

12%; large mononuclear, 37%; polynuclear neutrophils, 48%; eosinophiles, 3%.

Another examination on May 8 showed: Red corpuscles, 1,000,000; white corpuscles, 7,000; hemaglobin, 10%. The changes in the red corpuscles were more marked, and two megaloblasts were seen in counting 100 white corpuscles.

The patient was shown at this time at a meeting of the Clinical Club as a case of pernicious anemia. The long history of hematuria, as well as the condition of the urine which pointed to some disease of the pelvis of the kidney or bladder, seem to have been disregarded. The emaciation, which is unusual in pernicious anemia, might also have suggested that there was some cause for the anemia. The condition of the blood was, on the whole, pretty characteristic of pernicious anemia, although the normal white count and the very low percentage of hemoglobin are somewhat unusual when the number of red corpuscles is so low.

Attention was soon after directed more particularly to the bloody urine. On May 12 the urine was turbid, acid, of a specific gravity of 1.013, and contained a large trace of albumin. The sediment contained considerable pus, free and in clumps, considerable normal and abnormal blood and much squamous epithelium. On May 19 the urine was even more noticeably bloody. It was red, slightly acid, of a specific gravity of 1.009 and contained 1.5% of albumin. The sediment showed much pus, much normal and abnormal blood, some round and bladder cells. On May 31 the liver was palpable 4 cm. below the costal border. The abdomen contained a little free fluid, as did the pleurae.

On June 1 the examination of the blood showed: Red corpuscles, 2,080,000; white corpuscles, 8,000; hemaglobin, 15%. There was marked macrocytosis, microcytosis and poikilocytosis as well as polychromatophilia. No nucleated reds were seen. On June 6 a rather unsatisfactory cystoscopic examination of the bladder was made by Dr. Higgins. One ulcerated patch was seen. The bladder was treated by injections of gelatin. Examination of the blood on June 9 showed: Red corpuscles, 2,500,000; white corpuscles, 14,200; hemoglobin, 20%. She died suddenly on June 9.

During the whole stay in the hospital she had six or seven loose movements daily, and vomited occasionally. At times the stools contained a few clots of blood. The urine continued bloody. The temperature was irregular, ranging from normal to 100° F.

No autopsy was allowed. Several pieces of greyish-white, tough tissue with blood clots were removed through the urethra after death. Microscopical examination by Dr. Mallory showed connective tissue, muscle tissue and in places foci of round cells. Irregular cellular areas surrounded by connective tissue in which medium sized cell masses were irregularly grouped were also seen. The cells of these masses were epithelial in type, lay closely packed, had round or oval nuclei, and showed frequent mitoses. The anatomical diagnosis was carcinoma.

In this case the anemia was probably due partly to the continuous loss of blood in the urine and partly to the cachexia from the cancer. After the attention was directed to the bloody urine and other diseases duly considered, pernicious anemia was at once dropped from the list of probabilities. It is merely another instance to show how necessary it is not to attach too much importance to the blood condition alone to the neglect of other methods of diagnosis.

## A CASE OF POISONING BY THALLIUM.

BY WILLIAM N. BULLARD, M.D., BOSTON.

The metal thallium was discovered by Brookes in 1861, and since then we have obtained some knowledge, through experiment, of its toxic effect on animals. Cases of poisoning in man are, however, not common.

### POISONING IN ANIMALS.

The principal symptoms found in animals have been general listlessness, loss of appetite, nausea and vomiting, diarrhea with dejections often tinged with blood, and intestinal pain, sometimes severe. There is slowing of the respiration, and dyspnea. The chief action, however, seems to be upon the heart, on which it is supposed to act as a direct poison. It causes slowing and weakening of the heart's action, and the heart stops in diastole.

In addition to these symptoms, it produces general tremor of the limbs and a marked incoordination, usually more evident in the hinder extremities. Luck notes a marked swaying on standing, and a slow, uncertain, swaying gait. Richet found in chronic poisoning a generalized muscular atrophy: not a simple leanness, but an almost total wasting of different muscles.

Curci states that thallium does not act on the nervous system of animals, but that it is exclusively a muscular agent.

Both Buschke, in 1900, and Bettman, in 1901-1902, succeeded in producing alopecia in animals with acetate of thallium.

The only definite abnormal conditions found pathologically were swelling, congestion and small hemorrhages of the gastric and intestinal mucous membrane, sometimes congestion and small hemorrhages in the lungs, and mild parenchymatous nephritis. The heart is usually stopped in diastole, the right cavities dilated.

### POISONING IN MAN.

The instances of this are rare. Brookes states that he swallowed .065 to .130 gm. of thallium salt without any effect. Pozzi and Courtade employed the iodide of thallium in doses of .010 gm. daily in certain cases of syphilis, with favorable results. As unpleasant symptoms were mentioned pain in the stomach and vomiting. They also found in a few cases that the gums were painful and swollen, and that there was a blue line at their junction with the teeth. I have not found these symptoms elsewhere mentioned.

In 1898 Combemale advocated the use of the acetate of thallium in the profuse sweats of pulmonary tuberculosis, and found it most efficient for this purpose. The ordinary dose was 10 cgm., the maximum 20 cgm. He never observed any evidences of toxic action while the drug was being taken, but noticed a falling of the hair later. This was said to be *total* and extraordinarily rapid. Huchard, writing a report on this paper for the *Académie de Médecine*, states that

<sup>1</sup> Contributed to the Thirteenth Series of Medical and Surgical Reports of the Boston City Hospital, 1902.

he had tried this drug on two patients in the last stages of phthisis. They were attacked with very sharp pains in the lower extremities during the time thallium was taken, and he concluded that these pains could not have been due to the phthisis, because they ceased immediately on stopping the thallium.

Jeanselme, in the same year, reported a case in which a woman, fifty-nine years old, was given cachets, each containing 3 cgm. (.03) of acetate of thallium for profuse sweats. In the course of three days she took nine cachets, .27 gm., when the medicine was stopped, on account of diminution of the sweats and because of the occurrence of rather sharp pains in the abdominal and lumbar regions. Fifteen days later her hair suddenly began to come out in masses, and she lost about one-third of it.

Guinard also, in 1898, reports loss of hair after nine pills of .05 cgm. of acetate of thallium.

It was thus quickly established that thallium, when given even in small doses, was liable to cause a loss of hair or alopecia in men. This usually occurred some days after the administration of the drug had ceased. It was found that the loss of hair produced by the administration of thallium was so serious that the use of the drug has been practically abandoned, although it proved a most efficient agent for sweats. I have been unable to find any further reports of toxic symptoms in man from this drug.

My case was that of a gentleman, twenty-seven years old, a physician, who was admitted to the Boston City Hospital as a private patient of Dr. V. Y. Bowditch, and whom I saw in consultation a number of times. He had taken sulphate of thallium for purposes of experiment, "not over eight grains in all and probably not over half a grain at a time; four grains is probably nearer the exact amount." Later he writes: "From half a grain to a grain was taken at a time, and the first time was taken perhaps every other day for three or four doses. Then there was an interval of about two months, then three or four doses were taken again in the same manner. Nothing was noticed after the first lot was taken, but within two or three days after the last dose the numbness in the toes and finger tips was noticed."

On admission to the hospital he gave the following account of his symptoms: Three weeks ago slight diarrhea which readily yielded to treatment, and at the same time numbness in the toes of both feet and the fingers of both hands, which in the course of two or three days extended up the lower extremities and involved the lower abdomen, the perineum, the inside of the thighs and the inner surface of the legs, being less marked over the tibiae. The nerves of the lower extremities were painful, and there was considerable weakness and partial paralysis of the lower extremities. Almost from the onset he was confined to bed or to a wheel chair. He grew worse for the first seven to ten days, then his condition became stationary, and now he considers himself slightly better.

On admission the balls of his feet were exquisitely tender, and there was some tenderness over the whole metatarsal region of both feet and slight tenderness along the inner border of each tibia. There was loss of the power of motion of both big toes, which he could ordinarily move freely. The other toes could be moved without pain.

All other movements of the lower extremities were present though weak. There was some wasting of the lower extremities, and there was a diminution of sensation over all the toes. The muscles of the lower extremities were lax. Knee jerks lively. Plantar reflexes not obtained. No ankle clonus. There was also some diminution of sensation over the fingers. The internal organs were all natural and no other abnormal signs were found. The right pupil was slightly larger than the left, but he states that this had been the case since scarlet fever, when he was five or six years old.

The physical examination a few days later gave similar results. Has but little power of motion in lower extremities. Cannot move the big toes, but can now move the fifth toes, which he formerly could not do. There is now diminution of sensation over the external border of both feet and the internal third of the right leg. The most tender points now are on the soles of the feet near the middle of the metatarsi. Knee jerks increased. No clonus.

Eight days after entrance to the hospital it is noted that he has had for some days considerable difficulty in sleeping. The numbness has now extended so as to involve both knees. He has troublesome twitching pains in both legs and in feet.

Ten days later (eighteen days after admission): Improving. Limbs pain him much less. Sleeps better.

Twenty-sixth day after admission: Great improvement. Able to be up and out in wheel chair. Has had electricity since last report.

A week later we find that traces of lead were discovered in the urine; also  $\frac{3}{100}$  to  $\frac{4}{100}$  mgm. of arsenic, "probably too slight to account for symptoms."

Thirty-third day after admission: Discharged.

During his stay in the hospital the urine was frequently examined: it showed at first slight traces of albumin, which gradually disappeared. On the day of entrance the condition was as follows: Pale, acid, specific gravity, 1.016; slightest possible trace of albumin; no sugar. Occasional abnormal globules and degenerated small renal cells and leucocytes.

Twelve days later: High color; trace of albumin; much pus, mostly in clumps; many normal red corpuscles, some abnormal; occasional small and large round degenerated cells; calcic phosphate crystals.

Ten days later: It was normal; acid, 1.024.

The treatment, besides rest in bed and dry heat to his limbs, consisted only in iodide of potassium in small doses. Later, when the pains had ceased, electricity was applied to the lower extremities.

About three months after the onset of the illness the patient wrote: "I have resumed work but am not absolutely well. Played golf yesterday without discredit. Am getting used to the cold weather. After leaving the hospital there was total loss of hair."

## REMARKS.

The condition here was plainly a multiple neuritis. It followed the usual course of this affection, and the patient eventually recovered completely.

I do not consider the report of the existence of lead in the urine important. I cannot now determine with certainty by whom the examination was made or what tests were used. It is possible that the tests were really given by thallium. The patient lived in a large institution, where many other persons were exposed to essentially the same conditions as himself, none of whom showed any signs of lead poisoning. On the other hand, the source of the thallium was known and the symptoms occurred immediately after its ingestion.

## TETANY IN GASTRIC DISORDERS.

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(Concluded from No. 21, p. 563.)

CONTINUING the review of American literature, the cases which I here record, together with one reported by Bundy, one by Larrabee and one by Locke, are the only ones in adults which I have been able to find since 1894. Since Morse's last summary there have been four cases in infants reported by Adams and Davis.

A comparison of German and American ideas of tetany, as expressed by Frankl-Hochwart and by Morse, shows that the former leaves doubts, both in the definition and the classification as to whether it is a disease in itself or a symptom-complex, while the latter regards it simply as a symptom-complex. The fact that it occurs in so many varied conditions, of which presumably there is no common cause, is strong evidence against its being a disease in itself. It is possible that the first group of Frankl-Hochwart's classification, the epidemic form of tetany, may represent a disease in itself, infectious in character, which has received its name from its only objective symptom, the muscular spasm, tetany.

But one instance of this form of tetany has been reported in America, that of Vaughn in New York in 1893, where seven cases occurred in Italians, five being in the same family, with several other unrecorded cases in Italians in the same quarter at the same time. The cases were accompanied by mild fever. The hypothesis of an infectious disease, however, does not explain all features of Frankl-Hochwart's first group, such as its occurrence in individuals who are in other respects well, for although mild fever is common it is not invariable, and also its prevalence in cer-

tain occupations. This group and the epidemic in New York may equally well be explained by the supposition of a toxemia from working materials, foods or other conditions of the environment.

No other group of Frankl-Hochwart's classification appears as a disease in itself; the variability of the conditions making it plain that it is a symptom produced by various unknown causes.

No classification of the groups of tetany can be satisfactory in our present ignorance of the underlying causes. The divisions made by Frankl-Hochwart do not express these causes; they are groups of convenience representing frequency of occurrence which will ultimately be replaced by empirical divisions expressing the etiology.

We cannot assume, for instance, that Frankl-Hochwart's third class, where tetany follows the use of ergot, chloroform, morphin, antihelmintics, and in lead poisoning, is a true division. The natural explanation of these is an intoxication, but since the drugs mentioned are in common use, and only single cases of tetany have been referred to them, we cannot regard the drugs as the causative agents. The same may be said of tetany following infectious disease, and in connection with other nervous diseases.

An illustration of the uncertainty of the commonly assigned etiological factors is that Griffith gives rheumatism, or exposure to cold and wet, as a cause in almost one-fifth of his cases, while Frankl-Hochwart does not even mention this as a cause.

Notwithstanding its artificial basis, the classification is useful to separate epidemic, gastric and infantile tetany, and to point out its occurrence after thyroid extirpation and in the puerperium. Further than this it seems impossible to go, and even here it must be admitted that all these groups may be the same thing, and that many cases have been reported which cannot be assigned to any of them.

As to what symptoms are essential and pathognomonic, the German ideas are best expressed by Fleiner's recent article on gastric tetany. In a "festschrift" to William Erb, Leipsic, 1900, he published five cases of which he had previously published four in *Archiv. f. Verdauungskrankheiten*, Bd. i-v. While he regards ordinary tetany as a neurosis with a favorable prognosis, he considers tetany of gastric origin as a sign of bad import, implying a high grade of pyloric stenosis and marked gastric dilatation. Of his five cases Nos. 1, 3 and 4 are called tonic, muscular spasms, and 2 and 5 are actual tetany. The distinction is based upon the absence in Cases 1, 3 and 4 of Trousseau's and Chvostek's phenomena, and the presence of Trousseau's in Case 5, and of Trousseau's and Chvostek's in Case 2. In other respects the cases are alike. Apart from the fact that a series of five cases seems too small to establish positive laws for the essential symptoms, an examination of the various phenomena shows that they cannot be regarded as unvarying. Chvostek's phenomenon of hyperirritability of the facialis