

ABSTRACTS

TREATMENT OF GASTRODUODENAL ULCER WITH HISTIDINE MONO- HYDROCHLORIDE

David J. Sandrocias, M.D., J.A.M.A.
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Experimental Background and Rationale: The following experimental operation was performed on a series of dogs: "The pylorus was sectioned and the distal end inverted. The jejunum was transected and the distal end anastomosed to pylorus, the proximal end being anastomosed to ileum 30—60 c.m. from its termination".

This operation caused the gastric contents to be expelled from the stomach into jejunum without becoming mixed with secretions poured into the duodenum (bile, pancreatic juice and duodenal juice) which were drained into the ileum. In 95% of cases, peptic ulcers developed.

On the basis of above experiments, Weiss and Aaron suggested the following:—"Absence of duodenal juice especially effects protein digestion. Proteins arrive in jejunum as poly-peptides and cannot be broken down to assimilable form (amino acids) because pancreatic trypsinogen is lacking. Four amino-acids cannot be synthesized by the body. These are cystine, lysine, tryptophane and histidine."

Guided by these assumptions, Weiss and Aaron repeated the above experiment with daily injection of each of the above amino-acids (except cystine — too difficult) into separate groups of animals. They found that injection of histidine alone changed the evolution of ulcer. The inference is that the development of peptic ulcer is associated with a deficiency in histidine.

Clinical Reports on Use of Histidine: A number of reports by continental workers record a high percentage of successful immediate responses to histidine therapy in peptic ulcer cases. The efficacy of the treatment is based for the most part on symptomatic evidence. None of the observers have reported on long time follow-ups.

Author's Studies: Twenty-three cases were treated by the method under discussion, using a control group of forty-six patients treated by diet-alkali regimen. All showed ulcer on X-ray examination. In seventeen cases where diet-alkali failed, histidine therapy was substituted. In seven cases where histidine fail-

ed, diet-alkali regimen was instituted instead. Thus a total of forty patients received the histidine therapy, and fifty-three received the diet-alkali regimen.

Results, briefly summarized, were:—

1. For histidine, 75% favorable responses. For alkali, 71.7%.

2. Of patients not responding to diet-alkali regimen, 70.6% showed favorable response to histidine. Vice versa, 71.4%, showed favorable response to alkali, after histidine had failed.

3. Recurrence of symptoms after histidine treatment had caused remission, 85% in six months. For diet-alkali only 31% reported recurrence in same period.

4. Effect of histidine on gastric acidity—negligible.

5. Effect of histidine on ulcer as shown by X-ray or operation. Of the 40 treated, X-ray check was obtained in 23 cases. Six showed same lesion. One showed great enlargement of original crater. Of 16 with definite duodenal ulcer, 8 showed improvement by X-ray, but only 4 were symptom free; the other 8 showed no change by X-ray, but all were symptom free. (Persistence of deformity as seen by X-ray is not indicative of non-healing.)

Reaction: Of the forty cases thus treated sixteen showed mild reaction, i. e., fatigue, mild muscular pain in extremities. None suffered from fever, chill, vomiting or abdominal pain. Of the sixteen, eleven became symptom free, four moderately improved, and one showed no change. Of the twenty-four without reaction, eleven became symptom free.

Criticism of Rationale: Many experiments similar to that of Weiss and Aaron on which the rationale for the histidine therapy is based, were performed. Not all the results are in accordance with theirs. Study of these experiments raises the following questions:—Is histidine deficient? If so, is it the sole causal agent? What of the lack of enzymes and bile, per se? What is the effect of the disturbance of fat and carbohydrate metabolism? Why not consider the chemical and mechanical factors in the ulcer production in these experiments? It appears that there is not enough evidence that deficiency of histidine is the cause of peptic ulcer.

Remissions Explainable on Other Basis:

1. Intermittent nature of the condition.

2. Non specific protein reaction causing leucocytosis, mobilization of immune bodies, capillary dilatation, etc.

3. Psychic effect.

4. Non specific action on sympathetic nervous system leading to hypomobility and hypoperistalsis in ulcer area.

Treatment With Distilled Water: The author is at present treating twenty cases with injections of 5 cc. distilled water daily, to see if remission is the direct result of making up the deficiency of histidine, or otherwise. Of the twenty so far treated this way, 60% (twelve) have become symptom free.

Note: In this same issue, an article by Dr. Kirby A. Martin, N. Y., is published, on the same topic. Of the forty-one cases treated by histidine therapy, thirty are reported symptom free, of whom four-teen showed healing by X-ray. Recurrence of symptoms in twenty-six of these cases occurred in 6 - 12 months. A control group of forty treated by diet-alkali regimen showed thirty-one symptom free, with twenty-four recurrences in 6 - 12 months.

JACK HAIMOWITZ, B.Sc., '36.

THE PHYSIOLOGY AND PRINCIPAL INTERRELATIONS OF THE THYROID GLAND

by

David Marine, J.A.M.A. vol. 104, No. 25, June 22, 1935.

The principal function of the thyroid is to increase the oxidative processes in the body. This probably indicates that all bodily functions are influenced by the state of thyroid function. Three maxims are to be recognized:

(1) the thyroid originally comes from the alimentary tract;

(2) it has great capacity for the increase and decrease of its functional activity;

(3) hyperplasia indicates hyperactivity but not necessarily hyperfunction.

Chemistry:

According to Harrington, 40% of the iodine in the gland exists as thyroxine, while the remaining 60% is as di-iodotyrosine. The latter, though physiologically inactive in itself, is a stage in the synthesis of thyroxine in the gland. This synthesis takes hours, but the storage of iodine in the gland apparently is almost instantaneous, and the manner in which it is thus stored is not known.

Physiology:

In atrophy of the gland the metabolism is decreased greatly; treatment with thyroid extract raises the metabolic rate to normal or above. In hyperthyroidism, as is seen in exophthalmic goiter, the opposite occurs: the respiratory exchange is

increased, the nitrogen metabolism is increased, and in general we can say that the entire metabolic rate of the body is raised.

The administration of thyroxine, after a latent period of twelve hours, causes an increased oxidation in the body of protein, fat, and carbohydrate, and also causes an increased excretion of minerals, especially calcium and magnesium. It also increases the oxygen consumption of the liver, kidneys, and muscles.

Iodothyroglobulin, injected intravenously, causes a slight lowering of the blood pressure but the heart rate is notably increased after a certain latent period. This latter fact leads Oswald to believe that the thyroid secretion increases the irritability of all sympathetic nerve endings. The lowering of the iodine store and the tendency to thyroid hypertrophy as is seen in many of the infectious diseases clearly indicate that the thyroid is an important indirect factor in the resistance to infection.

Effects of Diet:

Fresh meats cause hypertrophy of the gland; sea fish increase the iodine store and reduce the size of the gland; fats also promote thyroid hypertrophy. As thyroid hyperplasia is now believed to be secondary to the depletion of the iodine store, these facts indicate that diets rich in proteins and fats increase the rate of discharge of thyroxine and suggest that thyroid activity is more necessary in the oxidation of fats and proteins than in the metabolism of carbohydrates. Starvation and subsequent wasting away bring about involution of the gland, i.e., a decrease in blood supply and an increase in the colloid and iodine store, all evidence of a diminished functional activity. The thyroid secretion is necessary for the specific dynamic action of foods.

Interrelations:

(a) PITUITARY:

The anterior pituitary is the master gland of the body in that it controls the functional state of many organs such as the thyroid, sex glands, suprarenals, etc. Hypertrophy of the thyroid, as is seen in parenchymatous goiters, is associated with a greatly enlarged anterior pituitary. Hypertrophy of the anterior pituitary is greater in younger animals to try to compensate for the great decrease in the already high metabolic rate of young animals. Removal of the anterior pituitary results in involution of the thyroid. Injection of anterior pituitary extract in such animals, i.e., injection of the thyrotropic factor, causes thyroid hypertrophy and hyperplasia resulting in a rapid loss of iodine from the gland, an increase in blood iodine, an increase in B.M.R., and an increased excretion of calcium and creatinine, when exophthalmos develops. However, immunity may be built up against this factor.

Hyperplasia may occur but the other symptoms are prevented from occurring by the anti-substance built up in the blood. Exhaustion of the thyrotropic factor is probably the immediate cause of atrophy in some cases of Gull's disease (myxoedema). Endemic cretinism is probably due to thyroid insufficiency and can be cured by the administration of iodine.

In exophthalmic goiter we find that two factors are necessary for its production;

(1) relative or absolute deficiency of thyroid secretion;

(2) excess of the thyrotropic factor. This explains why iodine administration with an intact thyroid, or thyroid extract administration after total thyroidectomy prevents exophthalmos. It also explains why thyroid insufficiency (myxoedema) alone is not usually associated with exophthalmos, because thyroid atrophy here seems to be primarily dependent on an insufficiency in the thyrotropic factor. The thyrotropic factor acts directly on the gland cells so that nervous connections are not necessary for the secretory or excretory activity of the gland.

(b) SEX GLANDS:

There is known to be a relationship between the thyroid and the sex glands, but the pituitary seems to be a necessary intermediary. The removal of the sex glands causes a slow involution of the thyroid and a slight reduction in the total metabolism. Large doses of thyroid extract produce an inhibition of sexual maturation but in small doses this is accelerated. Thyroid feeding also has an inhibitory effect on oestrus. Injection of anterior extract causes a greater hypertrophy of the male sex glands after thyroidectomy than before it. Hypertrophy of the thyroid occurs after five to ten days' injection of oestrogenic substance, but if this is continued for twenty days or more, the opposite effect is observed. The effects of the thyroid on the gonads and of the gonads on the thyroid can be explained as effects mediated through the anterior pituitary. The response of the pituitary to thyroidectomy is not limited to the stimulation of an increased production of the thyrotropic hormone, but also causes an increased production of the growth and gonadotropic factors as well. Conversely, a depression of the thyrotropic factor, brought about by the administration of thyroxine, probably depresses the gonadotropic factor. Injection of large doses of the oestrogenic substance appears to decrease the amount of the gonadotropic factor produced by the pituitary as well as depressing the thyroid glands. These effects are understandable if one assumes that the same pituitary cell can produce more than one hormonal factor; there is evidence that the eosinophilic cells may be

responsible for the secretion of both the thyrotropic and growth-promoting factors.

(c) THYMUS:

Feeding thyroid causes persistence of thymus. Thyroidectomy hastens the involution of the thymus. In hyperthyroidism the thymus hypertrophies. From the experimental and clinical evidence offered, we can say that there seems to be an antagonism between these glands, the nature of which we know not, till the function of the thymus is better understood.

(d) PANCREAS:

Experimental evidence shows that thyroidectomized sheep are more sensitive to insulin than normal animals. The thyroid hormone promotes glycogenolysis and therefore the hypoglycemic action is increased after thyroid removal and decreased by thyroid feeding. We can conclude that these two glands are antagonists.

(e) SUPRARENALS:

Thyroxin causes direct stimulation of the chromaffin system, and the adrenal cortex has a very definite inhibitory effect on the thyroid gland.

JONATHAN I. MORRISON, '40.

DIAGNOSIS AND TREATMENT OF EARLY MALIGNANT DISEASE OF THE UTERUS

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F.C.O.G.

Practitioner, January, 1937

Early Diagnosis:

The disease is symptomless in its early stages. Fully 90% of patients come too late for treatment. The age incidence ranges from the "cradle to the grave" but mostly between the ages of 45-60 years, especially in multipara.

Pathologically, two sites are encountered, viz.: outer surface of the vaginal portion of the cervix, and the cervical canal. In the case of the former, erosion will produce a flat malignant ulcer, or a large fungating cauliflower growth. In the canal the growth will be columnar-celled or sometimes metaplasia occurs to the squamous epithelioma type.

The first symptom which usually occurs is irregular bleeding between periods or after the menopause. This is the stage of ulceration. No pain is present, and the patient appears healthy. Pain and cachexia are late symptoms.

In carrying out the investigation, the history is of importance. Obstetrical, menstrual, family and personal background should be enquired into. A cervix torn as a result of childbirth, and which has later become infected, is an important predisposing cause to cancer. The presence of leucorrhoea is indicative of an infected cervix. The condition of the bowels and bladder are next enquired about. Constipation, incontinence, dysuria and frequency of micturition should immediately

put one on guard, even though these symptoms do not present themselves until late in the disease. The nature of the bleeding is important evidence. Bleeding connected with coitus, following douching, or some undue straining is particularly significant. The amount and duration of the flow should also be ascertained.

On examination, nothing can be ascertained externally in the early stages, and vaginal investigation must be carried out. Both speculum and the fingers should be used. Note first the vulva and whether there is any discharge. A urethral caruncle and varicosity often give rise to bleeding. A velvety feeling of the cervix is characteristic of erosion. The discovery of a bilateral or stellate tear is significant, since these are pre-disposing causes. Mucous polyps resembling stalked raspberries are sometimes seen projecting from the external os, and are the cause of bleeding. These should merely be snipped off. Cancer, however, may well be present along with any of these conditions so that thorough investigation is necessary. Enlargement of the cervix as a whole may mean radially-spreading carcinoma. On bimanual examination, any general enlargement of the uterus and any undue mobility is rated. When the finger is withdrawn from the vagina it may be blood-stained. A cervical erosion alone does not bleed on touching.

The "probe test" is of definite value in diagnosis. A probe or uterine sound is pushed into the suspected area. Erosion, by itself, is tough and restraint. A well-established cancer, on the other hand is friable, cheesy and bleeds readily when probed. Examine the entire cervical canal in the same manner. A negative probe test, unfortunately, does not exclude cancer.

Schiller's test or, as it is sometimes called, the Lugol test, depends on the fact that normally the vaginal and cervical epithelium contain a considerable quantity of glycogen. Epithelium of very early cancer does not possess glycogen, and therefore is not stained a dark mahogany color when Lugol's solution is introduced into the vagina. A portion of the unstained tissue is then removed for microscopical examination. The test has two main difficulties:

1. It cannot be applied satisfactorily to the cervical canal.
2. It is of no value where there is a previous erosion, since the latter is already a bright-red color.

The cervix should never be left in the pelvis in performing a hysterectomy. It is a frequent site for future cancer. The menopause must never be diagnosed as the cause of bleeding from the vagina until every other cause has been excluded by a vaginal, and, if necessary, microscopical examination.

LEONARD P. KLEIN, '39.

SOME THOUGHTS ON ACUTE OSTEOMYELITIS OF THE LONG BONES.

R. B. Deane, M.D., F.A.C.S., Can. Med. Assoc. Journ., 36, 3, Mar. '37

These remarks on acute osteomyelitis are intended for the man in general practice who sees such a case once in several years, and not for the surgeon specialist to whom they are a mere A.B.C. The amount of crippling from this source is appalling and lives are frequently lost. Early diagnosis would appreciably reduce disability. An important point is that diagnosis can be made at the bedside without laboratory aid. The X-ray is of no value and some may mistakenly think there is no bone disease on seeing a negative plate. Also acute osteomyelitis is not always accompanied by high temperature, excruciating pain and marked constitutional disturbances passing into coma. This fulminating type is rather uncommon.

Following slight trauma, a fall or a bump, a child develops an acute painful swelling of the knee region accompanied by slight temperature, not over 101 or 102° F. The pulse rate is somewhat raised and pain reveals a recent cutaneous focus of pus, as a pimple, insect bite, etc. Monoarticular pain with fever in a child should always make one think of acute osteomyelitis.

The pain is fairly well localized to the bone involved, is not excruciating and radiates some. The limb is held semi-flexed. Due to the pain it may be hard to determine if the lesion is above or below the knee. The part is distinctly swollen and is hot but not red. Clinch the diagnosis by palpation. Do not handle the limb as this causes generalized pain. With the finger tip press over the bone at half inch intervals from the middle of femur to the knee and similarly on the tibia. Press firmly for a few seconds in each spot. The site can be localized by the child's cries in response to the pain. A hypodermic may now be given and surgical exploration proceeded with at once. Soft parts and periosteum are incised and drill holes at least $\frac{1}{8}$ inch in diameter are made over the pus area. The holes are joined with an osteotome removing all overhanging edges of the bone. The endosteum should never be curetted. Wiping with gauze is sufficient. If pus is under the periosteum the bone should be drilled as above. In doubtful cases do not hesitate to explore by drilling two or three good size holes in the bone. Dressings must be of a type that will not dry, as drainage is all important. Splinting is also essential.

J. A. WEBSTER, B.Sc., '38.

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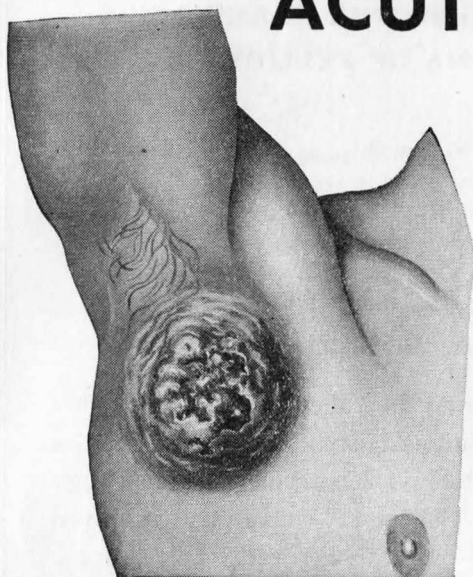
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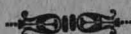
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