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DIFFUSE DEGENERATION OF THE SPINAL CORD.*

Clinical Analysis of Fifty Cases.

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Pathological Study of Five Cases.

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About nine years ago one of the writers published a brief discussion of certain diffuse degenerations of the spinal cord,¹ based on the observation of eight cases, four of them with autopsy. In one or two of these cases the spinal lesion had been associated with anemia of a profound type, and in the rest with other forms of mal-nutrition, not definitely classifiable but often attended with diarrhea and emaciation, and in one case with extensive pigmentation of the skin of high degree. Most of the patients were women and all were in the later stages of adult life.

Some of the descriptions, now classical, by Lichtheim, Minnich, and others, of the spinal lesions found in connection

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¹"A Group of Cases of Sclerosis of the Spinal Cord, Associated with Diffuse Collateral Degeneration; Occurring in Enfeebled Persons Past Middle Life, and Especially in Women."—JOURNAL OF NERVOUS AND MENTAL DISEASE, Feb., 1891.

with pernicious anemia had already been published, but the analogy between these and the degenerative, diffuse, or "combined" sclerosis associated with other forms of wasting disease, as described in the above mentioned paper, had not been noted. The subject was next taken up by Dana,² who has published from time to time papers of much value, the last of them containing a reference to the most important publications bearing on the subject, with an excellent summary of symptoms, etc., and the report of a new case, with autopsy.

Cases closely resembling those reported by Dana and myself have been described by various observers, but no serious attempt had been made by any European writer to utilize them for classification, or to point out the similarities and contrasts which exist between this group, where the disorder of nutrition is ill-defined, and the group of the spinal degenerations complicating the pernicious anemias, previous to the publication of Bastianelli's³ monograph in 1896.

Before speaking of Bastianelli's principle of classification I desire to call attention to another investigation which seems to me to throw light on the etiology of this disease from a new quarter. The belief has long been current that back of the changes in the bloodmaking organs and the nervous system, there was a toxic agent at work, derived perhaps from the intestinal canal, perhaps from other sources.⁴ A new step forward in the etiological study of pernicious anemia, and, we may hope, of the nervous diseases which are so frequently associated with pernicious anemia, as well as with other forms of mal-nutrition, has been made by the investigations of Adami and others to whom he refers,⁵ on the different forms of acute and chronic infection due primarily to the presence, in vari-

²JOURNAL OF NERVOUS AND MENTAL DISEASE, Feb., 1891; April, 1891; Jan., 1899.

³"Le Sclerosi Combinata del Midollo Spinale Nelle Anemie Perniciose," *Bull. della Royal Acad. Med. di Roma*, 1895-6, Fascicolo I. e II.

⁴Compare Eisenlohr: "Ueber Primäre Atrophie der Magen und Darmschleimhaut, und deren Beziehung zu schwerer Anemie und Rückenmarkserkrankung." *Deutsche med. Wochenschrift* 8, Dec., 1892, p. 1,105. See also Minnich's classical Monograph.

⁵"On Latent Infection and Subinfection and on the Etiology of Hemochromatosis and Pernicious Anemia." By J. George Adami, M.D. Annual address before Society of Internal Medicine, Chicago, Nov. 29, '99.

ous organs and tissues, of bacteria or bacterial poisons derived from the intestines, and to the reactive efforts of the tissue cells, which, though successful in overcoming the danger of specific infection, may be attended with a fatal exhaustion. The diseases which Adami and others have especially studied in this connection are hypertrophic cirrhosis of the liver, hemochromatosis and pernicious anemia, but at the close of his address the writer throws out a hint which should certainly be taken advantage of in the study of such affections as those now before us when he says: "Nay, more, I believe that in the development of many chronic fibroid conditions this subinfection will be found to play a definite part."

As regards, now, the classification proposed by Bastianelli, it may be briefly said that this writer attempts to divide all the cases in which the aforesaid degenerative spinal lesions occur, in connection either with pernicious anemia or with the more chronic forms of mal-nutrition, into two groups, between which, it may be, the line of separation is not to be too sharply drawn.

In the first group it is the anemia which dominates the scene, the spinal lesions making themselves felt only toward the end of life, when they develop with great rapidity. In this group many of the classical cases, as reported by Liehtheim, Minnich and many others, belong. It will be remembered by any one familiar with the literature that the records of these observers call particular attention to the rapidity with which the nervous symptoms run their course, the fatal issue often occurring in the course of a few months.

In the second group, in which the more chronic cases belong, including most of those reported by Dana and myself as well as others contributed by a number of European physicians and by the writer himself, the essential feature of the case, Bastianelli thinks, is the disease in the nervous system, the mal-nutrition being of secondary importance. The disease of the central nervous system in the cases of this second group occasionally strikes beyond the limits of the spinal cord, involving the optic nerves, for example, as in one of Bastianelli's cases. The anatomical lesions, too, he thinks, differ

somewhat in character. In the cases of the first group they are relatively slight and scattered, and the lateral columns in particular are relatively little affected, while in those of the second group they are more pronounced and the lateral columns more sharply and extensively involved.

As regards the lesions of the blood vessels, Bastianelli finds them less marked in the cases of the first group, where the lesions occupy relatively limited areas, and more marked in the typical, quasi-systematic, whole-column degenerations, though on the vascular-origin theory, as upheld by Marie, one might expect the reverse to be the case. In other words, he thinks that the vascular changes are secondary and keep pace with the intensity of the sclerotic process.

So far as our observations go this triple distinction between the two groups of Bastianelli is not fully maintained, though doubtless of importance and value. Substantially the same distinction has been drawn in the recent communication of Risien Russell, Batten and Collier, to be referred to later. We do not find it to be invariably true that in the more chronic cases, in which the nervous symptoms have played a prominent part for many years, the spinal lesions are necessarily most marked. Thus, we have one case, with autopsy (Pathological Report, Case IV.), where the patient, a lady small in stature and with a pale skin and feeble nutrition, suffered from the characteristic paresthesia, gradually leading to ataxia, for thirteen years, yet the spinal lesions were of relatively slight intensity, and that, too, in spite of the fact that the previous death of her sister from a similar affection had shown some degree of hereditary predisposition to spinal degeneration. In Case I. of the former series of cases, published in 1891 (*l. c.*), on the other hand, the lesions were of a quasi-systematic character and strongly marked, though the clinical course had been so short that it was difficult to believe it possible that the duration of the symptoms marked the duration of the disease.

It certainly cannot be true, and is apparently not claimed by Bastianelli, that the dividing line leaves all the cases in which pernicious anemia is present in one group and all the

rest in the other. In general terms this distinction is doubtless justifiable, but there are striking exceptions. In one of our cases (Pathological Report, Case V.) pernicious anemia was present and ran a typical course, yet spinal symptoms were recognizable for three years, their onset nearly coinciding with the onset of pallor and with a loss of flesh. It is noteworthy that this patient, like others of this series, had always been pale, even when thought to be well. The interesting fact should be borne in mind in this connection that routine examinations of the spinal cord in cases of profound or "pernicious" anemia have shown that degenerative changes may be present, though they have not been revealed by symptoms during life. These observations are borne out and paralleled by that of Nonne,⁶ who reports a case where recovery in a clinical sense occurred, though the spinal lesions were found to have persisted. The recognition of these facts should make us hesitate to assume that the development of the spinal lesions, which seems so extraordinarily rapid in some of the reported cases, as, for example, in Case I. of the first series, is really limited to the period indicated by the presence of clinical symptoms.

Among the most recent communications touching on this subject is that of Pitren,⁷ who examined the spinal cord in nine cases of pernicious anemia, in two of which spinal symptoms had been present. Not only in these latter, but in two other cases in which no symptoms of spinal degeneration had been noticed, slight signs of chronic change were found in the posterior columns. Similar observations had also been made by Nonne,⁸ who examined the spinal cord in thirty-one cases of anemia, and by Minnich.

The latest special study of this disease is recorded in an interesting paper by Drs. Risien Russell, Batten and Collier,⁹ reporting nine cases, with seven autopsies, and giving a full list of the literature, which is not, however, discussed in detail. The opinion expressed by these writers is much the

⁶Archiv. für Psychiatric, etc., 1893.

⁷Nord. med. Aek., 1896. (Abstract in the Neurol. Cbl., 1896, p. 747.)

⁸Deutsche Zeitschr. f. Nervenheilkunde, 1895.

⁹Brain, Spring, 1900.

same with that of Bastianelli (though his views are not cited) in that they think a distinction should be made between the spinal degeneration which appears toward the end of the severe anemias and runs a rapid course, forming perhaps only an incident in the main affection, and the more chronic cases in which the spinal degeneration is the essential feature, while anemia occupies a less prominent place or may even be wanting. They agree with him, too, that in the former group the lesions are more likely to occur in disseminated patches, while in the latter they are more systematic and defined. They see no reason for excluding from the second group such affections as Gowers' ataxic paraplegia. These writers range themselves with those who refrain from making a diagnosis of pernicious anemia from examination of the blood alone, and they adopt without reserve the view that the cause of the spinal change is neither degeneration of the gray matter, nor multiple hemorrhages, nor anemia, nor alteration of the blood vessels, but that it is due to the introduction of toxic substances of some sort. The arguments which they advance in favor of these opinions follow much the same line with those already advanced by Bastianelli. They divide the disease itself into three stages, characterized, in the main, by ataxia with slight spasticity, increased spasticity, complete paraplegia. While giving the prognosis as absolutely unfavorable, they cite a case, apparently of this sort, under the care of Ferrier, where the patient seemed to have recovered, although he had presented the characteristic symptoms, even including those of the third stage.

The peripheral nerves were examined in several cases and found normal in all but one or two, while in these fairly marked changes were present. While their account of the symptomatology is excellent and likely to be accepted as authoritative, it appears strange that they do not dwell more on the paresthesia of the early stage, which forms such a striking feature in my cases and in most of those hitherto published. The division into stages also seems to me to be of doubtful value, the passage from one to the other is often so gradual, and individual cases differ so much in detail from one

another. It has, however, quite as much importance as the corresponding division in tabetic cases.

On looking over my private clinical records (mainly of the past ten or eleven years) I find the notes of about fifty cases—if the group of eight cases reported in 1891 be included—which correspond pretty definitely to the type of the diffuse, sub-acute, sub-chronic or chronic spinal degeneration (in some of the cases perhaps more than spinal) which is before us for study. As only a few of these cases came to autopsy the correctness of the diagnosis in the majority is, of course, open to doubt. It is, however, difficult to see with what diseases this affection could be confounded, except unusual forms of chronic neuritis and multiple sclerosis.¹⁰ Doubtful cases have been excluded so far as practicable, and though mistakes in diagnosis may have been made, it is clear, at all events, that the affection is common enough to deserve far more attention than most text-books accord to it. It is also fairly certain that, although pronounced anemia is by no means always present, nor impairment of nutrition invariably, and though the patients may be men as well as women, and are not always advanced in years, yet on the whole, the designation given in the heading of the paper published in 1891 (*l. c.*) is justifiable and suggestive.

I have not attempted to utilize hospital records to any extent in the preparation of the following analysis, but have selected for the sake of convenience nine cases to bring the whole number, exclusive of those already published, up to fifty. It has not seemed worth while to burden the paper with the records of these cases in detail and I have attempted only to extract from the histories such clinical facts as are of practical value or special interest.

Sex.—Of the fifty cases there were seven (all private) in which profound anemia¹¹ was present, characterized by serious and well-marked blood-changes (low red-count, megalocytosis and

¹⁰Although the greater number of these patients were seen only in consultation, yet I have records of the later histories of most of them, by the aid of which the diagnoses are placed almost beyond question.

¹¹In a few others the diagnosis in this respect was doubtful.

poikilocytosis), and of these seven, five were males; two, females. In contrast with these figures, it is noteworthy that of the remaining forty-three patients thirty-one were women and twelve men, numbers which fully bear out the earlier statements of Dana and myself, to the effect that the lack of vigor or some other peculiarity of the female sex carries with it a certain degree of susceptibility to this affection. This fact, especially when linked with two others, namely, first, that the patients almost without exception were of relatively feeble health or advanced years, or both; and, second, that *indications of syphilis were exceedingly rare*, if not, indeed, wholly absent, is of value as helping to point the direction in which etiological research should tend.

Age.—As regards the ages of the patients, twenty-three, *i. e.*, more than half, were fifty years old or more at the time of the onset of the disease, and all but five were over thirty years old. The oldest patients were seventy-one and sixty-eight (a woman and a man, respectively) and the youngest twenty-two, all, it should be said, without autopsy. Erlicki and Rybalkin,¹² however, have reported a case where the patient was a girl of but seventeen. The case came to autopsy and the typical anatomical changes were found in the spinal cord. It is interesting to note that, in this case, although the ostensible exciting cause was a "cold" and fever of short duration, yet the patient was, from birth, of small stature. Death occurred at the end of a year and a half from the onset of the spinal symptoms.

Nutrition.—The next question is whether any characteristic disorders of nutrition other than severe anemia were present which might act as predisposing causes; or, in other words, whether the "general feebleness," so often referred to, can be more accurately defined, or can be considered as a causative factor.

A review of the cases shows that, as in the instance just reported, *small stature* or slenderness of frame was fairly common, though by no means always noticeable. It was present to a striking degree in Case I. of the group reported nine years

¹²Arch. f. Psych., etc., '86, p. 693.

ago. Other signs present in the same case were emaciation and an excessive pigmentation of the skin, which was as dark as that of an Indian. The patient was eccentric, excitable and addicted to coffee in excess, and perhaps to other stimulants. The same small stature was observable in one of the cases of the present series, which was followed by autopsy. (Case IV.) The case was a chronic one, the symptoms running over thirteen years. Pernicious anemia was not present, certainly not in a typical form, but the patient was excessively pale her life long, so that her face would attract attention as she walked the street. She, too, was eccentric to a marked degree, and without well-balanced judgment, yet spirited and full of plans and projects, which were carried out with remarkable energy, considering her feeble health.

It might be urged that in both these cases the eccentricity was analogous to the mental changes occasionally associated with pernicious anemia. Yet the peculiarities of temperament, not only in these two cases, but also in one of true pernicious anemia, to be spoken of later, were in a measure native, neurotic stigmata, and only accentuated by the later degeneration of the general nutrition. Meantime, the important thing at present is to record facts and coincidences as they appear, and it is certainly true that eccentricities of character, associated with other neuropathic signs, were present in several cases of this series.

General lack of vigor, usually from childhood, often accentuated by family or business worries, the strain perhaps resulting from the long illness and eventual death of a near relative, or the like; was conspicuous in a large proportion of the cases. Spare and sallow, when not distinctly anemic, men and women made up by far the greater number of the patients. Yet even this statement is not to be taken without exception, as there were a few who had no special complaint to make of their previous health.

Diarrhea,¹³ either chronic or of frequent occurrence, which seemed a prominent and important feature in the series of nine

¹³See also Bastianelli (*l. c.*). For the possible significance of diarrhea see Adami (*l. c.*).

years ago, and perhaps gains new importance through Adami's researches, was noted as present in a distinct form in only six or seven cases of this series.

Constipation, often quite obstinate, was much more common, but neither of them occurred so often as to remove the impression that if the penetration of germs through the walls of the intestine be indeed the essential cause of the toxemia, this may occur under the influence of impaired resisting power alone, or in association with latent disorders of the gastro-intestinal tract. Unfortunately, information is lacking as to the condition of the digestive secretions of the stomach, which Adami's citations show to be defective in some cases of pernicious anemia. This is certainly a point for investigation in future cases.

Pigmentation of the skin of high degree was seen in two cases,¹⁴ neither of them pernicious anemias, though both highly typical cases of Bastianelli's second group. It is also interesting to note, in connection with Adami's observations, that a physician who examined one of these patients at an early period of the affection pronounced her to have disease of the liver and intestine. Lesser degrees of pigmentation, amounting to no more than sallowness, were quite common.

In the earlier series of cases *lead* was noted as a possible partial cause of the severe anemia, and perhaps of the spinal symptoms in one or two cases.¹⁵ In the cases of the present series the same possible cause is occasionally seen. One patient came with a record of lead-poisoning in the past, and a trace of lead was found in the urine in another case, as also a large trace of arsenic in that of another. I do not, however, attach much importance to this fact, since it is one of such common observation.

Considerable *loss of weight* occurred in several cases as a part of the general nutritive impairment. It is worthy of mention that one patient, a woman of forty-six, besides presenting

¹⁴One of these patients is still living, but the blood certainly does not show as yet the characteristic changes of pernicious anemia. A sister has a progressive spinal affection which has led to paraplegia, and is probably of the sort now in question.

¹⁵One patient was a painter of many years' standing.

the characteristic sensory and motor symptoms of this affection, suffered and finally died with great enlargement of the liver, ascites, and jaundice. I do not, however, know which set of lesions was the first to appear.

A family history of neurotic tendency or nutritional weakness is fairly common. One patient (pernicious anemia) is an only child of parents, one of whom, the mother, died of tuberculosis at forty-one, the other of a "painful stomach disorder," of brief duration, at sixty-eight. The patient has one child, a delicate, hysterical girl, and has been himself from birth delicate and club-footed.

The family history of a second case (pernicious anemia) is of marked interest. The patient, a man of fifty, was one of a brilliant but highly neuropathic family of four sons and two daughters. The father, a man of unusual ability and energy, a tireless and successful man of business, and of fine personal traits, but excitable and positive, died of cerebral apoplexy at a moderately advanced age. The mother died of tuberculosis. The father belonged to a large family, many members of which were gifted but neurotic and eccentric. Of the patient's five brothers and sisters, three died with cancer, one of nephritis, one probably in consequence of dipsomania. In a third case (pernicious anemia) the patient's brother had suffered from an acute, severe and almost fatal attack of "multiple neuritis." In a fourth case, neurotic tendencies were absent, but the father had died with phthisis at forty, and the mother and sister had both been excessively pale before their death, the mother's skin having, too, it was said, a yellowish cast.

In a great majority of cases of the "simple debility" group,¹⁶ the patients' antecedents were not striking, and not other than one would expect in the family history of persons with poor nutrition. A few are, however, of importance. In one case (with autopsy, Case IV.), the patient being of small stature and of almost life-long pallor, and of an energetic and lively though eccentric disposition, an older sister had died, after a lingering illness, of a progressive spinal affection, probably of this same sort, characterized by exaggeration of the deep reflexes, asso-

¹⁶See also first report (*l. c.*), and Bastianelli's paper (*l. c.*).

ciated with tremor, and eventually with contractures of high degree and complete paraplegia. There had been occasional temporary disturbance of mind, but no affection of speech. This sister was seen by me a few times, towards the end of life, but before my interest in the present subject began. The patient herself was under my care, off and on, through the whole of her long illness.

In another case, characterized by pigmentation of the skin, though not by other signs of pernicious anemia,¹⁷ both the patient herself and also an older sister (one of three) were eccentric and addicted to chloroform-taking. This sister suffered from migraine. The father had died of phthisis. A second sister died in childhood from an unknown cause. A third sister and the mother had been well. In a third case,¹⁸ also characterized by pigmentation of the skin, an older sister became paralyzed below the waist, after a gradually progressive illness of three years' duration. Another sister, of rather small stature, is pale, delicate, and subject to sicknesses of hysteroid character. In a fourth case, both parents and a sister had been of delicate health, and the latter had died from a "complication of troubles" after a long period of invalidism. A fifth case¹⁹ is notable for the fact that a sister was said to have died of "pernicious anemia," though repeated examinations of the blood had failed to establish the diagnosis in the case of the present patient. A sixth patient of this group had two sisters, both of whom were said to have died with some disease suggesting softening of the brain.

Symptomatology. Paresthesias.—In the early history of my cases one or another form of this symptom was strikingly prominent. It was usually felt first in the feet, then in the hands—either all the fingers alike or in the median or ulnar areas by preference—but the proximal segments, as the shoulders or thighs, were occasionally attacked early, if not first, as occasionally in tabes. Sometimes the hands were involved first,

¹⁷Case seen but once, far in the country. No examination of blood, but a full and clear clinical record, partly personal, partly from the family physician.

¹⁸Patient still living.

¹⁹Patient still living.

but improved, while the legs then became involved and grew worse. In two cases the *genitals* were affected early, in one of them perhaps first, in like manner. With the numbness of this region an early loss of sexual power was associated. Drawing the finger along the penis caused an "electric thrill," like that sometimes seen in the hands under similar conditions. The loss of sexual power above referred to was preceded by herpetic eruption on the penis. In another case²⁰ (male patient), in which the blood examination likewise showed changes in size, shape, and number of the erythrocytes characteristic of a profound, if not a pernicious anemia, the *tongue* felt "numb" and as if a foreign body was on it, and there was a sense of constriction about the chest, although the illness had not yet reached so high a degree as even to prevent the patient from following his usual employment. Two other patients (females) had a similar involvement of the tongue, associated in one with "choking sensations," and slight impairment of swallowing and of speech. Bulbar symptoms of such sorts as these may, indeed, occur both early and in a serious form. Thus in one important case (with very serious blood changes) choking sensations, with difficulty in breathing, and both motor and sensory involvement of the lips (as well as of the limbs), came on near the onset and assumed a threatening character, but fortunately subsided later, after which the affection assumed its more usual form and course.

Sudden onset or rapid increase of numbness is occasionally seen, affecting one or another part, and on the other hand it may improve slightly or even pass away for a time, or recur, in the early stages, intermittently. The distress from this paresthesia, especially when it was felt as intense cold, or as like the burning of frost-bites, was sometimes extreme, and indeed almost unbearable without morphine.

Micturition may be involved early, in slight measure, and this symptom, too, is liable to variations in intensity or may temporarily disappear, as in tabes. Many patients complain early of *increased frequency of micturition*. Disturbance of the *rectal sphincter*, though met with, is not common until later in

²⁰Patient still living.

the disease, when it occurs in connection with paraplegia of the legs.

Reference has already been made to the *mental instability* exhibited by some of these patients, and to the fact that it is usually an exaggeration of native traits. It may be added that in one case (a typical pernicious anemia) this exaggeration reached an extravagant and almost unendurable degree. An examination of the brain in this instance (see Dr. Taylor's report, Case V) showed no changes of importance beyond those due to the very profound anemia in which the patient died. This fact is noteworthy, since, while mental symptoms have been repeatedly met with in pernicious anemia, but few reports have been made of anatomical studies of the brain.

I have recently seen for the second time (in consultation), after an interval of a year, a typical case of this series, with motor and sensory symptoms varying in intensity, but gradually getting worse, where mental changes of peculiar character had developed, though the spinal symptoms, though severe, had not reached the stage of complete paralysis. This is one of the cases where diarrhea had been prominent, and it was in convalescence from an attack of this that the patient became more or less incoherent (with relatively clear intervals), talkative, and noisy, delirious and even violent, and had spells of shivering and even, apparently, of complete unconsciousness, with rigidity. Extreme emaciation, incontinence of urine, and failure of strength, but without paraplegia and with but little fever, soon came on, and the patient died in exhaustion after a few weeks' illness.

Atrophy of the optic nerve, which was observed by Bastianelli and by Russell and his colleagues, was present in two, or perhaps three, of my cases. I will also mention one more case, probably of this sort, as perhaps indicating that the optic atrophy may occur as a very early symptom. The patient is a lady of sixty-six, energetic but never strong, always a sufferer from "stomach troubles," and weakened recently by an attack of pneumonia. On account of failing vision she consulted Dr. B. Joy Jeffries, who found $V = 20/32$, after correction of refraction, and relatively white disks, and kindly referred her to

me. She gave a history of slight paresthesia of the hands, feet, and tongue (as in other cases see below), where it had begun, and examination showed slight exaggeration of knee-jerks and wrist-jerks, and slight tremor of the head. There was no nystagmus, scanning speech, or intention-tremor of the hands, and no Romberg symptom, though a friend had noticed unsteadiness of gait.

In two cases *epileptiform attacks* occurred. In one they were very limited in number, and came on towards the latter part of the spinal disease (mental eccentricity was also present, and pigmentation of the skin); in the others they had occurred at intervals since the patient's fifteenth year of age.

The all-important problem of *etiology* admits of a solution only within narrow limits. An inheritance of feeble nutrition, special tendencies to disease of the sort in question, anxiety, overwork, gastro-intestinal disorders, perhaps metallic poisoning; such influences as these form a body of predisposing causes, the action of which we can in a measure guess at. Then come certain exciting, possibly localizing causes, which deserve mention. One patient, a physician, now considerably improved, but whose blood gives distinct evidence of primary anemia, found his hands numb for the first time immediately after a fatiguing obstetrical operation. In another case, where the anemia was also profound, though secondary, and the nervous symptoms progressive, the latter began during a severe post-partum hemorrhage, with which the disease, as a whole, was apparently ushered in. If all these influences are classified, they seem to fall into (1) those which lead to the introduction of poisons, among which the gastro-intestinal disorders are prominent; (2) those which induce lack of resistance on the part of the tissues to the action of these poisons, perhaps in the several senses indicated by Adami; (3) those which cause a native weakness of these special parts of the nervous system; (4) those which bring a special strain on the same parts, though just what the nature of this strain may be it would be guess-work to define.

The striking *absence of syphilis* from the histories of these patients has already been alluded to, and is of especial impor-

tance as accentuating the contrast between this disease and tabes, and the importance of that form of infection, not, indeed, as the sole cause of the latter affection, but as a frequent partial cause.

The relative predisposition of *sex* has also been noted above.

Finally, the great frequency with which prolonged *anxiety* and *worry* recur in the patients' histories leads one to realize anew the part mental influences play in regulating for good or evil the nutritive processes of the body.

The *duration* of the illness or of the patient's life seems to be very variable, and in view of the fact that in most of the cases reported some years ago by Lichtheim, Minnich, Nonne, etc., which were mainly examples of pernicious anemia, the nervous symptoms gained ground rapidly and led quickly to a fatal termination,²¹ while other cases have been of long duration, it appears reasonable to assume an acute and a chronic form of the disease, or else to assume that we have really to do with two different but kindred affections (as indicated above).

In thirty-eight cases I have been able to complete the histories up to date or up to the time of death. The hitherto fatal cases are seventeen in number, and of these, four were cases of pernicious anemia. The duration of life after the onset of the nervous symptoms²² was as follows:

(A) *Cases With Pernicious Anemia.*

Less than one year.....	2 cases
Between one and two years.....	1 case
Between two and three years.....	1 "

(B) *Cases Without Pernicious Anemia.*

Less than one year.....	1 case ²³
Between one and two years.....	4 cases
Between two and three years.....	5 "
Between three and five years.....	2 "
More than five years.....	1 case ²⁴

Of the patients who are still living, a good many have had symptoms for three to five years, and a few even longer.

In the analysis by Russell, Batten, and Collier (*l. c.*) the

²¹So also in some of the cases in my earlier paper, especially Case I, though not necessarily instances of pernicious anemia.

²²Subject to slight errors.

²³This patient was a woman 71 years old.

²⁴This patient had symptoms, consisting at first of paresthesia, later of ataxia and progressive weakness, for 13 years.

fatal ending was found to be the sequel of complete paraplegia. Doubtless this sequence is common, and perhaps the rule. Nevertheless, several patients²⁵ of the present series died from exhaustion or from an intercurrent disease before the paralysis had become complete.

Course of the Illness.—In the great majority of cases the patients grew worse steadily, or with trifling remissions from time to time, and this is usually true, as various other observers have noted, even when the accompanying anemia or other nutritional disorder has become temporarily less.

On the other hand, striking and prolonged remissions are sometimes seen, occurring spontaneously, though perhaps aided by treatment.

Furthermore, there is one special outlook for therapeutics which my experience shows to be of very great importance, namely, in the educational treatment of the ataxia by the method of Frenkel.

I give three outline histories to verify these important statements:

Case I.—A lady, fifty-one years of age, the patient of Dr. Henshaw, of Cambridge, to whom I am indebted for the later history, consulted me in August, 1898, on account of general lack of nervous endurance and sense of extreme exhaustion, and especially for a "stiffness," weakness and numbness of the feet and legs, and to a less degree of the hands. She had a sense of severe constriction or "tightness" down the backs of the legs and round the knees, which was particularly troublesome after she had retired for the night, and a feeling of rigidity of the muscles which was so great that walking out of doors cost her great effort. The abnormal sensations in the hands was of especial interest, from the fact that—as in other cases—their intensity varied much more than one can assume the actual neural depreciation to have varied. This patient had never been robust, though always cheerful and capable of enjoyment. She was naturally thin and spare, weighing usually about 115 pounds. Her family history seemed unimportant, and she had had four children, all of whom were said to have good health. For ten or fifteen years before her illness began she had had much cause for worry and anxiety about her

²⁵Only 4 died under my own observation, and I am dependent for information respecting the mode of death of the rest on the reports of their physicians and relatives.

domestic affairs, and this was the harder to bear from the fact that before her marriage she had been free from care and responsibility. Nine months before I saw her she had begun to have tingling in the hands, and this had continued ever since, although of late it had been less intense. The feet and legs had then become involved, and the symptoms relating to them soon became more serious than those in the hands, though at one time the latter had been so much affected that she was unable to pick up a pin without great difficulty. This pricking sensation was mainly confined to the palmar surfaces, and reached as far as the roots of the fingers. When these surfaces were rubbed it gave a feeling as if stung by nettles. The patient was put on tonic treatment, and was also recommended to Dr. R. W. Lovett in the hope that she might walk the better for careful treatment of the feet and muscles, and this proved to be the case. She improved steadily, and after about six months or less called to tell me that she felt entirely well. Unfortunately, this gain was not of long duration. After a few months the symptoms started up afresh, apparently in consequence of renewed anxiety. This time the hands were but little involved, but the legs became rapidly weaker, until very soon she was wholly paralyzed as regards both sensation and motion, and had incontinence of urine and feces. She was then transferred to the Adams Nervine Hospital, where she died some months later, two years from the beginning of the illness. During the last two or three weeks of her life her mental condition became much impaired. She would call out and even scream for persons who were perhaps in the very room, and ask to be turned in bed every few moments. In spite of the paralysis of sensation, she suffered much from discomfort which was referred to the lower extremities. There were no contractures, the paralysis being flaccid and complete. Death occurred apparently from exhaustion. No autopsy was obtained.

Case II.—Showing marked improvement under treatment for co-ordination.

The patient is a lady of thirty years, of slender build, weighing habitually only 105 to 110 pounds. She is married and has three children, two of them being twins. In connection with these confinements she had considerable uterine hemorrhage, and since the birth of the last child her health has not been as good as before. Four years ago she had jaundice for a week or two. She is of a worrying temperament, as she says her mother was before her, and has had a good deal of cause for anxiety on account of prolonged illness in her family. Her mother is of a nervous temperament, and walks, it is said, with

an ataxic gait. This difficulty in walking, it seems, began a good many years ago, but has been much worse for four years, since an attack of "rheumatic fever." Before that it was hardly noticed.

One year before her first visit to me this patient began to have blurring of the eyesight, although no error of refraction was discovered by the oculist who then examined her. This impairment of vision has continued to trouble her, so that she has difficulty in threading a needle and sometimes even in recognizing her friends as they pass on the street.

Soon after this, that is, nine months or more ago, her gait became somewhat ataxic, and at about the same time—perhaps in consequence of the impaired control—she fell and broke her arm.

At one time she had a strong sense of constriction about the thighs, midway between the knee and hip, and soon after the difficulty of walking was first observed she had a sense of numbness in the hands and arms, and some degree of actual impairment of the touch sense in the fingers; now no longer present.

On physical examination she was found to have static and motor ataxia of both upper and lower limbs, slight in the former, but strongly marked in the latter, so that it caused her serious inconvenience in walking.

Ophthalmoscopic examination showed a paleness of the disks, especially the right, the vessels standing out with undue sharpness. Vision was impaired at least one-half. The wrist, knee, and ankle reflexes were all somewhat exaggerated.

For the treatment of the ataxia, the patient was placed under carefully supervised gymnastic treatment, and although it is but three months since this was begun, the results have far exceeded my expectation. The patient has acquired a skill and confidence such that to a casual observer her gait would almost pass for normal.²⁶

I will say, in passing, that my experience in the treatment of true tabetic ataxia by this method leads me to think that it affects something more than a simple improvement in co-ordination. The paresthesias also are sometimes less complained of, and it may be that something is done toward a real arrest of the disease.

I am encouraged by this thought to recommend suitable gymnastic treatment even when no marked inco-ordination is present. The restoration of functional activity is the end to be sought at all hazards.

²⁶This patient grew worse again later, and is failing, but another in same condition has maintained her improvement for several years.

The histories of the cases followed by autopsy are given in brief in the latter portion of this article.

In glancing over these clinical histories, especially with the post-mortem findings in mind, two or three conclusions strike one as being almost inevitable. Firstly, it seems clear that we have to deal with a fairly definite form of disease, almost as definite as tabes, though with a somewhat less rich and varied symptomatology. In using the term "disease" for both these affections, we mean to imply that they represent, as it were, special "plans of cleavage," or modes of dissolution of the nervous system. Even if the morbid changes are due to a poison, nevertheless they imply, too, a definite construction, and definite liabilities of the nervous system, such as would make it react in almost the same way to a variety of (toxic?) causes.

Secondly, the question might be raised whether the progression of the disease implies the continuous action of some toxic agent. It does not seem, as a matter of fact, absolutely necessary to assume this to be true. One may imagine that if the first injury suffered by the nervous system interrupted the normal play of important functions, that very lack of functional activity itself might lead to further degeneration, and so on. To these interacting and mutually reinforcing causes of increasing decay would soon be added, of course, the unfavorable conditions of local nutrition due to the process itself acting on neighboring parts, and also the unfavorable conditions arising from the failure of general nutrition.

Finally, while we are ready to admit that the grouping suggested by Bastianelli, as well as by Russell, Batten and Collier, is useful as a working principle, and perhaps corresponds to certain real clinical and anatomical peculiarities; yet we cannot admit, with the latter authors, that the spinal degeneration attendant on pernicious anemia ought not to be classed with the chronic sub-acute degenerations such as they and we mainly describe. On the contrary, it seems to us that, whether one looks at the cases from the standpoint of the degree of the anemia, or of the duration of the spinal symptoms, or of the intensity and nature of the anatomical changes, gradations between the two groups referred to are everywhere apparent.²⁷

²⁷It is perhaps true that a loss of knee-jerks is more likely to occur early in the pernicious anemia cases.

If the spinal changes occurring in pernicious anemia do not belong in the same group with the others, the question would immediately arise where they do belong. For they, too, are certainly of toxic origin, and a study of them cannot fail to throw light on the other sub-acute degenerations of analogous character.²⁸

As regards *treatment*, we believe the essential point to be the *restoration of functional activity* so far as that is practicable, especially by graduated gymnastics.

(To be continued.)

²⁸Since the above paper was sent to press a case has come under my care which seems to me to bear out and illustrate the statement given in the text as to the relation between the spinal degeneration attendant on pernicious anemia and the subacute form associated with general cachexia or even occurring without any disorders of nutrition.

The patient is a lady sixty-nine years old, small in stature like many of the patients referred to above, and never robust, and with two daughters, of whom the same statement might be made. For ten or twelve years, that is, for a period which began apparently with the illness and death of her husband, after a distressing sickness, she has been particularly ill, though even previous to this her health had been impaired by a series of debilitating attacks of some inflammatory affection of the face, which recurred year after year. Two years ago she had an illness called the grippe, and at this time the anemia began to assume a distinctly pernicious character and the spinal symptoms also began to show themselves in the usual form of paresthesia of the fingers.

About a year ago the blood was examined by an expert pathologist, Dr. Mark W. Richardson, and unequivocal signs of pernicious anemia were found.

Except for slight and temporary improvement both sets of symptoms have been progressively increasing, so that now the patient is almost confined to the bed or chair, and presents a bloodless appearance and well marked anemic heart murmurs. The knee-jerk is absent on each side.

It will thus be seen that while the case is obviously one of pernicious anemia, the spinal symptoms have been of two years' duration while the early history of the case justifies the placing of it in the same category with a number of the others on which the statistics of the paper were based. It resembles, for example, Case IV of those reported with autopsy, although, unfortunately, in the latter, no blood examination was made during the later part of the patient's life when the anemia had become very great.