THE RELATION BETWEEN EPILEPSY AND TUBERCULOSIS.

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WHILE investigating the excessive epileptic incidence which obtains in the district served by this asylum, as far as mental alienation is concerned, some facts of general interest were ascertained.

Dividing the district into rural and industrial areas, and estimating the percentage of epileptics on the total number insane of each sex belonging to the different areas and resident in the asylum and workhouses, we arrive at the following figures: Males—rural areas 14.3, industrial 21.8; while for females the corresponding figures are 12.8 and 26.2. In the asylum alone the percentages are: For males—rural areas 13.5, industrial 15.4; females, 12.5 and 21.6 respectively. As the ratio for epileptics to the whole asylum population averages for England and Wales 12.8, it will be at once seen that it is to the industrial districts we owe our high epileptic ratio, and that urbanization tells to a very great extent on the females in this direction. This fact is emphasized by an analysis of 1,174 female admissions during the past ten years (1904–13), which showed a proportion of 8.54 per cent. of epileptics on the total admitted from the rural area and 15.08 from the industrial, the percentage of female epileptics on total female admissions for this period being 12.8. My colleague Dr. Bennett informs me that the male epileptic percentage is 11.4 for that period. As the corresponding figures for England and Wales given by the Lunacy Commissioners for the period 1907–11 are 6.6 and 9.2 for females and males respectively, the above analysis affords further proof that it is to the female sex that our excessive epileptic population is especially due, the male epileptic admission rate for the ten years 1904–13 being 2.2 per cent. above the average, while the female rate is 6.2 above—practically double the average.

From the following table it is apparent that in Wolverhampton at the ages when epilepsy becomes established there is a relatively greater male death-rate than obtains for females, as compared with the county totals:

Proportion of Deaths per 1,000 Living at Subjoined Ages in Staffordshire (Urban and Rural Aggregates) and Wolverhampton.

	0–	5–	10–
Staffordshire:			
Males	49.1	3.4	1.6
Females	40.0	3.5	2.0
Wolverhampton:			
Males	54.8	4.3	2.6
Females	46.3	3.1	1.6

This difference is really greater than appears, as the Wolverhampton figures are included in the averages for Staffordshire, but the fact that more females relatively to males survive in Wolverhampton at the ages when epilepsy develops is significant, also the fact that tuberculosis universally in early childhood is more fatal amongst boys than girls, the total figures for England and Wales being respectively 4,805 and 4,072 under the age of 5. These facts go far to explain our excessive female epileptic ratios, bearing in mind the relation between epilepsy and tuberculosis, to be referred to later.

Coincident with a high epileptic ratio, this asylum also has a high death-rate from tuberculosis—namely, 25.2. The thought occurs: Is it possible that epileptics may be potent agents in raising the tuberculosis mortality of communities they live amongst? The following statistics taken from the Commissioners' report help to support an affirmative answer. Taking the dozen asylums with the highest and lowest epileptic averages, we find that the first-mentioned group has an average epileptic percentage of 18.2, and a corresponding tuberculosis mortality of 17.8, while the dozen having the lowest epileptic percentages show an average epileptic rate of 7.9, and a correspondingly low mortality from tuberculosis—namely, 13.7.

Conversely, taking the dozen asylums showing the highest tuberculosis death-rate, we find this averages at 22.9, and the corresponding epileptic average is 14.0; again, those with the lowest tuberculosis mortality show an average of 10.1 and the corresponding epileptic ratio is 10.9.

When it is recollected that, as already stated, the epileptic average in asylums for England and Wales is 12.5 and the tuberculosis mortality 16.6, the significance of the above figures will be apparent. In this connexion it is also noteworthy that the institution for the feeble-minded at Darenth has an epileptic proportion of 18.7 and a death-rate from phthisis of 24 per cent.

An analysis of 100 deaths amongst epileptics here, taken seriatim, shows that tuberculosis was the cause in 33 cases. A similar analysis of 290 deaths amongst non-epileptic patients gives the figure 24.1. The tuberculosis mortality is therefore nearly 10 per cent. greater among epileptics, and it occurs to one's mind that this tendency to tuberculosis might be universal in this affection and not due to infection contracted here. To help in deciding this I have divided the deaths due to tuberculosis during the ten years under consideration into four periods of two and a half years each.

Table showing the Percentage of Deaths amongst those Admitted in each Period to the Total Admissions in that Period up to the Present Time.

	First Period.	Second Period.	Third Period.	Fourth Period.
Non-epileptics	30.2	21.1	20.3	15.7
Epileptics	28.5	25.0	13.2	36.3

It is apparent that there is a gradual increase in tuberculosis mortality depending on duration of residence amongst the non-epileptics which does not obtain with epileptics.

I have been in the habit for a considerable time of treating certain cases of tuberculosis here with tuberculin, and it occurred to me that it would help matters in this investigation to give diagnostic injections to all the patients in the epileptic ward, and at the same time to correlate the results with physical signs of pulmonary tuberculosis and alteration in weights during the past three months. I had already a series of controls amongst non-epileptics for purposes of contrast. Seventy cases from the epileptic ward were in all examined, ten of whom were non-epileptics. T. 0.001 c.cm. was the injection given; as regards physical signs I relied principally on the alteration in the apical percussion note and the variations in transmission of the tuning-fork note of definite intensity from the suprascapular to the infra-clavicular regions, auscultation being for the most part very unreliable in these cases owing to shallow breathing, which is very constant in all forms of insanity. A negative reaction I have considered as a rise of temperature of under 0.8° F., doubtful 0.8°, positive 1° and over. Of the 60 epileptics so investigated, the resultant reactions were negative in 3 cases, doubtful in 7, and positive in 50. The percentage of positive and suspiciously positive reactions to tuberculin amongst epileptics was therefore 95.0. The corresponding figure for the ten non-epileptic patients resident in the epileptic ward was 50.0, and, reviewing my previous diagnostic work here amongst non-epileptic patients, I find that 33.3 per cent. showed similar results.

A very noticeable peculiarity amongst epileptics is the marked depression of temperature after even a comparatively small initial rise and the quick response to the tuberculin in the first place. In 7 cases the temperature dropped to 96° and below (one reaching to 95.4°), in 4 cases to 96.2°, and in 6 to 96.4°, in 15 cases it dropped to between 96.8° and 97.2°, so that in 31 cases, or over 50 per cent., this sudden depression was marked. In all these cases the epileptic seizures were very severe and frequent, and in the 7 cases in which the temperature fell to 96° and below exceptionally so. The thought suggests itself that this peculiarity bears some relation to nervous instability. I have been very much struck by it in epileptics as compared with others.

The frequency of subnormal temperatures amongst epileptics is very marked. Out of the 60 cases under

consideration this condition was present in 35; physical signs were present in 22, doubtfully so in 6, and apparently absent in 7 cases. Of all those showing a positive reaction to tuberculin, physical signs were present in 61.6 per cent., and the number of cases in which the right apex was involved as compared with the left is remarkable; out of the total number showing signs of tuberculous deposit (namely, 38), in 33 the right apex was involved. This is a fact of very great interest when it is recollected that it is mainly on the right side that the tracheo-bronchial glands are implicated in children.

Of those showing a positive reaction, 40 per cent. lost weight during the past three months, while of those giving a reaction of 2° F. and over 63.6 per cent. lost weight, and 81.8 per cent. of these latter showed physical signs of pulmonary tuberculosis. It is therefore evident that, except in the later stages, loss of weight is by no means a valuable criterion of the presence of tuberculosis in epileptics.

Enumerated amongst the epileptics are five past middle age, who developed epilepsy after admission; four of these have undoubted signs of pulmonary tuberculosis, and the fifth had a reaction of over 1.5° and has suspicious signs at one apex.

Considering the results from the above investigation, also the facts ascertained from the Commissioners' report, together with the high mortality of epileptics from tuberculosis, it will at once be evident that there is a close relation between tuberculosis and epilepsy. It has heretofore been considered that epilepsy, by lowering vitality, predisposes to tuberculosis. No doubt in many instances this is so, but I suggest that the great majority of cases of idiopathic epilepsy met with in asylums—in which, as will be readily understood, the epileptic condition is very severe in degree and has begun at a very early age—are directly due to the toxæmia resulting from invasion of the child's system by the tubercle bacillus and its effect on a developing and naturally unstable nervous organization, or it may be to reflex irritation from diseased bronchial glands. Tuberculosis rarely affects children in the same way as adults; the lesion is mainly in the tracheo-bronchial glands. I have been from time to time struck, at *post-mortem* examinations on epileptics, by the size of these glands, especially those on the right side. Recently I made a *post-mortem* examination on an epileptic who had given a positive reaction to a diagnostic tuberculin injection, but who had had no physical signs pointing to pulmonary tuberculosis. She died later, showing all the signs of rapid tuberculosis, and the necropsy disclosed suppurating and caseous bronchial glands and invasion of adjacent bronchi, but the lung tissue itself showed no tuberculous deposit. In Vienna it has been shown that 90 per cent. of the school children under the age of 10 or 11 have been infected with tubercle. Hamburger, of Vienna, among 86 cases of localized tuberculosis, found the primary lesion in the bronchial glands in 85, Still in 81 per cent., and Carr in 80 per cent.¹

Chart showing marked reactive rise in temperature after a fit, previous to which and afterwards the temperature was subnormal. A, After fit at 9 a.m.; B, 11 a.m.; C, 1 p.m.; D, 3 p.m.; E, 5 p.m.; F, 7 p.m.

treatment. Bearing this in mind, I have had the temperatures of a number of epileptics taken, and am now constantly having this done, for diagnostic purposes, immediately after a fit and every two hours for ten or

twelve hours. I find that the results roughly correspond, but to a lesser degree, to the effects of the diagnostic tuberculin injection—in a few cases a surprising rise of temperature has occurred, and in some a fall, to be explained probably by the degree of toxæmia present. Tuberculosis is undoubtedly very rife amongst children in the poorest parts of thickly populated areas as compared with the rural districts, and it is apparent that the children in these industrial districts cannot get the same care and attention from mothers, who often have other than domestic occupations to attend to. The percentage of occupied to unoccupied married women is—for urban districts, England and Wales 12.9, and for rural 6.2. Now, when a child whose vitality is lowered through lack of care and proper nourishment, to say nothing of fresh air, and who may in addition suffer from unstable nervous heredity, contracts tuberculosis, it may very conceivably be either that a reflex effect is induced or that the toxins thrown into its system from the tuberculous focus have an action, centric or synaptic, on the child's partially developed and ill-regulated nervous organization, resulting in disturbance of the normal balance, and—especially in cases predisposed thereto by inherited nervous instability—the immediate result is an epileptic seizure, which, by bringing about autoinoculation, has the effect of rendering the toxic focus somewhat quiescent for a time. When the effects of this auto-tuberculinization wear off the fit recurs, and after a time the sensitive neurones acquire a habit, or synaptic changes take place from which recovery becomes unlikely. This constant autoinoculation either after a longer or shorter time brings about cure of the tuberculous lesion, the danger of recurrence of the epileptic seizures being in direct ratio to the length of such period, or it keeps the toxin-producing focus in check until debility from exhaustion of one kind or another deteriorates the defensive powers of the system, and rapid tuberculosis results. It will be familiar to every one having experience of epileptics what a low asthenic form the tuberculous process takes in them, and how advanced the lesions are *post-mortem*.

The percentage of epileptics in the urban and rural districts here under notice is respectively 24.0 and 13.5, and the Registrar-General's report shows in urban districts a similar preponderance of infantile mortality from tuberculosis, convulsions, and atrophy, debility, and marasmus. Thus for county boroughs all forms of tuberculosis amount to 3.57 and for rural districts 2.27. The corresponding figures for convulsions are 11.50 and 9.42 respectively, and for atrophy, debility, and marasmus 17.41 and 14.84. Just as at a very early age the toxæmia resulting from rickets will cause convulsions, laryngismus stridulus, and carpopedal spasms, so somewhat later epilepsy may become established, as I have endeavoured to describe, by the toxæmia of tuberculosis. If this is so, it is important that all cases of early epilepsy should be tested with tuberculin and the state of their bronchial glands thoroughly investigated by means of the Roentgen rays. At that early age, if taken in time, a course of tuberculin treatment might cure the epilepsy. I have given such a course to one epileptic without apparently any ameliorating effect on the seizures, but this result could scarcely be expected once the nervous system had firmly acquired the epileptic habit.

SUMMARY.

1. That it is to the industrial districts we owe our high epileptic ratio in the County Mental Hospital, Stafford, and that urbanization appears to principally affect the females in this direction in our neighbourhood.
2. That the high death-rate amongst male children in Wolverhampton relatively to female is probably associated with the great excess of female epileptics there.
3. That a high epileptic ratio is constantly associated with a high tuberculosis incidence and vice versa.
4. That the death-rate from tuberculosis amongst the non-epileptic is directly proportional to length of residence, which does not obtain amongst the epileptics.
5. That the number of positive and suspiciously positive reactions to tuberculin amongst epileptics here is 95 per cent.
6. That only 50 per cent. of non-epileptic patients associated intimately with the epileptics show a similar reaction.

7. That associated with a high ratio of epileptics in urban relatively to rural districts is a similarly high infantile and early childhood mortality from tuberculosis, convulsions, and atrophy debility and marasmus, and also a correspondingly high proportion of occupied married women, which it would be well for employers of female labour to bear in mind.

8. That, except in terminal cases of active tuberculosis, loss of weight is not a valuable criterion of the presence of tuberculosis in epileptics.

9. It is contended that epilepsy may be an evidence of tuberculous infection in childhood, probably affecting the bronchial glands initially, and that the convulsions are due either to reflex irritation so set up or to the resulting toxæmia acting on an unstable nervous system, either inherited or acquired. Further, that the constantly recurring seizures not only establish a vicious habit as far as the nervous system is concerned, but also effect tuberculin autoinoculation, thus tending to keep the tuberculous process in check, so that, instead of a fatal termination, epilepsy results.

10. Consequently, the advisability of carefully searching for tuberculous foci in children the moment epileptic fits develop, and also the immediate use of tuberculin in their treatment, should receive consideration.

REFERENCE.

¹ Riviere, *Early Diagnosis of Tubercle*.

STRYCHNINE-TUBERCULIN TREATMENT OF HOSPITAL TUBERCULOUS CASES.

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RECENTLY I called attention to the good results obtainable in the different forms of tuberculosis by the combination of tuberculin and strychnine, the former given weekly, the latter practically daily by intramuscular injection in large single doses.¹ Since then I have given larger doses of strychnine with improved results. I give the strychnine injections to all kinds of tuberculous patients, including cases in which tuberculin injections are contraindicated, with the best results. I give strychnine in acute and chronic cases, in the pyrexial and the apyrexial, in the early stages and in the most advanced, and with invariably good results. It always improves the appetite and general condition. Patients who have a loathing for food soon regain their appetites under its influence. Strychnine will frequently do away with the painful necessity of adopting Debove's gastric lavage and over-alimentation. But the drug must be given by intramuscular or subcutaneous injection, preferably the former. Administered by the mouth it has not the same effects and in large doses will cause tormina and diarrhoea, with possibly disastrous results in advanced cases. These effects are never produced by the injections.

Haemorrhage from the lungs I have found to be no contraindication for the strychnine injections. I have given them in such cases with remarkably good effects when the circulation had been quieted by morphine.

Has strychnine any special action in cases of tuberculosis other than that of a tonic? A bacteriological friend of mine says it probably makes the patient more resistant to the attacks of the bacilli. Personally I incline to the belief that it stimulates the formation of antibodies, especially when combined periodically with tuberculin, and of course it acts as a general tonic and nerve stimulant.

It may be thought that giving these daily intramuscular strychnine injections would be found very trying both to the patient and to the practitioner, but such is not the case. No patient of mine ever objected to them. In fact, the bad cases seemed to look forward to them, as they felt better after "in themselves." There is no strain on the practitioner, and he can give over thirty in an hour if necessary. The site of the puncture—deltoid or gluteal—is dabbed with a swab wet with tincture of iodine by the nurse. The doctor pours 20 to 30 minims of 1 in 400 strychnine hydrochloride solution into the barrel of an all-glass syringe with a fine needle in position; the piston is then adjusted, the instrument turned with the needle

upwards, and the air expelled from the barrel along with the surplus solution, and the dose given. The needle is then quickly washed in hot carbolic solution, wiped thoroughly with a sterile swab wet with spirit, and is ready to give the next patient his dose. The following is the solution I invariably use:

R. Liq. strych. hydrochlorid. (B.P.) 100 minims.

Sterile normal saline solution made with camphor water, add to make 400 minims.

Signa: 1 in 400 strychnine solution. Dose, 18 to 25 minims.

In febrile, haemorrhagic, and third-stage cases tuberculin injections are generally considered inadmissible. With this my experience coincides. But tuberculin may yet be used in these cases with good results in the form of Sahli's inoculation method. This is simply a multiple von Pirquet's test done weekly. Personally I make the inoculation over the affected parts. When reaction occurs there is, I take it, a local anaphylaxis with the formation of antibodies which find their way into the circulation, whereas the tuberculin does not. Patients who are having tuberculin injections react powerfully to the inoculations. In a few cases of severe pleuritic pain in chronic phthisical patients, the inoculations quickly relieved the trouble.

In suitable cases, as I have already said, I inject tuberculin once a week or less often. I generally use T.R., human and bovine mixed, but sometimes B.E. or T.O.A. I am a follower of Wright. Rapidly saturating a patient with tuberculin seems to me to be entirely wrong. We are not dealing with an autotoxin in tuberculin, but with a toxin whose only power for good resides in causing mild reaction and the stimulation of the production of antibodies—a process which takes at least a week in developing. To give it oftener than that does no good, in my experience. This is strikingly shown to be the case in the paper by Dr. E. H. T. Rigg, reporting the results of tuberculin treatment at the Brompton Hospital, printed in the JOURNAL. He says:

The dose was increased every second day at first and afterwards at intervals of four days.

The results as compared with patients not treated with tuberculin were strikingly bad.

Throughout my patients were fairly well fed. Cod-liver oil and creosote were given to all who could take those medicines. Antiseptic inhalations were freely used. I do not say as good results, if not better, are not obtainable by other forms of hospital treatment, but I have not seen such.

The function of the hospital in cases of tuberculosis on the medical side is to treat the febrile stages of the disease and arrest its progress in the shortest possible time. Another function is the segregation and modified isolation of patients whose sputa swarm with tubercle bacilli, and are therefore a real public danger outside.

I give in brief the last twelve cases I treated in hospital.

1. Lascar, aged 25, admitted with small cavity in left apex. Haemoptysis twice. Sick several months on board ship. Night sweats, cough, and anorexia. Had two tuberculin and eight strychnine injections, and left "cured" in three weeks.

2. Finnish seaman, aged 26, admitted with both lungs riddled with cavities and both petrous bones diseased. Cyanosed and apparently moribund. Hyperpyrexia. Case hopeless, but condition ameliorated by injections. Intolerable earache and cough disappeared, and he became contented and cheerful. Sent to workhouse infirmary after a month's treatment.

3. English apprentice, aged 19. Suppurating glands in neck. Reacted violently to second injection of Banderier and Roepke's tuberculin test. Well in three weeks, but relapsed six months later, when a month's treatment effected another cure.

4. Lascar, aged 26. "Skin and bones only." Crepitus over both apices. Chronic diarrhoea, anorexia, fever. Sputum very scant. Von Pirquet reaction positive. Sick two months. In six weeks had three tuberculin and sixteen strychnine injections. Left feeling quite well, only physical sign remaining feeble respiratory sounds over left apex. Gained 6 lb. last week of stay.

5. Irish stoker, aged 37. On admission, right side wet pleurisy, blood spitting, and night sweats. Von Pirquet's reaction strongly positive; 22 oz. of serum drawn off, and ten days later 40 oz. of sero-pus. Pyrexia quickly subsided. In six weeks had two tuberculin and twenty-eight strychnine injections. Gained 6½ lb., and left feeling quite well.

6. French stoker, aged 30. Admitted for "bronchopneumonia." Ill seventeen days. Profuse sputum; tubercle bacilli 10 to 50. Fever, but in a week temperature fell to normal.

In a month's treatment had two tuberculin and twenty-