tanum is pain in the suprapubic region. General practitioners have for a long time recognized that pelvic inflammatory lesions in women produce a wide range of referred pains, but there has not been a realization in the past that an even greater number of referred pains come from diseases in the male pelvis.

DR. WALTER BIERRING, Des Moines, Iowa: An instance of rather unusual results following a local infective focus in the prostate recently came to my attention. A traveling salesman sustained a rather simple injury, a blow on the thigh, after which the following sequence of changes occurred: He developed a typical femoral phlebitis of the left leg, followed by a local abscess formation, which was incised and the exudate permitted to drain. Three or four weeks of general septicemia followed and then death. There was a claim for accident insurance because of the local injury. At the necropsy a deep-seated abscess of the prostate, showing diplococci, was revealed. In addition, another interesting fact which was brought out by Dr. McCrae was a marked fibrosis of the myocardium, which also could probably be attributed to this latent prostatic infection. There had been a Neisserian infection five years before.

DR. W. O. BUDGES, Omaha, Neb.: One effect of disturbance of the prostate, which may be overlooked, has come under my observation within the last three or four years, with reference to several cases of abdominal tumor, dependent on obstruction of the prostate. The patient voided his urine apparently to his own satisfaction, but the residual urine eventually caused a tumor, which finally became distinctly palpable. I did not use the catheter, on the ground that the patient was able to pass 8 ounces of urine, in my presence, without any effect on the tumor of the abdomen. Two or three days later, a catheter was passed and the tumor entirely disappeared. When a catheter is passed into the prostate, in cases in which sufficient accumulation in the bladder has occurred to produce a good-sized tumor, it is surprising how much urine can be withdrawn without having much effect on the bladder. The reason is that for several weeks, or perhaps several months, the tumor has resulted in such back pressure of the urine in the kidneys that the urine drained down in the bladder about as fast as it was removed, up to a certain point. This is probably the reason for our failure in many of these cases. I recall one case in which the patient had a tumor for four months, and operation was recommended. He finally went to the hospital, the diagnosis of prostatic obstruction was made and the entire tumor was removed by the use of the catheter.

DR. J. M. ANDERS, Philadelphia: Dr. McCrae has called attention to certain causes of neurasthenic conditions that have been, to say the least, neglected by general practitioners in the past. He has well said that a most careful history is an important matter in the study of these cases. I have learned from experience one fact to which I wish to call attention, namely, that, in the absence of symptoms referable to these organs and in the absence of the history of a gonococcus infection, it will not do for the internist to exclude diseases of the prostate and deep urethra as a cause of neurasthenic states. The specialist knows that either arthritis or prostatitis may be caused by other organisms than the gonococcus, for example, *Streptococcus pyogenes*, *Staphylococcus pyogenes*, *aureus*, *albus* and *Bacillus coli communis* and others. The absence of a history of specific or gonococcus infection of the urethra is not proof positive that lesions do not exist which may cause, as I know from experience, reflex symptoms, particularly referred pains in the back.

Plague Universally Endemic.—The disease [plague] is endemic on every continent in the world and in practically all countries, excepting, possibly, those of continental Europe. In our own country any laxity of sanitary surveillance of the endemic centers on the Pacific coast would result in the broadcast spread of the disease. The same will apply to all endemic centers. It is a question of eternal vigilance.—R. H. Creel, *Pub. Health Rep.*

SOME NERVOUS SYMPTOMS OF PERNICIOUS ANEMIA *

C. EUGENE RIGGS, A.M., M.D.

ST. PAUL, MINN.

About seventeen years ago my attention was especially attracted to the distinctiveness of the nervous symptoms occurring in pernicious anemia, and at that time I reported a case before the American Neurological Association in which the pathologic findings were those of a subacute combined degeneration of the spinal cord. At this time I called attention to the fact that the sclerosis was apparently vascular, not systemic in origin. Stengel has stated that this type of anemic patients give the highest blood-count. Bramwell in 1910 reported a case in which the nervous symptoms were characteristically those of disseminated sclerosis and in which the cord symptoms developed three years before the anemia became marked, and he emphasizes the fact that the nervous phenomena may occur a long time before the anemia or cachexia which precedes or accompanies the degenerative changes in the spinal cord. This also has been my observation. Not only is the blood-picture not typical of that in pernicious anemia, but the nervous symptoms usually precede for months or sometimes even years the blood-findings characteristic of this disease. In Bramwell's case before mentioned the anemia was so slight that no blood examination was made and it attracted attention and became a feature of the case only a few weeks before death.

Some years ago I saw a patient in whom the clinical syndrome was that of a chronic myelitis; the nervous manifestations overshadowed by more than two years the typical blood-findings of pernicious anemia. Not infrequently the symptoms resemble those of a transverse myelitis or of a multiple peripheral neuritis.

According to Strümpell the nervous symptoms are similar to those of tabes; other writers compare them to ataxic paraplegia. It is an interesting fact that the nervous syndrome may be entirely wanting and yet there may be involvement of the spinal cord. Spiller has shown that the degenerative process may extend into the brain axis.

These symptoms may be purely subjective, such as numbness in the arms and legs. One of my patients complained that the bones were going through the flesh. According to Putnam paresthesias are strikingly noticeable. Knee-jerks may be normal, absent or exaggerated; ankle-clonus and the Babinski reflex may or may not be present; paraplegia may be partial so that the patient may move the legs freely in bed, or it may be complete. Associated usually with this is a loss of control over the bladder and rectum. Lightning pains and objective sensory disturbances are common. Wilson recently reported a case in which gastric crises were present. Dissociation, as in syringomyelia, has been observed. Dimness of vision is quite frequent and occurs early. Optic neuritis, optic atrophy, and hemorrhages associated with retinitis are occasionally seen. Mentality is as a rule unimpaired, although psychotic symptoms have been reported. Camp and others have described cases in which the mental symptoms and signs of paresis were clearly marked.

Dr. Addison, of suprarenal capsule fame, first described (and his description remains classical until

* Read in the Section on Nervous and Mental Diseases of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

to-day) a fatal and apparently causeless anemia which he designated idiopathic anemia, and it was while exploring pathologically the bodies of these patients to find the cause of this disease that he discovered the remarkable lesion which is basic in what we now know as Addison's disease. Dr. Pepper taught that this affection is fundamentally a disease of the bone-marrow, the most important red-blood-making structure. On the other hand, Dr. William Hunter contended that pernicious anemia was caused by an excessive destruction of the red blood-cells in the portal circulation, demanding of the bone-marrow an extreme effort, and in these cases, White tells us, the marrow is red like fetal marrow and is evidently in a state of great activity and "that in its hurry to cure the disease it is constantly pouring into the blood immature forms of red cells such as megaloblasts and normoblasts, poikilocytes and red cells staining badly, which give blood films so characteristic of pernicious anemia."

The ultimate cause of pernicious anemia is most likely a toxin absorbed from the gastro-intestinal tract, but as to the exact nature of this toxin we are entirely ignorant. This supposition affords us a plausible reason why in certain cases the nervous symptoms precede by so long a period those of the blood-picture, the time incidence in either case depending on the point of initial attack by the toxin. Marie's suggestion as to the anatomic arrangement of the pial blood-vessels would account for the occurrence of the combined lesion. Its relatively poor blood-supply in health would probably make the dorsolateral cord particularly susceptible to degeneration in abnormal conditions (Taylor). Certainly such an environment is favorable, and as to the selective affinity of toxins, who can say?

The following cases are a fair illustration of the nervous syndrome occurring in pernicious anemia:

CASE 1.—Miss K., aged 55, no nervous heredity, never robust but always well until fourteen years ago, when she had a nervous breakdown, was ill for two months. Two years ago she began to suffer from insomnia and loss of appetite; she complained at this time of a stuffed, bloated feeling in the stomach. She was very nervous and despondent and has continued so until the present time. Vertigo has been constant, worse in the morning; there has been continuous headache, the pain extending from the nape of the neck over the head to the forehead. Her eyes feel "as if they were pushed down." She complains of pain in both heels and small of the back, from which it extends to the front of the body and down the anterior aspect to both extremities. There is a burning sensation in the heels as though they were on fire and there is a constant shooting pain in the soles of both feet. Shortly after the legs and feet became affected she began to suffer pain in the hands; it extended up the arms, most severe between the hands and the elbows; it is intense and is of a burning, stinging character. Everything she touches hurts "as if she were touching hot glass." This pain is continuous, never lets up and seems to be steadily increasing. A year and a half ago she first noticed that her walking was unsteady and that when she attempted to wash her face she would almost fall over; she says that her legs feel as if they were wooden and did not belong to her. There is a marked weakness in both lower extremities and she finds it very difficult to arise from her chair without the aid of her hands. There is Rombergism; knee-jerks and Achilles jerks lost; the plantar reflexes plus; superficial reflexes all present with the exception of the gluteal; tactile sense impaired from below the umbilicus. Cold normal, heat exaggerated in the same area; urine normal. Hemoglobin 62 per cent, red blood-cells 4,061,000, white blood-cells, 4,112; color index .8; blood-picture normal, blood-pressure 130 mm. Hg.

CASE 2.—Mrs. O., aged 61; father died of pneumonia in his sixty-ninth year, mother of senility in her eighty-sixth year; three brothers living and well, two dead, one of diphtheria, one of acute Bright's disease; three sisters living and well, two dead, one of tuberculosis, one of apoplexy. The patient has had ten children of whom seven are living and well; one died of diphtheria, two died at birth. Climacteric at 48. For the past twenty years she has had a winter diarrhea. She began about five years ago to stumble in the dark. Although the weight is normal, yet there has been a progressive loss of strength; three years ago she noticed that she would tire very easily when walking up stairs; this effort was accompanied by rapid heart action. She complained of "rocking" feeling in the head. She has had three sinking spells lasting about a minute each time, but did not lose consciousness. The legs have grown steadily weaker and there is marked ataxia. She has been confined to bed since November, 1912. Lately she has had difficulty in starting the urine. There is a girdle sensation around the abdomen and a numb feeling in the legs to the hips and in the hands to the elbows. There is partial loss of tactile sense from the umbilicus downward. The loss of sensation in the upper extremities is more marked in the palms of the hands. Patient has a yellow color but says she has had this all of her life. Her eyesight has been poor for the past fifteen years.

When examined January, 1913, she was confined to her bed, would lose her legs in bed; there was marked Rombergism, knee-jerks normal, urine normal, hemoglobin 81 per cent., red blood-cells 3,584,000, white blood-cells 3,571, color index 1.1, no nucleated reds but poikilocytosis was marked.

CASE 3.—Mr. A., aged 53; father died of myocarditis in his fifty-seventh year, mother of apoplexy in her sixty-eighth year; a brother killed himself; two sisters are living and well. The patient had diphtheria in his twenty-second year. He denies venereal disease. In 1900 he first noticed that fluid began to gather in the knees and wrists, also in the ankles (hydrops articuli); the accompanying pain was intense. In 1907 he developed arthritis deformans. His face is a lemon color; this has been increasing during the past eight months. Paresthesia in the hands and lower extremities. Impaired sensation (tactile) in both arms from elbows to finger-tips, and in the legs from the lower level of the buttocks down. Aside from Rombergism the neurologic examination was negative. The hemoglobin was 36 per cent., red blood-cells 2,120,000, white blood-cells 5,130, color index 0.9; poikilocytosis, blood-pressure 180 mm. Hg; urine, albumin with granular and hyaline casts. This is the second case I have seen this year in which nephritis was associated with pernicious anemia.

CASE 4.—R., patient of Dr. Hammes, aged 42, mother died of apoplexy in fifty-fifth year, father of senility in his seventy-sixth year; five brothers living and well; one died of chronic nephritis; one sister living, but is asthmatic. The patient had acute articular rheumatism in his fifteenth year. No history of venereal disease. Five children living and well. About three years ago he began to suffer from numbness and a burning sensation all over the body. For the past eight months he has gradually grown weaker, bedridden for three months. In the last three weeks memory has failed notably. At present there is pain associated with cramp in both legs. During the last year the patient has suffered from alternating attacks of diarrhea and constipation. He can move his legs in bed with difficulty. There is marked ataxia, Babinski reflex in both feet and an impairment of all forms of sensation below the umbilicus. Hemoglobin, 46 per cent.; red blood-cells, 2,116,000; white blood-cells, 5,718; color index, 1.1; urine normal.

CASE 5.—Mrs. H., aged 71; father died of cardiac disease, mother of senility in her eightieth year; five brothers living and well; one died of diphtheria; one sister living in frail health, two sisters dead, one of apoplexy, one cause unknown. Two children living and well; two died at birth; there were two miscarriages; one child died of diphtheria. Patient always well; climacteric at 48. Suffered from chronic constipation. In May, 1912, she first noticed difficulty in using hands. A cold sensation soon developed in all four extremities, also a

tired feeling and loss of power. Patient gradually grew worse and she complained of a distressing numb sensation in heels and knees. There was at times tremor of right arm when trying to feed herself; also aching in the joints, especially of the wrists and in the bones of the forearm. There was a rapid loss in strength and weight. Diarrhea without any apparent cause occurred about every ten days. Profuse night sweats. The pain was so severe and so constant, with marked tenderness over the nerve trunks, that she was supposed to be suffering from multiple neuritis and was sent to us for treatment of that disease. Deep and superficial reflexes normal, urine normal. Hemoglobin, 62 per cent.; red blood-cells, 2,408,000; white cells, 4,280; color index, 1.3; marked poikilocytosis; nucleated reds were present.

Because leukopenia was present in all three cases it is well to recall Turk's statement that in pernicious anemia you must have leukopenia associated with the red blood-cell picture. While there is great reduction in both the red cells and the hemoglobin, this is proportionately much larger in the former, and hence each cell in order to compensate for their paucity has to carry an excess of hemoglobin. A higher color index therefore may be looked on as the constant of pernicious anemia and may be regarded as Nature's attempt at a cure (White).

The direct relation of the nervous syndrome to a diffuse primary non-systemic degeneration, occurring mostly in the spinal cord, has been definitely and clearly established. In my own case, reported before the American Neurological Association in 1896, these changes were most noticeable in the middorsal region; from this point they steadily decreased, ceasing at the third lumbar segment. Commonly the nerve roots, peripheral nerves and the gray matter escape; yet a number of cases have been reported in which the anterior horns were involved. The affection of the blood-vessels is usually slight. This degeneration is, without doubt, due to a variety of toxic causes, namely, toxins from the gastrointestinal tract, poisons, metallic and vegetable (ergot of rye). Without doubt also this pathologic process may occur in persons with a deficient initial life-impulse in whom degenerative tendencies manifest themselves early. Anemia may precede, associate itself with, or follow diffuse degeneration of the spinal cord, but in many instances, notably the cases of Russell, Batten and Collier, there was nothing in the blood to suggest pernicious anemia. In pernicious anemia the anemia, like the cord changes, is a direct result of the toxin, be it a germ toxin or a chemical one, we do not know which. Probably in each instance the personal equation determines whether the pathologic process be a pernicious anemia with or without cord lesion, or a diffuse degeneration of the spinal cord simply. The ultimate facts are that there is a nervous syndrome frequently found in pernicious anemia dependent on a diffuse, non-systemic, primary degeneration of the spinal cord, that this syndrome may antedate by months or even years the characteristic blood-picture, and that both the anemia and spinal cord changes are the resultants of toxic influence. Contrasted with this must be the nervous phenomena incident to subacute, combined degeneration of the spinal cord with which pernicious anemia is not associated.

Byrom Bramwell, in 1874, was struck with the fatty condition of the heart in pernicious anemia, and as he had observed that arsenic was beneficial in cases of fatty heart, he commenced its use in this disease. In 1910 he began the use of salvarsan and has since treated eleven cases with it. Of these four have been apparently

cured (remission?), two were strikingly benefited, one case improved at first with ultimate relapse and death, and another patient became somewhat better, but died of pneumonia while under treatment; yet another patient is slightly improved, but still under his care at the time of writing (May 24, 1913), while two patients received no benefit whatever. He regards the intramuscular injection of salvarsan as the best method of administration because it will produce a sustained and continued effect, and he thinks its use in this form much superior to the ordinary arsenical treatment. Neosalvarsan gives much less pain and swelling, and is therefore to be preferred. He uses 0.3 gm. Life being so precarious in grave cases he considers it safer to give the smaller dose. My personal experience in the use of this drug in this disease has been somewhat limited. I prefer the intravenous method and the larger dose, 0.6 gm. In Case 2 the patient was greatly benefited under its use; her nervous symptoms were rapidly disappearing when she left the hospital and she was getting so that she could walk fairly well. Current medical literature gives very conflicting reports regarding the benefit derived from this treatment; much further observation will be necessary before we can properly estimate its true value.

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ABSTRACT OF DISCUSSION

DR. GEORGE A. MOLEEN, Denver: There has been failure on the part of most neurologists, I think, to recognize the importance of blood-changes and their influence on nerve structure. The underlying systemic condition which lowers the resistance of the nerve elements to nervous influences has not been given sufficient attention. We shall, I believe, realize that this is particularly true when we recognize the increased irritability of the nervous reflex centers and the irritability of nerve structures generally in high altitudes, where, if physical factors are considered, we must remember that the amount of hemoglobin, consequently the number of red blood-cells sent to the tissues generally, must necessarily be greater in view of the lessened atmospheric pressure. That nerve structures are vulnerable to influences under anemic states, when otherwise they would not be, has, I think, been generally accepted. For example, it is not uncommon to find that a fatigue neurosis develops more readily in an anemic person than in those persons who might be considered as presenting the antipode of the anemic condition; in other words, in plethoric individuals. About two years ago I saw a number of cases of acute combined degeneration of the spinal cord. These cases have been considered as due to, or peculiarly associated with, blood-changes similar to those of pernicious anemia. I believe, however, the fact that they follow on acute infectious diseases, has been considered of more importance in producing the anemia than that the anemia is the cause of the disease itself. Most of those cases have followed influenzal infections.

Dr. Riggs has emphasized the importance which he attaches to the anemic states as bringing about nervous diseases, and this is a factor which should be given most careful attention. It is an underlying systemic factor in rendering the nervous system of these persons more susceptible to organic change under influences commonly recognized, than that of an individual supplied with a normal hemoglobin content and a full corpuscular count.

DR. HOWELL T. PERSHING, Denver: I should like to speak of a striking case that comes in one of the groups Dr. Riggs has been discussing. The patient was an able attorney. When about 60 years of age he began to show his age with great rapidity. He became quite pale, his hair whitened rapidly, he lost a good deal of weight and the expression of his face was considerably changed. While working hard at a summer

session in Washington, he noticed especially fatigue in the legs. He could walk all right for a short distance, then rapidly became fatigued, but after a rest could get along better. A few months later I had the opportunity of examining him with his family physician. At that time he was resting mentally and having some recreation; he wanted to play golf, but could not walk enough to do that with satisfaction. I could find no sign of organic disease, although he was examined with great care. In the winter he went to Honolulu and there he probably exercised too much. He had a stormy voyage coming back, and on arriving at San Francisco showed some signs of myelitis, having lost control of his legs and showing some sensory loss. He was at that time seen by Dr. Moffett of San Francisco, and later when I saw him he had definite signs of transverse myelitis. There was motor loss and distinct sensory loss, with some disturbance of the sphincters. He returned home and improved somewhat under rest in bed. The point that bothered both his physician and myself, however, was that while we thought this must be a case of pernicious anemia, and treated it accordingly, our examinations of the blood were, as we thought, quite inconclusive. There was only a moderate reduction in the reds, down to something over four million as I recollect, and the number of whites was about normal. The color index was slightly high, about 1.1. There were no normoblasts and there was no poikilocytosis. As time went on there was a continued slow reduction in the red cells, but not enough to account for his symptoms, so far as we could determine. Then an obstacle to further study occurred. The patient's daughter had died of pernicious anemia, and he had read much on the subject and studied his daughter's case with the utmost care. He was sensitive and begged to be relieved of the frequent tests of the blood. He had a horror of everything associated with anemia, even of the simple prick of the finger, and we had to respect his wishes. Toward the last week or two of his life the anemic appearance was striking. I think it was one of those cases spoken of by Dr. Riggs, without great changes in the blood. The changes in the cord were clinically distinct. It was the ordinary type of transverse myelitis, coming on with a sharp exacerbation at the time of the Honolulu visit, afterward showing slight changes and a gradual loss.

THE SERODIAGNOSIS OF PREGNANCY *

HENRY SCHWARZ, M.D.

ST. LOUIS

In speaking of methods for serodiagnosis of pregnancy, I refer to the biologic tests of Abderhalden only, because the method of Rosenthal, while of considerable scientific interest, appears to be of small practical value. It is applicable during advanced pregnancy only, and all conditions associated with increased destruction of the body proteins respond to the same test.

Abderhalden's methods of serodiagnosis of pregnancy, on the other hand, give reliable information just as soon as the ovum is permanently implanted; these methods are based on specific reactions and they are suited for the widest application in the study of physiologic and pathologic conditions.

To appreciate the value and the scope of these methods it is essential to have a clear understanding of the underlying principles and to be familiar with the monumental work of Abderhalden on cell metabolism and on protective ferments, which covers a period of more than ten years of intense activity.

It appears that each body-cell, including the white and the red corpuscles and the blood-disks, carries on its own

metabolism; it takes up nutritive substances from the blood, digests them with the aid of various enzymes, using the end-products of the intracellular digestion for the development of energy or linking them together into complex building-stones for the development or the repair of its own body.

The protoplasm of one group of cells differs from that of other groups of cells chemically and physically; difference of function implies difference in structure. The protoplasm of renal epithelial cells differs in structure from the protoplasm of muscular fibers; glands with internal secretion, sending out substances which act on special cells in distant parts of the body, require special structure both in the cells which send out these substances and in the cells on which they act.

Such intercommunication of two or more sets of cells is made possible by the fact that the intervening medium, the blood, is, under normal conditions, of pretty constant composition, and that the physical and chemical conditions in the various cell-groups likewise remain fairly even.

Nutritive substances pass into the blood from two sources: namely, from the gastro-intestinal tract and from the body-cells; before entering the blood-stream they must be divested of all individual character and be reduced to the simple cleavage products which form normal constituents of the blood.

For the purpose of this paper I shall limit this review to protein metabolism.

Protein foodstuffs, no matter what their source, are conglomerations of amino-acids; these are joined together into small groups like the blocks in a Chinese puzzle; the amino group of the one acid is always joined to the carboxyl group of the other; these small groups are joined together to larger and still larger groups, until they form the large albumin-molecule.

So firmly are these amino-acids joined together, that nothing short of repeated blasting will separate the albumin molecule into its original building-stones; this blasting is accomplished by the ferments of the gastro-intestinal canal with the aid of water, which enters at the points of juncture, that is, by hydrolysis.

The work of reducing the albumin molecule to amino-acids is a gradual one; the pepsin of the stomach in the presence of hydrochloric acid breaks it up into large fragments, proteoses and peptones; the trypsin of the pancreas, activated on entering the intestines, reduces these large fragments into smaller ones, the peptides and amino-acids; the enzyme found in the cells of the intestinal mucosa, the crepsin, completes the reduction into amino-acids.

Substances which are absorbed from the intestinal canal must pass through the liver before they can get into the general circulation. Here they are once more closely inspected by the liver-cells and, if anything has passed that is in the least degree foreign to the blood, it is held back and reduced to a blood-own substance. The liver likewise prevents a flooding of the system with blood-own substances by holding back an excess of such substances and letting them pass on in small quantities only, or by converting them to forms which can be stored up in the body for future use.

The other source from which nutritive substances and products of metabolism enter the blood-current is from the cells of the body.

All cell protoplasm is foreign to the blood; it has been built up by the cells from the amino-acids which are blood-own and it must be reduced to its original components before it can be allowed to enter the blood.

* Read in the Section on Obstetrics, Gynecology and Abdominal Surgery of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.