



Fig. 6. Small bowel enema study, May 13, 1946, showing normal intestinal pattern with no evidence of extension of the original process.

ileum were completely filled and satisfactorily visualized in about 40 minutes. The loops of the small bowel were freely mobile and presented a normal pattern. The colon was filled to the point of the colostomy. There was no leakage of the contrast medium during the 1½ hours of study. An interesting finding was the dilated cecum and proximal ascending colon which may have assumed the functions of a reservoir, similar to the rectum in the normal defecation, Figure 5.

He was x-rayed again in May, 1946, 22 months after operation. He had gained weight, felt very well, and continued to work at his trade as a jeweler. There was no evidence of recurrence of the original process.

COMMENT

The location of the pathologic process in the descending colon and sigmoid is sufficiently rare to warrant placing it on record. Follow up two years later showed that the pathologic process had been completely removed and that the large and small bowels proximal to the colostomy were normal roentgenologically, Figure 6. Its close similarity, symptomatically, to malignancy of the bowel should be borne in mind. Particularly noteworthy was the extensive area of necrotic involvement and the widespread and advanced changes noted in the blood vessels as previously described.

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Vitamins and Hormones in Nutrition — III. Infection

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THE FIRST report¹ of this series dealt with the synergistic action of vitamins and hormones, and the influence on vitamin absorption of such contributing factors as endocrine dyscrasia, infection, gastro-intestinal disease, reduced dietary intake, emotional upset, and trauma. The effect of hormone dyscrasia on vitamin absorption was discussed in detail in the second communication². The present report, the third in the series, is concerned with the significance of infection as an etiological factor in nutritional disturbances. Observations have been based on 200 cases, as analyzed in the original communication, in 60 per cent of which infection was the significant contributing factor, ranking second in etiological importance.

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Recently, considerable data have been presented in evidence of the important role of vitamins, specifically A, C, D, and the B complex, in resistance to infection. It has been demonstrated that a relative deficiency or complete absence of the vitamin B complex from the diet will lead to deleterious effects on normal growth, gastro-intestinal function, and the nervous system, followed by increased susceptibility to certain types of infection. Unfortunately, these facts have been so exploited commercially that many physicians are hesitant to accept them, or they prescribe vitamins with grave doubt as to their efficacy. However, in view of more recent findings, this increased susceptibility to infection in the presence of vitamin deficiency has been re-emphasized, and can be regarded as a manifestation of impaired metabolic activity.

And once established, infection will interfere with

the absorption and synthesis of vitamins. This has been demonstrated by clinical data, and corroborated by well-controlled experiments. The mechanism by which this is brought about has been clarified by recent investigations demonstrating that where there is infection the metabolic rate is increased. This induces a greater demand for essential food elements which must be provided by the reserves in body tissues. The health of tissues and organs of the body depends on the normal functioning of the individual cells of which they are composed. And each cell must play its part, not only in the metabolism of food, but in the chemical reactions concerned with the utilization of hormones and vitamins. In health a constant physiological balance of the cell chemistry is maintained and is delicately adjusted according to energy requirements. Now, infection, with its possible bacteremia and usual toxemia, interferes with the normal chemical processes in individual cell metabolism, and thus alters the absorptive capacity and nutrition in that cell. Infection, especially of the chronic type, sets up a barrier which obstructs, alters, or interferes with the orderly mechanism attending the important roles of hormones and vitamins. Under such circumstances physiological balance is bound to be upset.

As time goes on the deficiency states are being recognized quite accurately by clinicians, and therapy is directed to their correction. Surgeons, following the lead of endocrinologists and internists, realize the importance of correcting any known chemical imbalance. Not only that, but they actually anticipate the failure of cell function from the effects of infections and disease processes. As a result, the preoperative preparation and the postoperative care is carefully adapted to meet any possible imbalance. Experience, especially during the past decade in both civilian and military circles³, has taught surgeons to consider their patients from this physiological point of view. In patients with infections, before considering operative procedures, the surgeon thinks in terms of sodium, potassium, chloride, and water balance. He evaluates the nutritional³ and metabolic states. Knowing that in the presence of infection there is a pathological trend in the physiology, he supplies, fortifies, substitutes or replaces the needed minerals, chemicals, food elements, vitamins or hormones. These can all be given parenterally at first if oral administration cannot be utilized. Careful physical examination, laboratory studies and clinical judgment provide the clues toward the necessary corrective or substitutive measures that should be taken.

Some ten years ago, for example, in a case of acute cholecystitis complicated by empyema of the gallbladder, the surgeon would first drain the gallbladder, and later, when the patient's condition would be more favorable, he would perform a cholecystectomy. Today, extension of the empyema would likely be checked by a course of sulfonamides, antibiotics, or a combination of both. Preoperatively the patient would likely be fortified with intravenous or parenteral saline solution, hydrolyzed proteins, plasma, whole blood, glucose, vitamin B complex, and vitamin K, in order to

anticipate disturbances of the chemical and physiological functions which might otherwise appear. This present day approach has resulted in improved surgical convalescence and end results, simply because the nutritional status is considered before operation. In this way postoperative deficiencies, with lowering of nutritional levels, can be forestalled because preventative measures thus taken protect against the disruption of the normal metabolism of essential food elements.

From this brief discussion of the mechanism of infection in nutritional disorders it is evident that the true damaging agents are the toxins of pathogenic bacteria which produce a systemic toxemia. The site, extent, and severity of the infection are significant only as diagnostic and therapeutic guides. It makes little difference where the infection is, whether it be extensive or restricted in area, acute, subacute, or chronic. The resultant toxemia interferes with or inhibits vitamin absorption and synthesis, and therefore nutritional deficiencies result. Therapy must be directed toward eradication of all infective foci, and toward restoration of individual cellular nutritional levels by proper diet and complete replacement therapy.

Replacement therapy, as employed in such cases, attempts to replace the chemical balance of hormones and vitamins, similar to the chemical balance established in preoperative treatment. By substitution therapy or replacement therapy is meant a normal, well balanced diet, plus the replacement of all metabolic factors necessary in physiological balance, that is:

1. Elementary food factors:
 - a. proteins (hydrolyzed proteins)
 - b. Carbohydrates (intravenous glucose)
 - c. Fats (lipoids of liver)
2. Minerals
3. Vitamins
4. Hormones
5. Fluid balance

complete substitution therapy must take into consideration any upset in the normal levels of these essential nutrients, and in the event of such an upset, substitution must be made for that individual factor or group of factors.

The application of these etiologic and therapeutic principles to specific cases is illustrated in the six cases selected for analysis. It will be noted that the first three cases are males, in whom the prostate gland was the primary chronic infective focus. In the search for a focus of infection, chronic foci have, perhaps, most commonly eluded recognition. The prostate has been found to be one of the chief sites of chronic infection in the male. It has been notoriously overlooked as a possible focus of infection in a great majority of cases, or, when recognized, has frequently been inadequately treated. A large group of male patients, observed by the author, had previously been treated for prostatitis. Therapy consisted chiefly of massage, and in some cases bladder irrigations had been given at the same time. These patients had been discharged as apparently cured, but subsequent examination by the author usually revealed a large boggy gland, with prostatic

smears showing only a few pus cells at first. Soon after hormone and vitamin replacement therapy had been instituted, however, large numbers of pus cells were found in subsequent smears.

The reason for this increased discharge of pus cells becomes apparent upon analysis of the factors involved. That alteration in sex hormone balance occurs at the climacteric period in both sexes has been well established. Is it not conceivable, therefore, that hormonal imbalance can be an important factor in simple hypertrophy associated with infection of the prostate gland? Moreover, it was demonstrated in the second report of this series² that endocrine dyscrasia will interfere with the synthesis and absorption of vitamins. It seems reasonable to assume, then, that establishment of the hormone vitamin balance by replacement therapy produces further drainage of pus which could not be obtained by routine genito-urinary therapy. This accounts for the discovery of further infection in a gland which had previously been considered normal.

In many of these prostatic cases further investigation may reveal other foci of infection which contribute to the chronicity of the primary focus. Among these secondary foci are abscessed teeth, subacute sinusitis, subacute hepatitis, and chronic bronchiectasis. Treatment of these secondary foci by increased drainage or surgical eradication aids materially in alleviating the primary prostatitis. Along with the direct attention to the secondary foci of infection, replacement therapy, with both vitamins and hormones, must be continuously given. Presentation of specific cases may serve to illustrate these various points.

CASE I

The first case is that of a male at the climacteric period, with tertiary syphilis, and chronic infectious hypertrophied obstructive prostatitis, which complicated an old gonorrhoeal prostrate abscess. The patient, aged 56, complained of dysuria, nocturia, incontinence and impotence of several years' duration. Severe headaches, vertigo, blurred vision, and shoulder pain had persisted for three years. During this same period the patient had observed diminished pressure and narrowing of the urinary stream, and some dribbling. Mild constipation had occurred in the past year. The past history is rather ironical insofar as the patient had experienced sexual relations on only one occasion, at the age of 28. From this single contact he contracted both acute gonorrhoea and syphilis. The gonorrhoea had been treated and the infection arrested, but he was unaware of his luetic infection until the time of the present consultation, twenty-eight years later.

Physical examination revealed a thin, well developed male. The hair was dry with extensive achromotrichia. Numerous tophi were present on both ear lobes. The pupils of the eyes were irregular, with Argyll Robertson reaction. The sclerae showed a slight icteric tinge, and were slightly injected. Slight circulatory nystagmus and moderate arcus senilis were observed. Ophthalmoscopic examination of the ocular fundi showed moderate arteriosclerotic changes with yellow pigmentation and exudate along the central vein bilaterally. Moderate recession of the gums was noted, as well as extensive leukoplakial changes of the buccal mucous membranes. A chain of cervical glands was palpated, and there were slight pulsations of the external jugular vein. There was depression of the manubrium sternum, with a rachitic rosary of the sternocostal junctions. Medium crepitant rales were heard at the base of the left lung after cough. Abdominal examination revealed a slightly irregular, firm, non-tender liver edge, palpable two fingers below the right costal margin. The spleen was barely palpable. Rectal examination revealed the prostate to be tremendously enlarged, hard, tender, the median sulcus not palpable. The skin was thickened and dry. Moderate hypertrophic changes had occurred in the larger joints. Reflexes were hyperactive, with ankle clonus and absent knee jerks. Laboratory

data revealed the basal metabolic rate to be somewhat depressed, and blood counts and blood chemistry within normal ranges. Fasting non protein nitrogen was 38 mg. per 100 cc. of blood. Microscopic examination of the urinary sediment revealed 30-40 pus cells per high-powered field. Routine blood Wassermann was positive, as were repeated Hinton and Kahn tests, as well as the spinal fluid.

Specific anti-syphilitic therapy was instituted, parenterally and orally. A well balanced diet of high protein and high vitamin content was prescribed. Thyroid extract was given to increase the lowered metabolic level. Androgen, in the form of methyl testosterone, and estrogen, in the form of diethylstilbestrol, were prescribed orally to help maintain a normal androgen-estrogen balance. The subclinical avitaminosis was treated orally with vitamins A, D, C, E, and a potent elixir of the vitamin B complex. Sodium chloride, ammonium chloride, calcium gluconate, potassium iodide, and molybdenum were prescribed orally to restore the mineral balance.

The purpose of parenteral therapy was threefold: to establish a hormone and vitamin balance more quickly, to insure proper absorption, of ingested food, and to detoxify the liver in order to prevent destruction of hormones by that organ. Liver extract, vitamin B complex, thiamine chloride, and vitamin C were given parenterally for the avitaminosis. Testosterone propionate was substituted parenterally for the androgen factor, and ketohydroxyestrone and alpha estradiol dipropionate for the estrogen balance. For a short time an anterior pituitary like hormone was administered subcutaneously to aid establishment of an androgen-estrogen balance through the gonadotropic factors of the anterior pituitary gland.

During the routine anti-luetic treatment, toxic reactions were encountered in the intravenous administration of neoarsphenamine or mapharsen. Invariably, irrespective of the dosage, nausea and vomiting developed, either during administration or immediately after the injection. An elixir of the whole vitamin B complex and para-aminobenzoic acid were added to the oral medications, and the whole vitamin B complex was given intravenously, following which toxic manifestations subsided. The action of para-aminobenzoic acid and the vitamin B complex as detoxifiers has been mentioned in previous communications of the author's^{4,5} and elsewhere in the literature.^{6,9}

Prostatic massages were given twice a week for the first few months, then reduced to once per week. Microscopic examination of the prostatic smear after the first massage revealed 0.4 pus cells per high powered field, but at the third massage 80-200 pus cells per high powered field were seen. Prostatic smears continued to be loaded with sterile pus cells for months.

At check-up examination six months after the first consultation, the patient's general condition was greatly improved. There was improvement of the force and calibre of the urinary stream, with no further dribbling. On physical examination the hair was moist and of much better quality. Retinal vessels showed considerable dilatation, and the conjunctivae and sclerae were clear. The ear lobes were almost entirely clear of tophi. The gums were firmer, and only residual leukoplakial areas remained on the buccal mucous membranes. Only a few cervical glands were palpated. Heart measurements and blood pressure were within nearly normal ranges. Heart sounds were of much better quality, regular, with decreased intensity of the murmurs. The lungs were clear. Abdominal examination revealed reduction in the size of the liver, which could now be felt one finger's breadth below the right costal margin, and the spleen was no longer palpable. The prostate was reduced to about one-fifth its original size. The skin was more moist and of better tone. There was less crepitus in the larger joints, which were more freely movable. The reflexes were less active, but pathological reflexes persisted. Blood counts and chemistry showed definite improvement. Fasting non protein nitrogen was 35 mg. per 100 cc. blood. Basal metabolic rate was +4 per cent. Urinary sediment showed 2.5 pus cells. Prostatic smear revealed 25-50 pus cells per high-powered field.

Adherence to the therapeutic regime described has maintained the patient at fairly normal levels for the past three years, with very few subjective complaints. The blood Hinton remained positive, but the spinal fluid became negative. Prostatic massages have been continued, with gradual reduction in the number of pus cells.

A complication of diseases had occurred in this first case, which had upset the nutritional balance for many years. Symptoms became more pronounced at the climacteric period and were further enhanced by a focus of infection, the prostate gland. Eradication

of the infective focus, and establishment of hormone and vitamin balance by proper diet and complete substitution therapy resulted in an improved physiological balance, even though a positive luetic blood stream infection persisted.

CASE 2

The second case is that of a 44 year old, single, white mechanic who complained of bizarre symptoms over a four to five year period. Amongst his major complaints were listlessness, fatigue, constipation, headache, backache, mental depression, irritability, gain in weight, and loss of libido. Rapidly progressive graying of the hair had been observed over a three year period. He had just completed an eight-months' course of treatments for prostatitis by a competent urologist.

Physical examination revealed an obese male, with extensive achromotrichia, dryness of the hair and skin, and ridged thickened fingernails. The upper and lower eyelids were markedly edematous, and the sclerae were moderately injected. Ophthalmoscopic examination revealed early narrowing, tortuosity and arteriovenous nicking of the retinal vessels. There were leukoplakia of the buccal mucous membranes, atrophic changes along the tip and lateral borders of the tongue, and some sponginess of the gums. The thyroid was moderately enlarged. The heart was moderately enlarged, and the blood pressure was somewhat elevated. Numerous coarse to medium crepitant rales were heard at both lung bases. The liver was palpable just below the right costal margin. The prostate was enlarged, hard, and the median sulcus could not be palpated. Hypertrophic changes and thickening of some of the larger joints was observed, as well as coarse tremor of the extended fingers, and hyperactive reflexes. Laboratory findings were within essentially normal limits, with slight variations. The prostatic smear was loaded with sterile pus cells, with no predominating pathogenic bacteria.

A well balanced diet, of low caloric value, was recommended. Oral replacement therapy consisted of an elixir of the whole B complex, small amounts of thyroid extract, diethylstilbestrol, vitamins A, C, D, and para-aminobenzoic acid. Testosterone propionate, ketohydroxyestrone, the anterior pituitary like factor, and crude liver were administered parenterally. Prostatic massages were given once a week.

Response to therapy was prompt, with frank improvement of both subjective complaints and physical findings. After three months, major symptoms had entirely disappeared, and physical examination showed decided improvement. Weight was at a normal level. There was no further progression of the achromotrichia, the hair was moist, with improved luster. Edema of the eyelids had completely disappeared, and the retinal vessels showed some increased dilatation. Small residual leukoplakia were present on the buccal mucous membranes. Lingual papillae were more pronounced, and the gums were firmer. The thyroid was smaller. The heart was normal in size, and the blood pressure was within a normal range. There was greater expansion of the lungs, with no rales heard on auscultation. The liver was not palpable. The skin was moist, the fingernails less ridged. Reflexes were more normal. Laboratory data were entirely normal.

Mention should here be made of the fact that, at the original consultation, the patient complained of pain in the inter-phalangeal and tarsal-phalangeal joints of both great toes. A tentative diagnosis of gout was made, based on a fasting blood uric acid of 6.9 mg. per 100 cc. of blood. No specific treatment for gout was instituted, but after four months of treatment, as outlined above, pain in the great toe subsided completely. The blood uric acid taken at that time, and at intervals since, has varied between 1.2 mg. and 1.8 mg. per 100 cc. blood.

During eighteen months of persistent replacement therapy and prostatic massages, prostatic smears showed clumps and areas loaded with sterile pus cells. A secondary focus was discovered in an infected molar, following extraction of which prostatic smears gradually became negative. At the most recent examination the prostate was essentially normal in size, the median sulcus palpable, and of normal consistency. For four years, now, this patient has been maintained at normal levels, with no recurrence of symptoms. At intervals oral medication has been supplemented by short courses of parenteral therapy and prostatic massages.

This second case demonstrates clearly the end result of systemic symptoms produced by changes in cellular nutrition. These changes themselves resulted from a primary focus of infection, the prostate gland, which after previous treatment had been judged to be normal. An abscessed tooth provided a secondary focus of infection, complicating the primary focus, and both foci interfered with vitamin ab-

sorption and hormonal secretion. The therapeutic approach consisted of removal of the foci of infection, and restoration of hormone and vitamin balance by adequate balanced diet, and complete substitution therapy.

CASE 3

The role of the prostate as a focus of infection in the male climacteric is still further illustrated in the third case. A white male, aged 52, had for ten years been subject to mental depression, extreme nervousness, and crying spells, which had become worse during the past four years. He complained of headaches, palpitation, flushes, sweats, paresthesias, insomnia, partial impotence, slight constipation, and increased fatigue. He had particularly noticed increased difficulty in urination, narrowing of the stream with dribbling at the end of micturition, and nocturia six to eight times. His appetite was poor, and he had lost 20 pounds over an eleven year period.

Physical examination revealed a thin, well developed, male. The hair was sparse and dry, intermingled with achromotrichia. The scalp was dry and scaly. There was moderate edema of the eyelids; ophthalmoscopic examination of the ocular fundi revealed moderate arteriovenous nicking, calibre changes and tortuosity of the vessels, with areas of dark pigmentation along the larger vessels. The lips and mucous membranes were slightly cyanotic, with large areas of leukoplakia throughout the buccal mucous membranes; there was sponginess and recession of the gums; and atrophic lingual papillae. The thyroid was full, particularly on the right, and small cervical adenopathies could be palpated. There was moderate enlargement of the heart. Heart sounds were of good quality, with extra-auricular beats, accentuation of the first mitral sound, and the second aortic sound was greater than the second pulmonic. Blood pressure was moderately elevated to 178 systolic, 110 diastolic. The lungs were essentially negative except for a few fine crepitant rales at the bases. The abdomen was of the scaphoid type. There was marked voluntary spasm, with hyperesthesia. The liver was palpable one and a half fingers below the right costal margin. The prostate was enlarged and markedly boggy. The skin was thickened and dry, the nails thickened, the hands and feet cold. There was marked crepitus in the knee and shoulder joints. Reflexes were hyperactive. Laboratory findings were at generally low levels, but the basal metabolic rate was +22 per cent, and fasting blood sugar was 193 mg. per 100 cc. of blood. The urine showed 2 per cent sugar. Prostatic smear showed 6-8 pus cells per high powered field.

The patient was placed on a high vitamin and caloric diet, low in carbohydrate content. Complete substitution therapy was instituted, consisting of an elixir of the whole B complex, vitamins A, C, D, and diethylstilbestrol, all orally administered. A course of thiouracil was given over a five month period, the dosage varying from 100 mg. two times a day to 100 mg. four times a day. Parenteral therapy consisted of testosterone propionate, ketohydroxyestrone, alpha estradiol dipropionate, vitamin B complex, liver extract, and protamine zinc insulin. Prostatic massages were given once a week.

At check-up examination six weeks later his general condition showed considerable improvement with subsidence of some of the subjective complaints, and with complete disappearance of others. There was improvement in the force and calibre of the urinary stream, no further evidence of dribbling, and nocturia only once. He had gained 3¼ pounds in weight. The hair and scalp were comparatively moist. Edema of the eyelids had completely subsided, and on examination of the ocular fundi the vessels were more dilated, with no hemorrhage or exudate. Lips and mucous membranes were of good color, and the leukoplakia were diminished. The gums were firmer, and the lingual papillae were more pronounced. The thyroid was smaller, and only a few tiny cervical adenopathies could be palpated. Heart measurements showed a definite decrease in size, the sounds were of much better quality, regular, with less accentuation of the first mitral sound. There was considerable reduction in blood pressure, 142 systolic, 84 diastolic, as compared with the original level of 178 systolic, 110 diastolic. The lungs were entirely clear. Abdominal examination revealed less voluntary spasm and hyperesthesia. The liver was reduced in size, barely palpable at the right costal margin. The prostate was somewhat decreased in size, the right lobe was more normal, with some bogginess remaining in both lobes. The skin was quite moist and of good tone, the nails firmer, the hands and feet warmer. The joints were more freely movable, with less crepitus. Reflexes were more normal. Laboratory findings in general were at high normal levels, but the fasting blood sugar was still

high at 160 mg. per 100 cc. of blood, and the basal metabolic rate was +18 per cent. The urine showed but 0.5 per cent sugar.

After six months of therapy, check-up examination revealed even greater improvement. The patient had gained a total of 10 pounds in weight. The prostate was essentially normal, with smears showing no more than 1-3 pus cells per high powered field. Laboratory data at this time revealed a normal blood and urine. The fasting blood sugar was 110 mg. per 100 cc. of blood. The basal metabolic rate was +8 per cent, thiouracil having been stopped one month previously.

A typical male climacteric syndrome with resultant nutritional changes is illustrated in this case. Parenteral and oral substitution therapy partially re-established the vitamin hormone balance, but until the prostatic focus had been cleared, complete physiological balance could not be established. The patient's general condition has been maintained at nearly normal levels over a three year period.

The three cases just described exemplify a frequently encountered primary focus of infection in the male. An infected prostate which has been present for many years, can lead to a nutritional imbalance. The following three cases, all women, illustrate unusual instances of infection, any one of which can act as a primary focus. The fifth case represents not only an unusual focus, but an uncommonly encountered organism, one which should now be searched for more frequently with the return of our war veterans from the Pacific theatre. The sixth case illustrates a complicated deficiency state resulting from multiple foci of infection.

CASE 4

The nasal sinuses were finally revealed to be the chief focus of infection in this fourth case to be presented. A 26 year old, married female complained chiefly of obesity, with a weight gain of 46 pounds over a five year period, 20 pounds having been added during the previous year. Associated with the gain in weight were the usual complaints of fatigue, anorexia, headache, backache, constipation, and frequent excessive perspiration. Her past history revealed frequent colds, with sore throat. She had noticed dryness of the hair and skin, and brittleness of the fingernails. The menstrual cycle was normal in interval and duration, with dysmenorrhea the first day. The patient was sterile. The appendix and a polycystic left ovary had been removed at age 20.

Physical examination revealed an obese, well developed female. The hair was dry and lusterless, the scalp scaly. There was slight edema of the eyelids, and pallor of the conjunctivae. The nasal septum was slightly deviated to the right. Buccal mucous membranes were somewhat pale, with leukoplakia distributed throughout. The tongue was somewhat coated, protruded in the midline, with a coarse tremor; lingual papillae were atrophic. There was hypertrophy and erythema of the lymphoid tissue of the pharynx. Teeth showed evidence of decalcification, and the gums were somewhat spongy. The thyroid gland was barely palpable, with a few small cervical adenopathies. The heart was moderately enlarged, the sounds of good quality, with sinus arrhythmia. Slight dulness at the left base, broncho-vesicular breathing, and occasional fine crepitant rales were observed at the base of the left lung. Abdominal examination was negative except for a well healed postoperative scar. Pelvic examination revealed small areas of glistening, atrophic vaginal mucosa, first degree retroversion of the fundus, an ulcerated erosion of the cervix, and thickening in the left vault probably due to postoperative adhesions. The skin was dry and somewhat thickened. Fingernails were brittle and ridged, and there was moderate tremor of the extended fingers. Other findings were essentially normal, with laboratory data within normal ranges. The basal metabolic rate was -14 per cent.

The patient was placed on a well balanced diet, of low caloric content, and small amounts of thyroid were administered daily. Under this regime her condition improved somewhat, with gradual reduction in weight to normal levels. The severity and frequency of the colds persisted, however, proving intractable to therapy. Change to a warmer climate during the winter months afforded only temporary relief. The patient went along in this condition for about eighteen months. At this time she was greatly concerned about her

sterility, and at her request a plastic operation was performed on the right fallopian tube, and salpingostomy on the left tube. In the course of the next year a severe *Trichomonas vaginalis* infection developed and was treated successfully. At check-up examinations during this period signs of avitaminosis and endocrine dyscrasia had become more evident, there had been further weight loss, and laboratory data were considerable below normal standards.

A well balanced, high caloric diet was prescribed, and parenteral substitution therapy was administered, consisting of ketohydroxyestrone, corpus luteum hormone, anterior pituitary like hormone, liver, and the vitamin B complex, in potent dosage. Under this regime, and following clearance of the pelvic infection, the patient's general condition improved, but upper respiratory infections still persisted. At this point the patient contracted a tracheo-bronchial infection, complicated by pleurisy, and right nasal antrum infection. Examination by a competent nose and throat surgeon, his findings corroborated by x-ray examination, revealed a severe pansinusitis with an abscess in the right antrum. The presence of an abscess in the antrum, along with marked thickening of the antral mucous membranes, indicated clearly that the nasal sinuses had long been the hidden primary focus of infection, even though a number of examinations and x-rays done previously had been reported negative.

Daily irrigations, with other appropriate treatments, were given by the laryngologist to clear the infected sinuses. The patient continued on a high-caloric diet, and a regime of complete substitution therapy with vitamins and hormones, consisting chiefly of thyroid extract and the whole B complex orally, and ketohydroxyestrone, corpus luteum hormone, anterior pituitary like hormone, and liver extract parenterally administered. At check-up examination six months following institution of this regime the patient volunteered that she felt better than she had in years. She had regained 10 1/4 pounds of the weight loss which had occurred during the period of infection. She had been entirely free from colds during this period, and her subjective complaints had subsided. Physical examination at this time revealed definite improvement. Her hair was moist and of good luster. There was no edema of the eyelids, and the conjunctivae were of normal color. The sinuses were clear on transillumination. The buccal mucous membranes were of good color, with only slight residual leukoplakia. Atrophic areas of the tongue had filled in almost completely, and the throat was more normal. Cervical adenopathies had disappeared. Heart measurements were within normal limits, the sounds of good quality, and regular. Blood pressure was within normal ranges. The lungs were entirely negative. Pelvic examination revealed a normal vaginal mucosa. The cervix was entirely healed. The skin was moist and of better tone. The fingernails were firmer, with disappearance of ridging. There was no tremor of the extended fingers. Laboratory data showed definite improvement, with normal blood counts, and differential smear. Blood chemistry was within normal levels. Basal metabolic rate was -2 per cent.

Here we have an example of persistent nutritional changes which at first improved only slightly under hormone and vitamin substitution therapy. Until the hidden primary focus of infection, the nasal sinuses, had been cleared, general physiological balance could not be established. But, with eradication of the infective focus, substitution therapy with vitamins and hormones was effective in restoring the body to a normal nutritional condition, which has been maintained for four years. The patient during this period has been free from symptoms, and has had only a rare, mild cold.

CASE 5

The fifth patient is an unmarried female, aged 26, whose chief complaint was paresthesias of the upper extremities of six weeks' duration. Three months previously the patient first became conscious of pressure low in the right lower quadrant, which radiated through to the back and spine, and was aggravated by bending the head forward. Paresthesias of the left upper extremity were first noticed six weeks prior to consultation. Two weeks later the patient noticed paresthesias of the right upper extremity. Muscular weakness then developed in both hands, for she found it increasingly difficult to dress herself. This was followed by paresthesias and coldness of the left foot, along with general paresthesias throughout the left side of the body. She noticed increasing fatigue, with sleepiness during the day. Her hearing had become less acute. Her appetite remained normal, constipation became more marked. Her weight had remained constant for the past two years, although a year previously

she had lost 15 pounds by voluntary dieting. She complained of intermittent headaches, soreness and bleeding of the gums, precordial pressure, and slight hacking cough. Menstrual flow had decreased in duration and volume over the past few months. She had developed headaches the last two days of the period during the same interval. One week before consultation the patient observed edema of the entire left arm which was tender to palpation. The past history was irrelevant except for a fractured nose sustained during an automobile accident four months previous to consultation. As a child, at age 4 to 5, the patient had been kept on a sugar free diet because of a question of diabetes mellitus. As far as could be determined a glycosuria had been found, but at no time had hyperglycemia been looked for. Achromotrichia had developed over a period of ten years, but became more pronounced during the past year.

Physical examination revealed a thin, well developed female, showing marked evidence of avitaminosis: dry lusterless hair, extensive achromotrichia, scaly scalp, dry thickened skin, atrophic lingual papillae, extensive leukoplakia of the buccal mucous membranes. There was edema and redness of the eyelids. Ophthalmoscopic examination showed definite haziness of the nasal side of the optic disc bilaterally. The gums were spongy, hypertrophied, and bled on slight pressure. There was fine tremor of the tongue. The pharynx showed follicular hypertrophy. The neck was somewhat rigid with limited motion. The thyroid gland was moderately enlarged, and a few small cervical glands could be palpated. The heart was slightly enlarged, the sounds of good quality, the first mitral sound was somewhat accentuated, with a grade I systolic murmur at the base. Abdominal examination revealed a slightly tender, smooth liver, palpable one finger below the right costal margin. The spleen was barely palpable at the left costal margin. Pelvic examination was essentially negative except for slight enlargement of the right ovary with questionable cystic changes. The skin was somewhat dry and thickened. The extremities were cold, particularly on the left side, with some mottling and redness of the feet. Dorsalis pedis and posterior tibial vessels were feebly palpable on the right, entirely absent on the left. The muscles of the left hand and forearm were slightly atrophied. The nails were soft, yet brittle. There was coarse tremor of the extremities, more pronounced on the left. On the left side the knee and ankle reflexes were hyperactive, and the Babinski reflex was positive. Abdominal reflexes were absent. No Kernig, Oppenheim, or Gordon reflexes were observed. Biceps and triceps reactions were two plus on the left, and the muscular power was slightly diminished on the left side. Pass pointing was found bilaterally. Laboratory findings were all at low normal, or subnormal levels, but the white cell count was elevated to 10,400. Basal metabolic rate was -5 per cent. Hinton test was negative.

One week later the patient was hospitalized, where a regime of substitution therapy was strictly followed. Oral medications included thyroid extract, the whole vitamin B complex, para-aminobenzoic acid, and vitamins A, C, D, with calcium and minerals. Parenteral therapy consisted of thiamine chloride, pyridoxine hydrochloride, liver extract, alpha estradiol dipropionate, and the whole B complex. Complete laboratory studies were repeated at regular intervals. On the third day of hospitalization there was a moderate drop in the blood counts; a lumbar puncture revealed increased initial pressure, increased pressure with left jugular collapse; spinal fluid examination showed a lymphocytic count of 20, an increase of total proteins, a negative Wassermann and goldsol reaction. After neurological consultation a provisional diagnosis of mild virus meningitis was made. Sulfadiazine was administered, and the patient's condition improved somewhat under continued therapy.

In the sixth week of hospitalization the differential smear showed 16 per cent monocytes, suggestive of agranulocytic angina, or infectious mononucleosis. At about the same time the temperature began to assume a picket fence variation with a three day cycle, that is, three days elevated, three days flat. The temperature chart became suspicious of estivo-autumnal type of malaria, although on differential smear red cells showed no plasmodium malaria. Agglutination tests for typhoid, para-typhoid, and undulant fever were negative. A therapeutic quinine test was undertaken at this time, following which the temperature subsided and finally remained normal. Despite the absence of the plasmodium bodies in the blood smears, the therapeutic response to quinine prompted a search for other possible sites which might harbor the organism. The enlarged, tender liver was not consistent with the tentative diagnosis of virus meningitis. Gallbladder drainage was performed, and the bile on both microscopic

examination and bacteriological culture revealed the plasmodium malaria. This finding substantiated a final diagnosis of chronic malaria. Quinine therapy was continued, plus gallbladder drainage, and substitution therapy was continued. Under this regime the entire picture cleared, with complete subsidence of the neurological symptoms.

Oral and parenteral substitution therapy was continued after the patient's discharge from the hospital, the regime being essentially the same as outlined at the beginning of treatment, and a well balanced, high caloric diet was prescribed. With the clearance of the infective focus, definite gradual improvement was first observed, and then a rapid return to normal health. Evidence of her restored physiological balance is provided by the fact that three months after her discharge from the hospital she contracted a mild virus pneumonia, the course of which was uneventful. Convalescence was rapid, with no impairment of physiological levels, no return of earlier symptoms, nor sequelae of any kind.

For three years this patient has been maintained at completely normal levels, chiefly on oral medications, but with some short courses of parenteral therapy. There has been no return of symptoms. At her last check-up examination she had gained 8 pounds in weight, and her general condition was remarkably improved. Her hair had a normal sheen and luster, with a decrease in the achromotrichia. There was no redness of the eyelids, and only slight edema remained. Ophthalmoscopic examination was negative. The lips and mucous membranes were markedly improved, with only a few small areas of residual leukoplakia. The gums were firm, the lingual papillae pronounced, and there was no tremor of the tongue. There was normal motion of the neck, the thyroid was normal in size. Heart measurements were within normal limits, the sounds of good quality, the rhythm regular. Blood pressure was at a normal level. Abdominal examination was essentially negative with the liver and spleen no longer palpable. On pelvic examination the right ovary appeared to be normal in size. The skin was moist and of good tone, the nails firm. Extremities were warm. Dorsalis pedis and posterior tibial vessels were palpable bilaterally. There was no tremor of the extended fingers. The reflexes were slightly diminished in the upper extremities, normal in the lower. Laboratory findings were all at normal levels, basal metabolic rate was +2 per cent.

CASE 6

The sixth case presents one of the most pronounced nutritional deficiencies in our group, complicated by several foci of infection, a marked endocrine dyscrasia, chronic gastro-intestinal disease, reduced dietary intake, emotional upset, and trauma. Classification of this case is difficult, since every etiological factor mentioned in the original communication is included but infection seems to be the principal individual factor.

The patient was a 55 year old, white, married, business woman, who complained of ill health of more than fifteen years' duration, with such symptoms as extreme fatigue, headaches, colitis, weakness, nausea, vertigo, palpitation, sweats, anorexia, dysuria, insomnia, and loss of weight. She was first seen in consultation in 1942. Fifteen years before, following a "gum infection," the patient had developed osteomyelitis of the mandible, because of which she was hospitalized for eight months. During this period surgical intervention was required on seven different occasions. Following one operative procedure, apparently in the post-anesthetic stage, she sustained a fracture of the mandible. Other complications arose when she contracted spinal meningitis of a mixed streptococcus-pneumococcus type. Later during the eight months' hospitalization she also developed mucous colitis, acute cholecystitis, acute hepatitis, and broncho-pneumonia. Loss in weight amounted to some 60 pounds.

Here we have infection, faulty dietary intake, and trauma as obvious etiological agents. Endocrine dyscrasia was a further etiological factor as disclosed by the following menstrual history. The patient at that time was 40 years old. Catamenia had become somewhat irregular, with varying degrees of dysmenorrhea. Menstrual flow had increased, lasting seven to ten days, although her normal period of flowing had been only three or four days. Persistent flushes, headaches, pruritus vulvae, mental depression, and palpitation had become increasingly pronounced over the past ten years. Thus endocrine dyscrasia of the thyro-ovarian type, complicated the case still further.

Emotional disturbance also entered into the etiological picture as can be seen in the occupational history. The patient had been engaged in many business ventures, among them conducting a small chain of hotels. The responsibility involved in this enterprise cre-

ated such severe mental strain that it added to her physical difficulties.

During the fourteen years between her hospitalization and the present consultation, the patient had felt poorly, and most of her earlier subjective complaints had persisted. For the three years directly prior to consultation, fatigue, weakness, headache, vertigo, joint pain, anorexia, abdominal distention, extreme constipation alternating with attacks of mucous colitis and insomnia had become pronounced. Extreme debility, with marked hypochromic anemia, followed the slightest infection. According to the patient she had received massive doses of iron by mouth, as well as parenteral injections of iron, arsenic, liver, and foreign protein, without correcting the anemia.

Physical examination revealed a thin, pale, hyperactive individual, with dry thickened skin, and lusterless, brittle hair. Pronounced edema of the upper and lower eyelids was seen, and considerable darkening of the skin peri-ocularly. The conjunctivae were pale and the sclerae were moderately injected. Ophthalmoscopic examination of the ocular fundi revealed slight irregularity of the discs on the nasal side, marked vascular tortuosity, arteriovenous nicking, and calibre changes of the vessels, with areas of light brown pigmentation throughout. The nasal septum was slightly deviated to the left, and the inferior turbinates were somewhat hypertrophied. Areas of leukoplakia were scattered throughout the buccal mucous membranes, and some areas were seen on the hard palate. There were marked atrophic changes of the papillae on the dorsum and lateral border of the tongue. The pharynx was red, edematous, with some follicular hypertrophy. The thyroid was full, and small cervical adenopathies were palpated. Partial ankylosis of the right temporo-mandibular joint was found. The heart was enlarged and the sounds were of fair quality, but somewhat distant. There was slight accentuation of the first mitral sound, and the second pulmonic sound was greater than the second aortic. Blood pressure was low. Slight dulness and somewhat diminished tactile and vocal fremitus was found at the base of the left lung, with numerous medium crepitant rales. The abdomen was markedly distended, with superficial tenderness. The liver was palpable three fingers below the right costal margin, smooth and slightly tender. On deep palpation there was spasm and moderate tenderness over the gallbladder. There was some tenderness along the course of the ascending and descending colon. Slight spasm with tenderness was evident at the left costo-vertebral angle. On auscultation peristalsis appeared to be markedly decreased. Pelvic examination revealed atrophic vaginal mucous membranes, with glistening areas. The uterus was of the senile type, the adnexa normal. Examination of the joints revealed crepitus in the larger joints, with pronounced Heberden's nodes at the interphalangeal joints of the fingers. The skin was thickened and dry, and there were numerous pigmented nevi throughout the body, with a large number of keratotic dark brown papillae scattered over the upper and mid abdomen. The extremities were cold, with beginning hallux valgus, and some clubbing of the fingers. There was coarse tremor of the extended fingers, and reflexes were hyperactive throughout, except for the knee jerks and abdominal reflexes which were somewhat diminished. Laboratory data were at low normal levels. Basal metabolic rate was -6 per cent.

In view of the fact that obvious nutritional deficiency had existed for fifteen years, frequent parenteral therapy was essential. This consisted of massive doses of the whole vitamin B complex, thiamine chloride, pyridoxine hydrochloride, amino acids, crude liver extracts, adrenal cortex hormone, insulin, and intravenous glucose. Small doses of endocrines were administered parenterally, namely, alpha estradiol dipropionate, ketohydroxyestrone, anterior pituitary like hormone, and deproteinized pancreatic extract. Injections were given daily for a short time, then on alternating days over a two month period, and then twice a week. Oral medication was also indicated, consisting of thyroid extract, alpha estradiol, vitamins A, C, D, E, the whole B complex, hydrolysed proteins, banana powder, decholic acid, and mineral oil.

After the first month of therapy, gallbladder drainage was done, with washings of essence of caroid and 50 per cent magnesium sulphate. Thickened, viscous mucus, black-green bile, and crystals of black bile salts were obtained. Microscopic analysis showed large numbers of mixed bacteria. Two weeks later duodenal drainage was repeated. 20 cc. of 10 per cent solution of the sodium salt of dehydrocholic acid was slowly administered intravenously, followed by 50 cc. of 50 per cent glucose, and the whole B complex with ascorbic acid 500 mg. An injection of regular insulin, Units XXX,

was given subcutaneously. The patient's response was dramatic. Before the drainage the liver was tender, its edge could be palpated 4 fingers above the pelvic brim, but within twenty minutes after the drainage an actual decrease in size and tenderness could be noted, the edge being palpable at a level 2 fingers below the right costal margin.

The patient improved rapidly following this procedure. Gastric distress, distention, and nausea subsided. Attacks of mucous colitis became less frequent. Four weeks later a second duodenal drainage and treatment was done, similar to the one just described, except that 10 cc. of a 20 per cent solution of decholic acid was used. Following this treatment the patient had no further major attacks of colitis.

After six months of treatment the patient showed a marked systemic improvement, with complete absence of her major symptoms. In the first two months of therapy she had gained 10 pounds in weight. For the first time in fifteen years her blood counts and chemistry attained normal levels, and have been maintained at these levels up to the present time. Over the past eighteen months two major infections were overcome with the aid of penicillin, with comparatively little change in the blood picture and relatively little debility. The last infection was a severe nasal pan-sinusitis which responded well to large doses of penicillin, and daily lavage of the sinuses. It is the author's belief that the sinuses were the hidden focus of infection in this case.

At her last check-up examination physical findings corresponded with the subjective improvement. The hair was moist and of good luster, the scalp clean. Edema of the eyelids had completely subsided, and fundal examination revealed no increase in arteriosclerotic changes of the vessels. Nasal turbinates were more normal. Lingual papillae were more pronounced, a few atrophic areas still remaining at the tip and lateral borders of the tongue. The thyroid was smaller, and only a few small cervical glands were palpated. Heart measurements were nearly within normal range. Heart sounds were of good quality, regular, the first mitral sound was only slightly accentuated, and the second pulmonic and second aortic sounds were equal. Blood pressure was at a more normal level. The abdomen was soft, with no tenderness nor distention. The liver edge was barely palpable at the right costal margin. Peristalsis was normal on auscultation. Pelvic examination revealed more normal vaginal mucosa. The joints were more freely movable, with somewhat less crepitus in the larger joints. The skin was moist and of good tone. There was a reduction in the number of verrucous papillae on the abdomen, and a marked lightening of the brown pigmented nevi. Extremities were warm, dorsalis pedis and posterior tibial vessels were forceful on palpation. There was no edema of the extremities, and no tremor of the extended fingers. Reflexes were essentially normal. Laboratory data showed definite improvement. Basal metabolic rate was +2 per cent.

Of particular significance in this case is the fact that a persistent mucous colitis of thirteen years' duration was entirely cleared by the prescribed therapy, with no recurrence over a two year period. This fact further emphasizes the relationship between endocrine dyscrasia, avitaminosis, infective foci, and hypoproteinemia.

The patient is now maintained on oral medication, with parenteral injections once or twice per week. At intervals injections have been omitted for six to twelve weeks at a time, but oral therapy has been uninterrupted. Recognition of recurrent mild symptoms has at times prompted the patient to voluntarily request extra "booster" injections. Recently, a whole liver factor*, with added factors of the vitamin B complex, and inclusive of the lipoids of liver, has been added to the oral medications. This new factor is regarded as an important therapeutic addition in this and similar cases, which may decrease the necessity for prolonged parenteral therapy. It has been employed for too short a time to draw any definite conclusions as yet, but clinical evidence obtained over a four-month period is most encouraging. A detailed report on this new whole liver factor will be sub-

*Material supplied through the courtesy of Rawl Chemists, Brooklyn, New York. Trade name "Rawl Whole Liver Vitamin B Complex Capsules," each capsule containing: Whole liver substance (1-5) 500.0 mgs. containing all the lipoid and water soluble B complex factors as found in whole liver; thiamine hydrochloride 1.0 mgs.; riboflavin 2.0 mgs.; niacinamide 5.0 mgs.; choline chloride 12.0 mgs.; pyridoxine hydrochloride 0.2 mgs.; calcium pantothenate 0.2 mgs.; biotin 600.0 mmcg.

mitted later, when more clinical data are available, and based on a longer period of observation.

On the basis of the six cases just discussed in detail, the role of infection in the production of nutritional disorders, by disruption of the synergistic action of vitamins and hormones becomes apparent. Further substantiation is provided in the fact that infection constituted the chief etiological factor in 60 per cent of the original series of 200 cases. In every case previous therapy had been of little benefit until active foci of infection were cleared, and vitamin and hormone deficiencies were corrected by restoration of individual cellular nutritional levels through proper diet and complete replacement therapy. Not until all of these factors had been considered, corrected, and adjusted, could subsidence of subjective complaints, with corresponding improvement in physical findings and laboratory data be obtained.

Maintenance of normal levels over a long period of time is equally important. In order to accomplish this, no single therapeutic factor can be neglected. For example, as illustrated in the sixth case, in the presence of gastro-intestinal disorder, absorption of ingested food or oral medication was embarrassed. Therefore, parenteral substitution therapy was administered during that period in order to restore and maintain nutritional levels. After clearing up the gastro-intestinal upset, oral medication sufficed. The same is true in the majority of cases, that oral medication will be adequate,

for limited periods, once a precipitating factor like infection has been eradicated, and normal physiological balance is achieved. But it is imperative in all cases that constant observation be maintained in order to detect those periods of mild regression, when a short course of parenteral therapy may be required to re-establish and preserve chemical balance. Only by continued vigilance and observation can physiological balance be achieved and maintained.

CONCLUSIONS

1. Infection constituted the chief etiological factor in 60 per cent of a series of 200 cases of nutritional disorders.
2. Six representative cases have been selected from the original series for detailed discussion and analysis.
3. The prostate has been demonstrated to be a common focus of infection in the male, but one which is frequently overlooked, or inadequately treated.
4. Therapy must be directed toward eradication of all foci of infection, and toward restoration of vitamin and hormone deficiencies by complete substitution therapy, as herein defined.
5. Proper diet and substitution therapy, along with eradication of infection, in these cases attempts to restore to normal the chemical processes which have been disrupted. By so doing, the synergistic activity of vitamins and hormones can be re-established and normal nutrition and health maintained.

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