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Relation of thyroid disease to blood disorders

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RELATION OF THYROID DESEASE TO
BLOOD DISORDERS

SENIOR THESIS

SUBMITTED BY: JAMES H. BENA

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INTRODUCTION

In recent years the importance of the endocrine system has reached a prominence far above any single phase of medicine. It is entirely possible that the endocrines have been over emphasized and that in future years they will drop to their proper place in the practice of medicine. More probable however, is that the wide spread effect of the endocrine glands and their secretions is at present as a large book of which only the title page has been read.

Perhaps the most commonly known types of endocrine disturbances are those referable to the thyroid gland. The symptoms of certain types of thyroid dysfunction are usually easily diagnosed by the majority of clinicians. There are, however, certain conditions brought about by thyroid dysfunction which are not only misunderstood but often are never noticed. This type of phenomena is especially true of the blood changes in thyroid disease.

The blood in thyroid disease is ordinarily thought a secondary change, however, certain blood conditions which are thought to be primarily from the blood forming organs might possibly be referable to an abnormally functioning thyroid gland.

This article is written and presented in an attempt to give a brief resume of the literature on the subject.

HISTORY

The relation of the thyroid gland to hematopoiesis was practically an unheard of subject until 1893. At this time Putnam (29) made a study of cases of myxedema and the result of treatment with Sheeps thyroid. As a result of his studies he made the following statement: "The point has not attracted as much attention as it deserves that the directly hematopoetic functions of the thyroid gland, if they are of real importance, ought not to be met by ingestion of the thyroid secretion." This statement is given credit for the beginning of investigation on the subject.

Cuifini (5) is said to have discussed relative lymphocytosis in exophthalmic goiter. His works however apparently did not receive great attention.

Kocher (16) in 1908 received considerable attention. He found a triad in Basedows disease he felt to be highly diagnostic. This triad consisted of leukopenia relative Hypopolynucleosis and relative lymphocytosis. This work was confirmed by Crotti (3). Crotti also studied the blood post operatively.

No further important chemical work was done on the subject until 1919 when Plummer (28) made a study of 578 cases of hyperthyroidism. Plummer noticed that the blood in hyperthyroidism was often altered but he did not believe that the blood picture was diagnostic.

Emery (7) in 1923 made an extensive study of the blood in myxedema and decided that there were definite changes in the leucocytis but no constant changes in the red blood cells.

Menkin (24) in 1928 made a study of 100 cases of hyperthyroidism and noted a relative lymphocytosis.

PHYSIOLOGY OF THE THYROID GLAND

The physiology of the thyroid gland outside of its endocrine functions are practically unknown. The normal thyroid gland contains a relatively small amount of lymphoid tissue. When the thyroid gland undergoes changes leading to hyperthyroidism the lymphoid tissue becomes more prominent. MacCallum(22).

The presence of lymphoid tissue in the thyroid gland has lead some investigators to believe that the gland functions as a part of the lymphatic system as well as being an endocrine gland. This belief becomes more significant when in hyperthyroidism the Hyperplasia of the lymphoid tissues of the gland is followed by lymphocytosis. (Chapter on blood in Hyerthyroidism.)

Gottleibe (10) states that in hyterperthyroidism the thyroid vein contained 75%-80% more lymphocytes then the thyroid artery. Sharpe and Bisgaard (32) have not been able to find the percentage as high as this however. It is reasonable to assume in view of these facts that the lymphatic function of the gland in proportion to the amount of lymphoid tissue present. The lymphoid tissue present, as compared with the body as a whole, is almost negligble. The various activities for which the thyroid gland is directly responsible are probably largely, if not entirely, an endocrine effect.

EXOPHTHALMIC GOITER AND CHRONIC LYMPHATIC LEUCEMIA

Perhaps the most interesting phenomena occurring in thyroid dysfunctions are those which correspond to chronic lymphatic leucemia. These phenomena occur particularly in exophthalmic goiter.

Exophthalmic goiter and chronic lymphatic leucemia are both particularly characterized by an elevated basal metabolic rate. No other condition except chronic myeloid leucemia produces this disturbance to such great extent.

In both of these conditions there is considerable similarity in regard to the various pathological, physiological, and clinical findings.

These findings are so similar in some instances that various authors have given special attention to attempting to find a common basis for each disease Dameseshek (6) has even discussed a case of lymphatic leucemia with hypermetabolism that reacted very favorably to total ablation of the thyroid gland.

The ocular findings are not as consistent in chronic lymphatic leucemia as they are in exophthalmic goiter. Friedgood (8) reported that ocular phenomena occurred in six of ten cases of chronic lymphatic leucemia. Five of these had unilateral exophthalmos and four had bilateral ocular prominence.

It is obvious that in making a study of the relationship of two conditions that are ordinarily considered

separately that more than the rare phenomena of each are considered. For this reason a discussion of the common phenomena of each condition is warranted.

CLINICAL FEATURES OF EXOPHTHALMIC GOITER AND CHRONIC
LYMPHATIC LEUCEMIA

Perhaps the first clinical finding of exophthalmic goiter which attracts the attention of the patient or physician are the evidences of increased metabolism. An individual who complains of nervousness, weakness and fatigue is ordinarily classified as a possible thyroid dysfunction.

The same type of clinical picture may bring the leucemic patient to the attention of the physician. The patient may present such symptoms as nervousness, irritability, insomnia, flushing of the skin, gastro-intestinal disturbances and menstrual difficulties. These symptoms however are more constant in hyperthyroidism. The majority of clinicians in the process of a routine physical examination attempt to demonstrate a tremor of the hands in a suspected case of hyperthyroidism. Minot and Means (26) called attention to the fine tremor of the hands which is present in conditions of lymphatic leucemia. They attribute this condition to the associated anemia.

LYMPHADENOPATHY

Although the generalized lymphadenopathy and splenomegaly are accepted and widely recognized physical findings in chronic lymphatic leucemia they are also found in hyperthyroidism. Baldrige and Petersen (1) reported an incidence of these conditions in 30% of his cases of hyperthyroidism. This enlargement is usually found at autopsy but frequently is so large that it is discovered during a routine physical examination.

The etiology of the lymphadenopathy, and splenomegaly is unknown. It is reasonable to assume however it is a part of the generalized lymphoid hyperplasia which is reflected in the pathological picture of the thyroid in exophthalmic goiter. This will be discussed in the Pathology of Exophthalmic Goiter.

BASAL METABOLISM

The laboratory procedure of the most value in the diagnosis of hyperthyroidism and in exophthalmic goiter is the basal metabolic test. This test is so important that Emery (7) believed that the diagnosis of thyroid dysfunction was unreliable before the advent of the basal metabolic test. However the basal metabolism is increased in both cases of lymphatic and myelogenous leucemia (17-1) Friedgood (35) has observed an increase in basal metabolism in some cases of acromegaly, diabetes mellitus, essential hypertension polycythemia vera and pernicious anemia. The causes for the increased basal metabolic rate in both hyperthyroidism and in leucemia is not established. In hyperthyroidism the degree of increased metabolism is evidently dependent on the amount of excess thyroid hormone thrown into the blood stream. Whether the difficulty rises purely from a thyroid gland dysfunction is not known. Hicken (12) states that the changed function of the thyroid gland is probably only the local manifestation of a more or less unknown disease. In lymphatic leucemia the basal metabolic rate is more comparable to the patients general condition, the degree of anemia and inversely to the number of platelets in the blood (17-30).

Minot and Means (26) made a rather extensive study of the pulse rate and metabolic rate in hyperthyroidism and in leucemia. They decided that if the tachycardia of leucemia is purely a result of increased metabolism then the same must apply to exophthalmic goiter. They further decided that

the damage done to the heart was probably a result of overwork although the anemia was a definite factor.

In the various studies they discovered that the pulse rate and basal metabolic rate in both exophthalmic goiter and chronic lymphatic leukemia show a high degree of correlation. The variations that occur in relation to each other seemed to be quantitative rather than qualitative.

PATH OF EXOPHTHALMIC GOITER

Perhaps the most striking pathological finding in exophthalmic goiter is the extra ordinary lymphoid hyperplasia in the thyroid gland. MacCallum (22).

This hyperplasia is attended with the formation of well defined germinal centers. In the normal thyroid gland small foci of lymphoid tissue are occasionally demonstrated but are never marked. MacCallum (22).

The degree of epithelial hyperplasia seems to have little bearing on the basal metabolic rate. Simpson (33) Simpson discovered that thyroid glands showing only lymphoid hyperplasia the basal metabolic rate was often as high as 100%.

The significant feature of these changes in the thyroid gland is that they are only a part of the generalized increase in the lymphoid tissues throughout the body. Baldrige (1). This lymphoid hyperplasia is especially noticeable in regional lymph nodes of the neck. This feature is also present in leucemia.

The splenomegaly which is discovered at autopsy quite frequently in exophthalmic goiter is also marked by a generalized lymphoid hyperplasia. This hyperplasia is attended by enlargement of the Malpighian corpuscles. Baldrige (1)

It is generally known and accepted that the thymus is enlarged and persistent in most cases of exophthalmic goiter MacCallum (22)

This enlargement of the thymus gland is supposed to

to parallel the generalized lymphoid hyperplasia. MacCallum (22) However suggests that the histologic changes of the thymus represents an accentuation of the condition corresponding to the age at which the disease develops. Menkin (25) however has noted that all cases of exophthalmic goiter treated by thyroidectomy to not respond favorably. He suggests that possibly the thymus gland is acting by itself.

PATH OF CHRONIC LYMPHATIC LEUCEMIA

The pathology of chronic lymphatic leucemia has been studied quite extensively and is well recognized. In a study of the latter and a comparison with exophthalmic goiter the striking similarity of the two is revealed even on superficial examination. The difference seems to be one of quantity, the hyperplasia of the lymphoid tissue and the splenic enlargement of exophthalmic goiter being less extensive. Friedgood (8)

In lymphatic leucemia the lymphadenopathy is generalized with enlargement of the solitary nodules. There is frequently an infiltration of the liver, kidney, lungs and bone marrow with lymphocytis. The splein is practically always enlarged sufficiently to be palpable. Because of the extensive lymphoid hyperplasia frequently distorts the architecture of the stroma but the pulps still discernable Friedgood (8) Ordway (27)

Cases of lymphatic leucemia have been reported in which the regional lymph nodes and splein have not been enlarged. (Quoted from Rossle and Bensis by Friedgood. (8)

THE BLOOD IN EXOPHTHALMIC GOITER AND CHRONIC LYMPHATIC LEUCEMIAErythrocytes

The blood picture in chronic lymphatic leucemia need not be discussed at great length as they are well known. In the early stages the red blood cell count and hemoglobin content are normal or nearly so. ^a As the disease progresses the blood count and hemoglobin become reduced. The color indexes low. In exophthalmic goiter the red blood count and hemoglobin do not show a great deal of change. Plummer (28) in his study of five hundred and seventy eight cases noted that the erythrocyte count averaged around 4,790,000 while the hemoglobin averaged 83.1%. From his studies he felt that the slight anemia was secondary to a change in the general body condition. Lerman (20) believes that the Red blood count and hemoglobin in exophthalmic goiter have no relation to the basal metabolism.

LEUCOCYTES IN CHRONIC LYMPHATIC LEUCEMIA AND IN EXOPHTHALMIC
GOITER

The leucocyte picture in chronic lymphatic leucemia is a well known phenomena. The leucocyt count is as a rule lower than in myelogenous leucemia averaging between 100,000 and 200,00 per millimeter. The count rarely exceeds these figures. Ordway (27)

The leucocyte count and differential studies in exophthalmic goiter has been a subject of considerable topic. Kocher (16) in 1908 received considerable attention for his treatise on the blood picture in hyperthyroidism. Kocher believed that the blood count was definitely diagnostic of Hyperthyroidism. He decided that the blood picture consists of leukopenia, relative hypopolynucleosis. Most modern investigators however do not believe that the blood picture is of great diagnostic value.

That there is a leukopenia seems to be more or less well established; Jackson (15) in his studies of 600 cases discovered that 80% of patients with exophthalmic goiter had White blood counts below 7000. The average counts were not so definite. The concensus of opinion in this matter, however, is that the leukopenia is not marked (11-26). Plummer (28) feels a leukopenia may occur in the early stages.

Perhaps the most definite blood finding in exophthalmic goiter is that there is a lymphocytosis. Practically all investigators agree that there is a relative lymphocytosis however there is a dispute as to whether or not the lymphocytosis is absolute. Crile (2) felt that the relative lymphocytosis is the only significant change. That this

lymphocytosis is more apt to occur in exophthalmic goiter is apparently a well established fact. Menkin (25) discovered that of 100 patients with hyperthyroidism 56% had exophthalmus and of these 80% showed definite lymphocytosis.

Plummer (28) in his studies of 578 cases computed that the small lymphocytes averaged 34.8% while the large lymphocytes averaged 4.4%. This percentage was large enough so that there was an absolute lymphocytosis, that is there was a lymphocytosis greater than normal in spite of the leukopenia. Jackson (15) concluded that there is a significant lymphocytosis of 4.8%.

LEUCOCYTES OTHER THAN LYMPHOCYTES

In leucemia the count of other leucocytes is generally reduced both relatively and absolutely. Ordway (27). In exophthalmic goiter the same obviously holds true for the poly nuclear neutrophils however Jackson (15) claims there evidently is a monocytosis to some degree. He found that the percentage of monocytes was approximately 8.4% in 600 cases of hyperthyroidism.

The effect of iodine on the various systems of the body is as yet wrapped in obscurity. This fact remains true even though the iodides have been used in medicine more than any other drug. Gushney (4) states that the central nervous system and blood stream is unaffected by iodides. Friedgood (8) states that iodine is a sedative of the sympathetic nervous system.

It is well known that lugols solution has a temporary effect on exophthalmic goiter with remission of the clinical findings for a few days. The reason for this is unknown. (Marine(2) suggests that there is a blocking of the colloid and this pressure temporarily blocks absorption of the secretion.

In leucemia the effect of lugols on the metabolism is less marked. Friedgood (8) has noticed there is a definite decrease in the various symptoms. He believes this is due to a sedative action on the sympathetic nervous system. He also believes that the effect of lugols on exophthalmic goiter is due almost entirely to its sedative action on the sympathetic nervous systems.

EFFECT OF SURGERY

Present day medicine accepts surgery as the only practical treatment of exophthalmic goiter. The surgical procedure usually consists of a sub-total removal of the gland after which a period of rest is instituted. The result of surgery usually is remission of the clinical symptoms.

The blood ordinarily under goes changes approaching normal. Menkin (25) states that thyroidectomy removes the cause of the various disorders. Hertz and Lerman (11) noticed that after operation there is a reversion of the blood picture toward normal. Occasionally however after surgery the blood symptoms do not regress to any great extent. It has been suggested that the thymus gland maintains the abnormality. Menkin (25).

DAMESHEK AND SURGERY

A very interesting case of the effect of surgery on leucemia by surgical removal of the thyroid was reported by Dameshek (6).

A forty two year old woman presented all the signs and symptoms of an aleuemic lymphatic leucemia and with a basal metabolic rate of plus 65. The patient underwent continuous loss of weight, profuse drenching sweats, increased nervous symptoms and beginning circulatory failure. Xray therapy, Lugols solution and rest having no effect complete ablation of the thyroid gland was resorted to.

After surgery the basal metabolic rate began dropping immediately, the clinical signs and symptoms of hypermetabolism and circulatory failure disappeared. The patient immediately began to gain weight and the nervous instability receded. Perhaps the most striking feature of all was the regression of the spleen and lymph nodes almost 90% from their former size. The blood picture became almost normal.

Dameshek reports that the patient is continuing to be healthy a year and a half after the procedure. Dameshek feels that the surgery was at least partly responsible for the result.

In cases of incurable lymphatic leucemia that fail to respond to any other treatment, surgery of the thyroid warrants consideration as a final attempt at treatment.

SYMPATHETIC NERVIUS SYSTEM IN EXOPHTHALMIC GOITER AND LEUCEMIA

Friedgood (8) made a rather extensive study of the relation of the sympathetic system to these diseases. Because of the various phenomena which were suggestive of sympathetic disturbance he suggested that the sympathetic system probably plays an important part in each. Friedgood even goes so far as to say that exophthalmic goiter is not hyperthyroidism but rather a sympathetic disturbance.

Menkin (25) suggested that if the exophthalmic goiter is a sympathetic disturbance then the continuous contraction of the spleen and lymph nodes may be the cause of the lymphocytosis. Whether the sympathetic nervous system findings are primary or a result of primary disturbance in the thyroid remains as yet a problem.

THE BLOOD IN HYPERTHYROIDISM

The blood changes occurring in hyperthyroidism have been discussed in 'The Relation of Exophthalmic Goiter and Chronic Lymphatic Leucemia'. Briefly those changes are as follows:

In hyperthyroidism the Red blood count is not altered to any great extent however there is a slight anemia which probably is secondary.

There is usually a slight leukopenia which is a result of a hypopolynucleosis. This leukopenia is so slight that it is disputed by many.

Practically all investigators agree that there is a relative lymphocytosis and many claim that this is absolute.

There is a definite monocytosis in hyperthyroidism.

THE BLOOD IN HYPOTHYROIDISMIntroduction

It has been recognized for many years that that in myxedema the blood picture is altered, this however is not generally known. The main difficulty has been in making a clinical diagnosis of myxedema. With the basal metabolism test the diagnosis of myxedema became more positive.

Myxedema not infrequently is confused with other conditions. A rather good example of this is pernicious anemia.

In pernicious anemia the basal metabolic rate is occasionally diminished, Tomkins(35). This diminution is not as constant nor as great as in myxedema. Emery (7) felt that the diagnosis of myxedema could be made fairly accurately when clinical evidence was confirmed by the basal metabolic rate.

THE RED BLOOD CELLS IN HYPOTHYROIDISM

Perhaps the most significant blood finding in hypothyroidism is the marked anemia. Lerman (19) believes that there is a high degree of correlation between the red blood count, basal metabolism and hemoglobin. He also believes that anemia is more liable to appear in hypothyroidism when there is an achlorhydria.

Mackenzie (23) found that two out of three patients showed marked yellow pallor and the symptomatic findings of anemia. Emery (7) however states that the anemia is not constant but that usually there is a moderate secondary anemia and a reduction of the hemoglobin. He further states that the anemia has no definite relation to the metabolic rate. Experimental research however indicates that an anemia is a characteristic finding in experimental hypothyroidism. Sharpe and Bisgaard (32) Kunde (18).

The anemia of hypothyroidism will often give symptomatic findings suggesting a primary anemia, namely Pallor, decreased perspiration and dyspnea. However a study of the blood reveals no abnormality of the cells. Mackenzie (23)

The cause of this anemia of hypothyroidism in common with most endocrine disorders is unknown. Most investigators however believe that the anemia is only another manifestation of the general slowing down of the tissues. Stone (34) believed that the anemia was a result of a direct depression of the erythropoietic tissues due to a lack of thyroid secretion. Mac Kenzie (23) believed that the bone marrow functioned improperly due to the sluggish oxidation that occurs in all the tissues in myxedema.

LEUCOCYTES IN MYXEDEMA

The white blood count in hypothyroidism is evidently of no great importance. Literature does not reveal any serious discussion on the subject. Emery (7) states the white blood count average was about normal but varied some with the R. B. C.

GASTRIC SECRETION IN HYPOTHYROIDISM

That there is a definite gastric anacidity in hypothyroidism seems to be well established. Lerman and Means (7) noticed that in myxedema there is often a gastric anacidity. Lerman (13) states that when gastric achlorhydria is present there is a greater tendency toward anemia. Lerman suggests that a study of the gastric secretion may help present anemia.

Because of this phenomena in myxedema there has been some discussion of the relation between pernicious anemia and myxedema. Emery (7). Most investigators more or less avoid the question. Experimentally the anemia of myxedema does not resemble the anemia of pernicious anemia Kunde (18).

The relationship between anemias for which no cause is known and the anemia of myxedema however warrants careful investigation.

TREATMENT OF THE ANEMIA OF MYXEDEMA

That the logical treatment of the anemia of myxedema is to be found in the thyroid secretion is only logical. In as much as thyroid extract causes a regression of the symptoms of myxedema we can also expect a return of the Blood toward normal.

MacKenzie (23) in treating two cases of myxedema with thyroid found that the blood of one returned to normal while the other showed definite improvement. The same effect was found by Lerman and Means (19). They noticed that some patients made a complete recovery while others showed a return of either the R. B. C. or Hb. The process in each case was slow.

The effect of other hemopoetic substances is evidently negligible; but as yet has not been studied extensively. Lerman and Means (19) in a study of seven cases discovered that liver increased the Red blood cell formation somewhat but did not change the hemoglobin. Iron alone was of little value but was a great help when used with thyroid extract. They suggest that iron and thyroid should be given together in the treatment of the anemia of myxedema.

EFFECT OF THYROID EXTRACT IN ANEMIA

The effect of thyroid extract in the various anemias not primarily a part of myxedema has not been noted to any great extent. The work of Hoskins and Jellinek (13) however is of considerable interest.

107 male schizzophrenics were selected for the experiment. The patients all showed underweight and sec. anemia 47% showed leucocytosis, 16% showed slow metabolism.

After the administration of thyroid extract the average R. B. C. was increased while the leucocytes were decreased especially the polynuclear cells. The lymphocytes were increased. The erythropoetic effect was in oxygen consumption rate. The erythropoetic effect however was transient.

CONCLUSIONS

1. The difference between exophthalmic goiter and chronic lymphatic leucemia is apparently one of quantity rather than of quality.
2. Blood changes in hyperthyroidism.
 1. Little or no change in Red blood cell or Hb.
 2. A slight but definite leukopenia.
 3. A relative and an absolute lymphocytosis.
 4. A relative monocytosis
3. The blood picture in hyperthyroidism is neither diagnostic or prognostic.
4. Iodine has a slight beneficial/^{effect}in hyperthyroidism.
5. Surgery usually causes the blood picture to return to normal.
6. There is evidence that the various changes in hyperthyroidism are a result of a sympathetic nervous system disturbance.
7. Total ablation of the thyroid gland is to be considered in progressive chronic lymphatic leucemia.
8. The anemia of hypothyroidism is probably a secondary change.
9. The leucocytes in hypothyroidism do not show any definite abnormalities.
10. The Blood picture is neither diagnostic or prognostic in hypothyroidism.
11. Thyroid extract is almost a specific treatment for the anemia of hypothyroidism.

12. Thyroid extract is beneficial in some cases of anemia where there is also a low Basal metabolic rate.

BIBLIOGRAPHY

1. Baldrige C. W. and Petersen F. R. - Splenic Enlargement in Hyperthyroidism-J. A. M. A. 88: 1701, 1927
2. Crile G. W. and Ass - Clinics Of - The Thyroid Gland W. B. Saunders & Company, Phil. 1922
3. Crotti Andre - Thyroid & Thymus - Lea and Febiger Phil., P. 40: 1924
4. Cushney - Pharmacology and Therapeutics -Lea and Febiger, Phil 9th Ed P 560
5. Cuiffini - Quoted by Hertz and Lerman (10)
6. Dameshek W. - Complete Ablation of the Thyroid Gland in a case of chronic Lymphatic Leucemia with Hypermetabolism New Eng. J. of Med 210:723 1934
7. Emery E. S. The Blood in Myxedema Am. J. Med. Sc. 165: 577 1923
8. Friedgood H. B. - The Relation of the Sympathetic Nervous System and Generalized Lymphoid Hyperplasia to the Pathogenesis of Exophthalmic Goiter and Chronic Lymphatic Leukemia Am J. Med Sc. 183:841 1932
9. Friedgood H. B. The Effect of Lugols solution on the Basal Metabolism and Pulse Rate in Polycythemia vera) acromegaly and Chr Myelogenous Leuc. Quoted From Sharpe (31)
10. Gottleibe Blood Studies in Hyperthyroidism J. Lab. and Clin. Med 19: 37 1934
11. Hertz S. and Lerman J. - The Blood Picture in Exophthalmic Goiter and its changes Resulting From Iodine and Operation. J. Cl. Inv. 2: 1179, 1932
12. Hicken N. F.- Personal Interview
13. Hoskins and Jellinek Endocrinology 16:455 1932
14. Hubble D.- Influence of the Endocrine System in Blood Disorders Lancet P. 113 July 1933
15. Jackson A. S. - The Blood Picture in 600 cases of Goiter J. A. M. A. 1954:97, 1931
16. Kocher - Quoted by Hertz and Lerman (10)
17. Krantz C. I. and Riddle - The Basal Metabolism in Chronic Lymphatic Leucemia Am. J. Med. Sc. 175: 229 1928

18. Kunde Blood Changes in Hypo and Hyperthyroidism
19. Lerman J. Means J. H. -Treatment of Myxedema-
Endocrinology 16:455 1932
20. Lerman J. and Means J. H. - The Gastric Secretion
in Exopthalmic Goiter and Myxedema J. Clin. Invst.
21. Marine Quoted by De Bois Cecils Textbook of Medicine
3d Ed. Saunders and Co. Ph 1 1933
22. Mac Callum W. G. A textbook of Pathology - W. B.
Saunders and Co. Phil. 3rd Ed. 1924
23. Mackenzie G. M. - Anemia In Hypothyroidism J. A.
M. A. 86:422 1926
- (24. Menkin Rel Lymphocytois in Hyperthyroidism Arch
(25. of Int. Med. XLIII: 419 1928
26. Minot G. and Means J. H. - The Metabolism-Pulse Ratio
in Exopthalmic Goiter and Luecemia Archives of Int. Med.
576 1924
27. Ordway T., Whittington-The Leukemias-Cecils Textbook
of Medicine-Saunders and Co. 3rd ed 1029 1933
28. Plummer W. A. The Blood Picture in Exopthalmic
Goiter,Minnesota Med. 2:330 1919
29. Putnam J. J. - Myxedema Treated by Sheeps Thyroid
Tr. Am. Phys. 8:333 1893
30. Riddle M. C. and Sturgis C. C. Basal Metabolism in
Chronic Myelogenous leucemia Arch Int. Med. 39:255
1927
31. Sharpe J. Personal Interview
32. Sharpe J. and Bisgaard Relation of the Thyroid
Gland to Hematopoesis J. of Lab. and Cl. Med Vol. 21;
347, Jan. 1936
33. Simpson W. M
Am. J. Surg. 7:22 1929
34. Stone C. T. The Occurrence of Anemia in Myxedema
Am. Int. Med 1:215 1928
35. Tompkins E. H. Brittingham and Drinker- Bassal
Metabolism in anemia Arch. Int. Med. 23:441
1919