

ball. A fungus was demonstrated among the debris of the iris and exudate, and a few days afterward sporothrix was obtained in culture. The patient bore potassium iodid poorly, and finally the eye was enucleated because of the pain.

CASE 16.—The last case described is by Morax¹⁹ in a man aged 37, who had nodular lesions on the skin of the thighs and a nodule on the outer surface of the lower lid, below the internal palpebral ligament. This nodule was violet-red, firm and easily movable without pain. It was about 0.7 cm. in diameter and projected 2 mm. above the surface, with the center slightly depressed like a lacrimal fistula. The conjunctiva appeared normal and there was no cutaneous reaction or congestion of the surrounding tissues. Exploration by means of a probe showed that there was no connection of the lesion with the eye. Cultures from this nodule gave sporothrix. Cure followed treatment with potassium iodid.

In experiments by Fava²⁰ and others, following the injection of a culture of sporothrix into various parts of the eye of a rabbit, lesions were produced resembling those of sporothrix infection of the human eye. The incubation period generally lasted from twelve to eighteen days. The organism was recovered from the eye lesion.

CLINICAL CONSIDERATION

From a study of the cases that have been recorded and of the one we have observed, we should say that infection of the conjunctiva by sporothrix causes a marked congestion of the membrane, particularly the palpebral portion, the fornix and the semilunar folds. The bulbar portion is not so frequently infected.

Numerous follicular prominences appear in the palpebral conjunctiva and in the fornix.

Small yellowish nodules, varying in size and shape, develop rapidly in the conjunctiva, and these may ulcerate. When opened, the contents of the nodules do not escape rapidly as from small abscesses, but seem to be of a gummy consistence. These little nodules developed so rapidly in the case we observed that on the second day new ones presented that had not been seen the day before.

Secretion is rather scanty and hardly sufficient to stick the lids together at night, but lacrimation is rather abundant. The eyelids are somewhat edematous and thickened, and palpation shows a well-marked induration of the subcutaneous tissue. Enlargement and tenderness of neighboring lymph-glands is also present.

Subjectively, there is a sensation of a foreign substance under the lids, and so much discomfort that use of the eyes is almost impossible. The discomfort comes on rapidly after the infection. The two cases of laboratory infection (that of Fava and the present one) and the absence of a history of trauma in the other cases, seem to show that the sporothrix is able to penetrate the normal conjunctiva. It also appears from the reports of cases that infection of the eye may be secondary to a generalized sporotrichosis. Probably in most of these cases the infection is ectogenous, but the suspicion that it may be endogenous is aroused by the case of LaPersonne, in which, after a violent iridocyclitis and perforation of the eyeball, sporothrix was obtained from the contents of the bulb.

That general symptoms may arise from a primary lesion of the eye is indicated in our case by the fever, leukocytosis and pains in the bones of the extremities.

DIAGNOSIS

Some of the clinical features of this infection are common to other conditions. Lymphadenopathy would be present with chancre of the conjunctiva, but in the initial lesion of syphilis it is very unusual to have such multiple erosions or ulcerations, and scrapings from such an ulcer would probably show the characteristic spirochete.

Tuberculosis of the conjunctiva would probably not be so rapid in its course, and it would be a week or more before the caseous tuberculous nodule would break down and form the ulcer, whereas in sporotrichosis the little ulcers develop in a few days.

Parinaud's conjunctivitis presents more points of similarity, and it is possible, as mentioned by Morax, that cases of sporotrichosis may have been mistaken for Parinaud's conjunctivitis.

In the latter, the vegetations on the conjunctiva are different from the follicles and the yellowish nodules of sporotrichosis. The adenopathy in Parinaud's conjunctivitis points to a severe infection, but all attempts to isolate an organism from the lesions have failed. Recently, however, Verhoeff has observed in such conditions an organism like leptothrix. On the other hand, the diagnosis of sporotrichosis is easy if scrapings from the nodules or ulcers are inoculated on appropriate mediums and left at from 18 to 20 C. for the organisms appear in from three to ten days. The presence of Gram-positive, spore-like bodies in a direct smear from the conjunctiva should suggest sporothrix.

We wish to acknowledge the kindness of Dr. L. Hektoen, director of the Memorial Institute for Infectious Diseases, for valuable suggestions offered in the study of this case.

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CLINICAL REPORT OF FIVE HUNDRED AND SEVENTY-ONE CASES OF PULMONARY TUBERCULOSIS TREATED WITH TUBERCULIN *

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Early in the spring of 1910, and following my presentation of a short paper on tuberculin at one of the meetings of the medical staff of the Otisville Sanatorium, of which I was a member, Dr. E. S. McSweeney, the physician then in charge, asked me to reorganize the tuberculin class among the patients.

After rather an extensive perusal of much of the literature on the subject, I was struck by the divergent views held by the different investigators on tuberculin therapy in general and the matter of dosage and reaction in particular. I then decided to lay aside all my preconceived notions on tuberculin and begin injections with a dose well below any possible reaction, such as 0.000,000,01 gm., and to double each previous dose at weekly intervals, using Koch's B. E. In the last year of this work, patients in the class were started on Koch's Old Tuberculin exclusively, and when they were standing well from 0.003 to 0.006 gm. at a dose, they were then changed to Koch's B. E., 0.000,1 gm., which was later progressively increased according to the table. The

19. Morax: Sporotrichose primitive des paupières simulant une fistule lacrymale, *Ann. d'ocul.*, 1913, cxlix, 183.

20. Fava: Sporotrichose expérimentale de l'appareil oculaire du lapin, *Ann. d'ocul.*, 1910, cxliv, 77.

* From the Department of Health Sanatorium for tuberculosis at Otisville, New York.

gain was twofold: there were less reactions to the smaller doses on account of the O. T. being weaker, and there were also fewer reactions to the larger doses of B. E. because of the previous immunizing effect of the O. T. Incidentally, the patients were thus immunized to both the endogenous and the exogenous toxins of the bacillus. After over two thousand injections were given of less than 0.000,001 gm. each, with not a single reaction in any one of them, I decided that this amount was needlessly small to begin with, after which injections were begun with 0.000,001 gm. B. E. As a matter of fact, the earliest reaction dose was clinically found to be about four times as large, namely, 0.000,004 gm. B. E.

One reason for trying to make the tuberculin treatment as brief and decisive as the patient's tolerance would permit was due to the short stay in the institution of the average patient (about five months), which practically excluded the method of administering very small doses of tuberculin over long periods of time. The idea was to have each dose come as near as possible to producing a clinical reaction without actually doing so, as whatever advantage there may be in beginning treatment with very small doses very slowly increased in those who have the time and means to carry it out, it is entirely unsuited to the vast number of curable tuberculous patients who have their living to make, and cannot spend more than about six months in a sanatorium, to say nothing of the fact that after all, tuberculin such as B. E. is no more than a vaccine, in the successful use of which one must apply the same rules as govern vaccine therapy in other diseases in which we know that the prolonged administration of minute doses will lead to no therapeutic results, though it may produce an immunity to itself.

The cases were unselected male patients,¹ varying in age from 16 to 50, the great majority of whom were moderately advanced, or the so-called Stage II (Turban). The other treatment of the patients in the class, such as rest, exercise, etc., differed in no respect from those who did not receive tuberculin. The dilutions of the tuberculin used were made with sterile normal saline, no preservative being added. The diluted tuberculin was put up in sterile rubber-stoppered vials of 5 c.c. capacity, and were kept in the ice-chest. What was left in the vial at the end of the day it was used, was discarded. The tuberculin was diluted fresh from the stock bottle every three weeks. The O. T. was that prepared in the research laboratories of the department. The B. E. was Mulford's and Alexander's, 0.005 gm. to the cubic centimeter. The number of patients in the class at any one time varied from seventy-five to 110, and the period covered by the subject-matter of this paper was from June, 1910, to January, 1913, or two and a half years in all.

The actual injections were made under strictly aseptic conditions, and were given hypodermically in the outer aspect of the upper arm, except for the large doses such as 0.001 gm. B. E. and over, which were always given in the back between the vertebral border of the scapula and the spine, the two sides being used alternately. No undesirable local by-effects were noted except occasional slight tenderness, though sterile "abscesses" may develop at the site of injection of large doses of B. E., resulting from the intense local *Stichreaktion*.

1. The clinical impressions and conclusions were really drawn from about two hundred more cases (all female), making a total of seven hundred and fifty cases in all, but unfortunately the collected records of the former have been mislaid.

In passing, mention should be made of the great difference existing in the minds of tuberculous patients between the tuberculin treatment of tuberculosis and the other accepted therapeutic measures as used in our sanatoriums. Custom has given the patient latitude in choosing or rejecting (particularly the latter) tuberculin injections often against the physician's advice in the matter, in contradistinction to stopping the chest, rest in bed, taking cough-mixtures, etc. In these hardly any patient dreams of questioning his physician's judgment and skill; but let tuberculin be suggested, and the patient immediately puts himself on the defensive. Not only were we hampered in recruiting new members in the class, but it was hard to keep many otherwise desirable patients after they joined. If the patient happened to be injected with tuberculin earlier in the day before being weighed, and found that he had lost some pounds during the week, the tuberculin was to blame, etc., on the strength of which he would not only refuse further treatment himself, but would try to get other members in the class to refuse also. The result was that while half of the patients in the class dropped out because they were leaving the institution, the other 50 per cent. refused further treatment with tuberculin for reasons no better than the foregoing. Practically none were found to be unsuitable for treatment once they were in the class, because no matter how hypersensitive to tuberculin a patient was found to be, the dose could always be attenuated to his tolerance.

The terms "reaction" and "allied conditions," as used in this work, were standardized for purposes of comparison as follows:

$$\text{Clinical Tuberculin Reaction} = \begin{cases} \text{Afebrile} & \frac{a}{b} \\ \text{Febrile} & \end{cases}$$

Persistent Accentuated Symptoms.

All tuberculous persons in the active, and many even in the quiescent stage of the disease, will react subjectively, and often clinically, to very small doses of tuberculin, such as 0.000,000,1 and 000,000,01 gm. B. E., or even less. The term "reaction" as used in that sense is practically always afebrile and is defined as: (a) a distinct change in subjective sensation, difficult to define, but quite a real condition to the one injected, which, while hardly pronounced enough to make the person feel sick, yet is far from agreeable; (b) a condition occurring in less than twenty-four hours after the injection of tuberculin characterized by the presence of some or all of the following: slight feeling of malaise, mild disinclination to food, and greater ease because more fluid expectoration. These conditions occurring and to be expected in practically all cases were, therefore, not looked on as a reaction in the clinical sense, and not of enough importance in themselves to affect the progressive increase in dosage.

The kind of reaction which did affect the progressive dose increase follows tuberculin injection usually within less than twenty-four hours, and is characterized by the presence of some or all of the following: distinct increase in cough and expectoration, also headache, anorexia, pain in back and joints, with lassitude, sufficiently pronounced to make it inadvisable either for the patient so affected or for the physician treating him to continue him at his exercise. This condition is usually, but may not be, accompanied by a rise in temperature from 99.5 to 103 and more.

The term "persistent accentuated symptoms" was used to define the condition of a tuberculous patient (who may or may not use tuberculin), when for an

indefinite period of time his cough, expectoration, temperature-curve and nutrition show a distinct tendency for the worse. This was considered of sufficient importance either to stop tuberculin injections altogether until the symptoms subsided, or else materially to diminish the weekly tuberculin dose. In other words, it was acted on the same as a tuberculin reaction.

TABLE 1.—LENGTH OF TIME INDIVIDUAL PATIENTS WERE UNDER TREATMENT WITH TUBERCULIN

No.	Patients Per Cent.	No. of Weeks per Patient	Total No. of Weeks
92	16.1	1	92
89	15.5	2	118
34	5.9	3	102
37	6.3	4	148
19	3.3	5	95
22	3.8	6	132
26	4.5	7	182
32	5.6	8	256
22	3.8	9	198
18	3.1	10	180
4	0.7	11	44
8	1.4	12	96
21	3.6	13	273
4	0.7	14	56
11	1.9	15	165
10	1.7	16	160
4	0.7	17	68
11	1.9	18	198
9	1.5	19	171
6	1.0	20	120
6	1.0	21	126
8	1.4	22	176
4	0.7	23	92
3	0.5	24	72
3	0.5	25	75
5	0.8	26	130
3	0.5	27	81
7	1.2	28	196
2	0.3	29	58
3	0.5	30	90
3	0.5	31	93
3	0.5	32	96
5	0.8	33	165
4	0.7	35	140
1	0.1	36	36
2	0.3	39	78
1	0.1	40	40
1	0.1	41	41
3	0.5	42	126
6	1.0	43	258
1	0.1	44	44
1	0.1	46	46
1	0.1	49	49
16	2.8	*	1,248
571	100—	11.3	6,470

* Eighteen months each or 78 weeks.

On the occurrence of a clinical reaction, tuberculin was discontinued until all symptoms of the same had subsided, when injections were recommenced with fourth lower dose removed. Only the two conditions "clinical reaction" and "persistent accentuated symptoms" were considered in influencing tuberculin dosage.

A clinical tuberculin reaction occurring in the course of treatment in no demonstrable way permanently influences for the worse either the disease or the subsequent course of tuberculin treatment, as the same patients later stand with impunity many times the dose at which they formerly reacted.

If a large dose is reached too quickly, a hypersensitiveness to tuberculin supervenes, necessitating going back to a very small dose indeed. The determination of dosage is purely arbitrary, as sensitiveness differs not only in different patients, but at different times in the same patient. On the other hand, should a reaction occur after a large dose with a slowly progressive dose increase, it merely shows the limit of that patient's maximum tolerance to tuberculin for the present, after which it is best to leave off injections for a time, according to results obtained.

While a patient who has once been thoroughly treated with tuberculin probably never reacts to his disease the way he did before treatment, yet the immunity so acquired to the tuberculin does not last much over two

months, if that long, although the good effect persists for a variable time after the acquired immunity to tuberculin has been lost.

Much has been said of the mental effect of tuberculin, as if that were something separate and distinct from its physical effects. If the psychic effect is for good, it is because the tuberculin is having a favorable influence on the lesion and the patient feels more nearly normal owing to diminished toxemia. If the patient feels depressed after tuberculin, it is due to doses which are either too large, or given at too frequent intervals, or both. In other words, the patient is near a clinical reaction, and his depression is nothing less than its earliest manifestation.

Tuberculin may be *tried* in all cases of pulmonary tuberculosis of whatever stage, provided the patient is given a small enough dose, with the effects carefully watched. At Dr. Turban's sanatorium, in Davos Platz, Switzerland, which I visited early in the spring of 1912, they use as small a dose as 0.000,000,000,1 gm. Bovine T. R., and they assert that if persisted in, it will often bring a patient's temperature down to normal, when other measures fail. Tuberculin, however, is to be *used* in all cases which run the chronic course, so common in this disease, particularly in the vast number of patients whose improvement seems to have stopped short of a clinical cure under sanatorium treatment alone, and also in those patients who, for one reason or another, cannot leave their families and affairs and go to a sanatorium in the country.

While not sufficient time has elapsed after the treatment of the patients on whom this report is based, to permit any conclusions from the effect of the treatment, on their own prognosis, there is good authority for the statement that the clinically cured, following the use of

TABLE 2.—NUMBER AND DOSES OF B. E. TUBERCULIN INJECTIONS WITH PERCENTAGE OF REACTIONS AND PERSISTENT ACCENTUATED SYMPTOMS

Dose Gm.	No of Injections	Reaction		Persistent Accentuated Symptoms	
		No.	Per Cent.	No.	Per Cent.
0.000,000,001 to 0.000,001	2,040	0	...	0	...
0.000,001	275	0	...	0	...
0.000,002	272	1	0.3	0	...
0.000,004	261	0	...	5	1.9
0.000,008	232	3	1.2	7	3.0
0.000,016	211	5	2.3	3	3.3
0.000,032	182	5	2.7	3	1.6
0.000,064	163	6	3.6	4	2.4
0.000,1	171	4	2.3	2	1.1
0.000,2	155	7	4.5	3	1.9
0.000,4	151	8	5.2	0	...
0.000,8	74	6	8.1	4	5.4
0.001	115	19	16.5	0	...
0.001,25	37	5	13.5	1	2.7
0.001,5	26	3	11.5	0	...
0.001,75	18	2	11.1	0	...
0.002	54	5	9.2	2	3.7
0.003	23	2	8.6	0	...
0.004	10	3	30.0	0	...
0.005	8	0	...	0	...
0.006	7	2	28.5	0	...
0.007	4	0	...	0	...
0.008	3	0	...	0	...
0.009	2	1	50.0	0	...
0.010	1	1	100.0	0	...
	4,515	88	1.9	38	0.8

tuberculin, are not so apt to relapse, or to develop tuberculous complications, as those who had sanatorium care alone.

RESULTS

In figuring the result of tuberculin therapy in pulmonary tuberculosis, the most important and at the same time the most difficult factor to standardize is the patient and his disease. For one thing, there is no known way of determining with any degree of exactness

the length of time a given tuberculous patient has had the disease, or in other words, his resistance. This fact makes it very difficult to determine accurately how much of the improvement during tuberculin administration was due to that, and how much to the native resistance of the patient to his disease, supplemented by the usual sanatorium treatment. Therefore, until more exact means of determining the extent of the patient's resistance to his infection is discovered, we have to rely solely on clinical observation. One thing which we do know beyond question is the specific effect for good of subcutaneous injections of tuberculin on localized visible forms of tuberculosis in the eye, skin, glands, etc. This has been noted repeatedly by numerous independent observers all over the world. While none but the over-enthusiastic claim as much for it in the treatment of pulmonary tuberculosis, still it is no more than to be expected that it would have some definite good effect in that disease, and I have found this to be as follows:

The first few injections will slightly increase expectoration, making it more fluid, and brought up with less coughing; later on, expectoration and with it cough is

TABLE 3.—NUMBER AND DOSES OF O. T. TUBERCULIN INJECTIONS WITH PERCENTAGE OF REACTIONS AND PERSISTENT ACCENTUATED SYMPTOMS

Dose Gm.	No. of Injections	Reaction		Persistent Accentuated Symptoms	
		No.	Per Cent.	No.	Per Cent.
0.000.001	262	0	...	0	...
0.000.002	181	0	...	0	...
0.000.004	157	3	1.9	1	0.6
0.000.008	153	2	1.3	2	1.3
0.000.016	165	1	0.6	2	1.2
0.000.032	130	0	...	1	0.7
0.000.064	103	2	1.9	3	2.9
0.000.1	146	1	0.6	0	...
0.000.2	126	3	2.3	2	1.5
0.000.4	83	3	3.6	1	1.2
0.000.8	66	4	6.0	1	...
0.001*	0
0.001.25*	0
0.001.5	42	2	4.7	1	2.3
0.001.75	11
0.002†	0
0.003	43	2	4.6	0	...
0.004‡	0
0.005§	0
0.006	15	2	13.3	0	...
Total	1,683	25	1.4	14	0.8

* Not given, as last dose 0.000.8 was almost doubled to 0.001.5.
† None given, as 0.001.5 was doubled at next dose to 0.003.
‡ None given, as 0.006 was given after 0.003.

distinctly diminished. The tendency to toxic manifestations of the disease such as rapid pulse, dyspnea and slight elevation of temperature on exertion, is inhibited to a great degree in those who receive tuberculin as opposed to those who do not. Routine examination of the sputum will disclose a much greater tendency (50 per cent.) to absence of bacilli in those who are treated. Physical examination of the chest will show the lesion to be much less active; the râles, particularly, will be drier and scant. There is a somewhat better showing in weight increase in the tuberculin-treated.

To sum up, the most constant effects of tuberculin in those who do well under it are the diminished sputum and cough, particularly when the latter is dependent on the amount of sputum, and the distinct tendency for the sputum to become non-bacillary, thus demonstrating clinically the specific effect of the tuberculin on the site of the disease. The other signs of improvement are the natural results of the diminished activity in the lesion.

SUMMARY

The net results of tuberculin treatment in the patients forming the basis for this paper may be summarized as follows:

1. Those who were distinctly improved and apparently cured (clinically), 25 per cent.

2. The indifferent (60 per cent.), who may be subdivided into (a) 40 per cent. who responded indifferently while the tuberculin was continued, but on the cessation of which did distinctly better than before tuberculin treatment, an indeterminate number of

TABLE 4.—NUMBER OF PATIENTS AND THEIR HIGHEST DOSE, ALSO PERCENTAGE OF HIGHEST DOSE REACHED TO TOTAL NUMBER GIVEN OF THAT DOSE (B. E. TUBERCULIN)

Highest Dose Gm.	Patients		Total No. Given of that Dose	Times this Was the Highest Dose Reached	
	No.	Per Cent.		No.	Per Cent.
0.000.001	82	14.3	2,040	82	4.0
0.000.001	20	3.5	295	20	6.7
0.000.002	20	3.5	272	20	7.3
0.000.004	21	3.6	261	21	8.0
0.000.008	26	4.5	232	26	11.2
0.000.016	17	2.9	211	17	8.0
0.000.032	16	2.8	182	16	8.7
0.000.064	13	2.2	163	13	7.9
0.000.1	20	3.5	171	20	11.6
0.000.2	10	1.7	155	10	6.4
0.000.4	17	2.9	151	17	11.2
0.000.8	12	2.1	74	12	16.2
0.001	21	3.6	115	21	18.2
0.001.25	7	1.2	37	7	18.9
0.001.5	3	0.5	26	3	11.5
0.001.75	2	0.3	18	2	11.1
0.002	26	4.5	54	26	48.1
0.003	9	1.5	23	9	39.1
0.004	2	0.3	10	2	20.0
0.005	3	0.5	8	3	37.5
0.006	1	0.1	7	1	14.2
0.007	0	...	4	0	...
0.008	0	...	3	0	...
0.009	1	0.1	2	1	50.0
0.010	1	0.1	1	1	100.0

whom often come in later under 1, and (b) 20 per cent. who remain indifferent.

3. Those who are apparently made worse (15 per cent.); that is, under the use of the same dosage as the others in the class, but who not only come in under 2, but some even under 1, if the tuberculin is given in doses attenuated enough to meet their hypersensitive-ness.

TABLE 5.—NUMBER OF PATIENTS AND THEIR HIGHEST DOSE, ALSO PERCENTAGE OF HIGHEST DOSE REACHED TO TOTAL NUMBER GIVEN OF THAT DOSE (O. T. TUBERCULIN)

Highest Dose Gm.	Patients		Total No. Given of that Dose	Times this Was the Highest Dose Reached	
	No.	Per Cent.		No.	Per Cent.
0.000.001	4	0.7	4	4	100.0
0.000.001	45	7.8	262	45	17.1
0.000.002	19	3.3	181	19	10.4
0.000.004	15	2.6	157	15	9.5
0.000.008	17	2.9	153	17	11.1
0.000.016	18	3.1	185	18	10.9
0.000.032	18	3.1	130	18	13.8
0.000.064	21	3.6	103	21	20.3
0.000.1	9	1.5	146	9	6.1
0.000.2	20	3.5	126	20	15.8
0.000.4	16	2.8	83	16	19.2
0.000.8	9	1.5	66	9	13.6
0.001	0	...	0
0.001.25	1	0.1	1	1	100.0
0.001.5	6	0.1	42	6	14.2
0.001.75	0	...	11
0.002	0	...	0
0.003	3	1.5	43	9	20.9
0.004	0	...	0
0.005	0	...	0
0.006	10	1.7	15	10	66.6
0.007	3	0.5	11	3	27.2
0.008	0	...	0
0.009	0	...	0
0.010	1	0.1	1	1	100.0

4. Effect of tuberculin on localized visible tuberculosis such as fistulae in ano, glands, etc., which is specific, particularly in the case of tuberculous glands in the neck, in which condition tuberculin is by far the treatment of choice.

While the number of the distinctly improved and apparently cured under sanatorium care and tuberculin does not appear to be any greater than under sanatorium

care alone, the value of the former is in bringing up to the same percentage a type of case that under sanatorium care only would by no means fare so well, if clinical experience is worth anything.

CONCLUSIONS

As there is no way of telling beforehand what case of pulmonary tuberculosis will benefit the most from tuberculin, every patient with that disease should be treated with tuberculin, and only those ruled out who seem unsuitable by reason of their hypersensitiveness, as proved after injection; and even these may receive all the benefits that tuberculin has to offer, if it is given in small enough doses very slowly increased.

I wish to acknowledge my indebtedness for valuable aid in the work on which this paper is based to Dr. Herman M. Biggs, who as general medical officer of the Department of Health spared no effort to further the scientific interests of the institution; to Drs. Edward S. McSweeney, Walter L. Rathbun and William H. White, my associates at the sanatorium, and to Drs. Charles F. Bolduan, assistant to the general medical officer, and Robert J. Wilson, superintendent to the hospitals of the department, for much valuable criticism of this paper.

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AN INTERESTING CASE OF CHRONIC LEAD-POISONING WITH RELAPSE FOLLOWING FRESH EXPOSURE *

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PHILADELPHIA

The following case, showing the effects of lead intoxication, principally on the nervous system, is presented here because of the fact that it illustrates some interesting points in the clinical course and urinary findings of the condition:

History.—Mr. N. E. H., aged 45, weight 151 pounds, height 5 feet 9 inches, was referred to me, Nov. 21, 1913, by Dr. W. H. Hartzell. The family history was negative except that the patient's father, who was a worker in lead, died of paresis due to plumbism. He had had no lead colic, but wrist-drop, ptosis of one eyelid and optic atrophy followed by symptoms of general paralysis of the insane. No members of the family, other than father and son (the patient) were exposed to lead, and hence no additional cases of intoxication occurred in the household. We may, however, assume that susceptibility, which varies markedly in different families, was fairly well marked in that of the patient since he employed the usual precautionary measures with minute care. The patient had had the usual infections of childhood, and had been subject to frequent "attacks of biliousness" since early adolescence. He was married and had been a traveling salesman for the past fifteen years, during which time he had not been in contact with lead except for one and a half days (as described below). From 14 to 30 years of age, however, he had been a house- and sign-painter. During the first seven years of this period, not all his time was devoted to his trade, but from 21 to 30 years of age it was. The patient had used three cups of coffee a day and alcohol in moderation, but no tobacco. He walks from 3 to 5 miles daily in the open air, but otherwise takes no exercise. He denies venereal infection.

Present Illness.—At about the time he began to work in lead, he began to be subject to attacks of "biliousness," which recurred frequently at first but later at longer intervals until

four years ago, when they disappeared for one year. The symptoms in detail manifested during an attack of "biliousness" are, in the order of development, diplopia, transitory blindness, headache, dizziness, aphasia and repeated vomiting, followed by abdominal soreness lasting one week. The arms become numb and the heart-beat drops frequently to 46 a minute.

Three years ago Mr. H. sandpapered the casings of his home, which was attended with the production of much dust. Following this marked exposure, which lasted only one and a half days, he painted the house alone. Almost immediately the attacks returned in a modified form: vomiting and abdominal soreness were absent, while the diplopia, transitory blindness, vertigo and aphasia were present. At the same time (three years ago) he developed lead arthralgia affecting the entire right arm and the sacral region. All of the foregoing symptoms after persisting a year and a half were relieved by treatment directed to the lead intoxication, principally the use of potassium iodid, lasting four months. The symptoms, however, recurred later, and four months ago he resumed the treatment with immediate improvement, but he soon gave it up. During the past week daily slight attacks occurred. The average duration of one of the paroxysms described above is at present about one hour, but formerly it was not so brief—from two to three hours.

Laboratory Examinations.—An examination of the urine resulted as follows: specific gravity 1.020, faintly acid; albumin, glucose, indican and casts were all absent; a few leukocytes and epithelial cells were present. Dec. 5, 1913, Dr. Matthew Beardwood reported that he had found an appreciable quantity of lead in a specimen of the urine which had been submitted to him for chemical analysis.

Blood: Erythrocytes, 4,990,000; hemoglobin, 96 per cent.; leukocytes, 7,400. There was no basic granulation of the erythrocytes.

Physical Examination: This revealed an adult white male, moderately well nourished, musculature fairly good; no evidence of any palsies; reflexes: knee-jerks diminished, Babinski and ankle-clonus absent.

Local Examination: There was no lead-line on the gums, but a faint bluish-black line around a single decayed tooth. Dr. William L. Estes had observed a distinct lead-line in 1912. The heart and lungs were normal. Blood-pressure: systolic, 122 mm. Hg; diastolic, 90 mm. Hg. Abdomen: The liver was slightly enlarged downward; otherwise the examination was negative in its results.

Eyes: These showed interesting changes, as shown by Dr. L. Webster Fox's report, which follows: Marked astigmatism in both eyes and a low-grade muscle insufficiency. Visual fields normal (no reversal of color field). Ophthalmoscopic examination showed marked stasis of the veins, sheaths of both optic nerves thickened, showing evidence of chronic meningeal thickening.

It may be doubted by some whether this case is really one of lead intoxication. The absence of basophilia, however, does not rule out plumbism, for it is generally held at present that it is of little or no diagnostic value. Moreover, Oliver¹ failed to find granules in the blood in 40 per cent. of the cases. Again, the absence of the history of either lead colic or palsies during the time that his occupation entailed exposure to lead, weighs against the diagnosis of saturnism, but does not exclude the condition, since these typical manifestations have been absent in well-authenticated cases to be found in the literature. No evidences of contracted kidney existed in the case here reported. The majority of cases of chronic lead-poisoning that show a progressive tendency, it is true, develop chronic interstitial nephritis, which commonly proves to be a fatal

* Read before the Section on Medicine, College of Physicians, Feb. 24, 1914.

1. Oliver: Quoted by Alice Hamilton: Industrial Lead-Poisoning in the Light of Recent Studies, THE JOURNAL A. M. A., Sept. 7, 1912, p. 777.