of whom, with one exception, had been resident for periods under one year, showed a deficient reactive power when compared with the chronic cases, many of whom had been many years resident. This conclusion is also supported by comparing the opsonic indices of the insane patients as shown in Table I where, as has already been pointed out, the more recently admitted cases, who were also the acutely insane, had a lower tuberculo-opsonic index than the patients who had been longer resident, and were, therefore, chronic cases of mental disease.

That so large a proportion as 91 *per cent.* of the insane cases should show a negative phase after injection with $\frac{1}{800}$ mgr. T.R. as against 50 *per cent.* in the control cases seems to indicate that the resistive power of the insane to tubercular infection is less than that of sane persons. That such a large proportion of both the sane and insane should give a negative phase after injection is probably due to the fact that $\frac{1}{800}$ mgr. T.R. is too large a dose. In none of the twelve patients injected with this dose, however, were any constitutional symptoms produced.

Eighteen insane patients were injected with $\frac{1}{700}$ mgr. T.R. Of these only four showed a negative phase—that is to say, 22·2 *per cent.*, as compared with 91 *per cent.* of those injected with $\frac{1}{800}$ mgr. T.R. Only one of these four patients showed evidences of old tubercular disease, and this was a case of general paralysis. The average tuberculo-opsonic indices of these four cases for the five days prior to injection did not lead one to expect that a negative phase would follow injection. One of them had an index of 1·07, and the average for the four cases was '99.

In the remaining fourteen cases of this series in whom no

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negative phase supervened, the maximum rise of the positive phase was reached much more slowly than in the two control cases injected with the same dose. In only two of these cases was there an immediate rise in the tuberculo-opsonic index on the day following injection, while in the majority of the cases four days were required to reach that point.

All the patients injected with $\frac{1}{100}$ mgr. T.R., with the exception of four who suffered from general paralysis, were subacute or chronic cases, and, with only two exceptions, they had been resident for more than two years in the asylum.

The difference between the reaction in the two control cases and the four insane patients injected with $\frac{1}{100}$ mgr. T.R. who showed no negative phase was the slow reaction of the insane after injection. Both the control cases reached their maximum on the day following the injection, while the insane patients took an average of four days to reach the same positive maximum. There was, however, no difference in the maximum positive level ultimately reached in both the control and insane patients.

The result obtained in these two control cases corresponds with that recorded by Lawson and Stewart in the four healthy persons they examined.

Wright has stated "that the result of his observations seem to suggest that the development of a negative phase following a dose of T.R., smaller than that which would produce this result in a healthy person, may prove to be an index of tubercular infection. Such a conclusion would be in harmony with our experience in connection with the therapeutic inoculation of T.R. vaccine (new tuberculin). We find in this connection that the negative phase supervenes upon a very much smaller dose, and persists much longer in the case where the patient is the subject of extensive infection than in the contrary case." As the result of the observation made by Lawson and Stewart upon the four healthy persons whom they injected with tuberculin, they state: "The appearance of a negative phase after inoculation with a small quantity of tuberculin (T.R.) should enable one to distinguish between the blood of a subject of tubercular invasion and that of a person in sound health." Of the six control cases whom I injected with tuberculin, two, as previously stated, gave a negative reaction. Both these control cases, as well as the eleven of the non-tubercular insane patients

who also gave a negative reaction, were injected with $\frac{1}{300}$ mgr. T.R. I therefore conclude that this dose is too large for diagnostic purposes. The results obtained with an injection of $\frac{1}{750}$ mgr. T.R. were very different. Neither of the control cases so injected showed a fall in the tuberculo-opsonic power, while of the eighteen insane patients similarly injected only four, or 22·2 per cent. presented a negative phase. Of these four, one presented signs of former tubercular disease. The other three presented no signs or symptoms of tubercular infection, but the evidences of early tubercular disease are admittedly difficult to detect in the insane.

The tuberculo-opsonic indices prior to injection in these four patients, who showed a negative phase, were much more irregular than the tuberculo-opsonic indices in the fourteen cases who gave no negative reaction. The same fact was noted in the tuberculo-opsonic indices of the control cases and insane patients injected with $\frac{1}{300}$ mgr. T.R. In those who gave no negative phase the tuberculo-opsonic indices prior to injection were very regular, showing little variation from day to day, while the tuberculo-opsonic indices of those who gave a negative phase showed considerable daily variation.

Wright has shown that a fresh injection of tuberculin given during the negative phase, induced by a previous injection, produces a cumulative effect, that is to say, it still further emphasises the negative phase. It is, therefore, possible that in those who are already infected with tubercle an injection given when the tuberculo-opsonic index was much below or much above the healthy average might produce very different results. In the control persons and the insane patients upon whom I made these observations, however, I could detect no connection between the level of the tuberculo-opsonic index on the day of injection and the subsequent presence or absence of a negative phase. It is, therefore, probable that the amount of tuberculin administered has a more important bearing on the production of a negative phase after injection in non-tubercular persons than the level of the tuberculo-opsonic index at the time of injection, and, as I have already pointed out, the amount of variation in the tuberculo-opsonic index prior to injection has also to be considered in estimating the occurrence or absence of a negative phase after inoculation.

Summary and Conclusions.

(1) That the average tuberculo-opsonic index in persons free from tubercular disease varied between '97 and 1'32.

(2) That the tuberculo-opsonic index of persons free from tubercular disease varied considerably from day to day, but that the weekly average of the tuberculo-opsonic index in the same persons varied very little from week to week.

(3) That the average tuberculo-opsonic index of thirty insane persons, all free from symptoms of active tubercular disease, was '88, the variation being between '65 and 1'23.

(4) That the daily variation in the tuberculo-opsonic indices of insane persons is much greater than in healthy persons.

(5) The results of these observations lead me to conclude that the insane, as a class, are more liable to tubercular infection than the healthy sane population.

(6) That the tuberculo-opsonic indices of the insane, classified according to their length of residence in the asylum, is '92 in those patients who had been in residence for more than one year, as against '82 in those who had been in residence under a year. From this I conclude that asylum residence does not predispose the insane to tubercular infection.

(7) That the tuberculo-opsonic indices of the insane, classified according to their mental state, *vis.*, acute, sub-acute, and chronic, indicate most clearly that the acutely insane with an average index of '87 are more liable to tubercular infection than the chronic cases who had an average index of '93.

(8) That the low tuberculo-opsonic index of cases of general paralysis, namely, '79, explains the frequent occurrence of tubercular disease in this class of patient.

(9) That the tuberculo-opsonic index of the acutely insane patients, classified according to the form of their mental disease, is lower in cases of adolescent insanity than in adult cases suffering from mania and melancholia. The tuberculo-opsonic index of the adolescent cases was '84 as against '89 in the adult cases.

(10) That the tuberculo-opsonic index of cases of melancholia in adults is '88, as against an index of '91 in adults suffering from mania.

(11) As the result of Observations 9 and 10, I conclude that the acutely insane adolescent is more prone to contract tuber-

cular disease than the acutely insane adult, and that adults suffering from melancholia are more liable to tubercular infection than adults suffering from mania.

(12) That an injection of $\frac{1}{800}$ mgr. T.R. in healthy, sane persons produced a negative reaction in two out of four cases. As I have no reason to suppose that these two controls who gave a negative reaction were tubercular, I believe $\frac{1}{800}$ mgr. T.R. is too large a dose to use for diagnostic purposes.

(13) That out of twelve insane persons injected with $\frac{1}{800}$ mgr. T.R., eleven showed a negative phase, from which I conclude that the insane, as a class, have a low resistive power to the tubercle bacillus.

(14) That the reaction after injection in the non-tubercular insane persons, who showed a negative phase, was more prolonged than in the healthy, sane persons who gave a similar reaction.

(15) That the negative phase induced by the injection of $\frac{1}{800}$ mgr. T.R. in the acutely insane cases was more marked than in the chronic cases, and that the succeeding positive phase was more delayed. From this observation I conclude that the acutely insane have a lower resistive power to tubercular infection than the chronic cases.

(16) That so large a proportion as 91 *per cent.* of the insane patients gave a negative reaction after injection with $\frac{1}{800}$ mgr. T.R. is probably due to the dose being too large for diagnostic purposes.

(17) That out of eighteen insane patients injected with $\frac{1}{800}$ mgr. T.R. only four, or 22.2 *per cent.*, gave a negative reaction.

(18) That the remaining fourteen cases in this series injected with $\frac{1}{800}$ mgr. T.R., although they showed no negative reaction, reacted much more slowly than the two control cases injected with the same dose.

(19) That although an injection of $\frac{1}{800}$ mgr. T.R. is probably a sufficiently small dose for diagnostic purposes in the healthy sane population, it is still too large a dose for diagnostic purposes in insane persons.

(20) That in estimating the occurrence or absence of a negative phase after injection with T.R. it is necessary to take into consideration the variations in the tuberculo-opsonic indices for at least five days prior to injection.

(21) That in both the sane and the insane persons who gave

a negative phase after injection it was noted that the tuberculo-opsonic indices, prior to injection, show greater daily variation than in those who gave no negative phase.

(22) That I could discover no connection between the level of the tuberculo-opsonic index on the day of injection and the subsequent presence or absence of a negative phase.

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The Care of Children in County and Borough Asylums.

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THE normal English child has thriven apace of recent years, as the result of a healthy popular tendency to foster his mental and physical well-being as thoroughly as may be. But there exists among the poor a race of unfortunates—happily a small one—whose interests have rarely met with adequate recognition. It consists of the imbeciles who find their way into pauper lunatic asylums—the children legally certifiable as idiots. They cannot, I admit, pay a dividend in hard cash on the money sunk in their education, and their appeal for special attention mainly rests on their helplessness. My aim is to speak briefly of the measures already taken in their interest elsewhere, and to describe in a little more detail those adopted with success at Hellingly. Lastly, I propose to discuss the