an equal amount is injected into the portal vein. Equally competent observers doubt the accuracy of these conclusions, believing that the explanation lies in the slow absorption of the sugar and not in the avoidance of the portal circulation. Without further experimental evidence it cannot be concluded that the greater part of sugar enemata does avoid the liver or that sugar is better tolerated when thus introduced by rectum. Clinical experience has failed to yield any positive evidence on this point. It is reported on the one hand that with the same quantity of sugar given by rectum as by mouth, the acidosis subsides and the glycosuria diminishes; on the other hand, cases are reported in which the glycosuria is not favorably influenced, and in certain instances a marked acidosis has developed when sugar by mouth was withdrawn and the same quantity given by rectum.

OTHER FACTS REGARDING ENEMATA.

Dextrine is said to be preferable to dextrose, as it irritates the rectum less. Its ultimate absorption compares favorably with dextrose, although more time is required. Inasmuch as infant foods consist largely of dextrin it is more easily obtainable.

Much has been said regarding the advisability of the drop method in giving enemata, but the preference of the patient must be always taken into consideration. Absorption is slower by the drop method, consequently this method is preferable in cases of diabetes.

Whenever repeated enemata are given it is essential to note with accuracy the quantity of fluid injected. This is especially true in unconscious or collapsed or extremely debilitated persons, since in such cases it may happen that absorption is retarded or fails altogether, with the result that the fluid finds its way into the small intestine and stomach, and if large quantities are injected these organs may become distended, giving rise to urgent symptoms.

The addition of ten drops of tincture of opium to the enemata may allay the mechanical irritation somewhat and does not delay absorption to any degree.

It has been claimed that nutritive enemata cause a reflex secretion of gastric juice which contra-indicates their employment in cases of gastric ulcer. Experimentally a flow of gastric juice of a half hour's duration has been shown to follow enemata. This corresponds to the period of psychic secretion; consequently it is attributed to the desire for food rather than to a reflex from the rectum. No secondary secretion of gastric juice has been noted.

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A STUDY OF LEUKEMIA.*

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LEUKEMIA is ordinarily defined as a disease characterized by an enormous increase in the number of leucocytes in the circulating blood. Some of the familiar facts concerning the disease are as follows:—

Its course may be chronic, lasting from six months to several years; or acute, from a few weeks to six months. The termination is invariably fatal. The chronic cases are much the more common, and the diagnosis is readily made. The acute cases, on the other hand, although at present they are much more often recognized than they formerly were, are comparatively rare. They are characterized by severe anemia, weakness and a tendency to hemorrhage.

An interesting feature of acute leukemia is that the patients often present some evidence of infiltration of the normal tissues outside the blood vessels by the white cells from the circulating blood. These "leukemic infiltrations," so-called, may be demonstrable only on microscopical examination of the various organs, or they may be sufficiently prominent to be easily recognized as definite tumors. Sometimes they are large and numerous enough to be the most striking clinical feature of the case. Many of these tumors are on section of a definite green or greenish color, and to such the name "chloroma" has been applied. The relation of chloroma to the leukemic process has been but recently demonstrated.

* Received for publication, November 5, 1913.

In dealing with a case of leukemia, the practitioner ordinarily classifies it as either myelogenous or lymphatic in type, according as he finds granular or non-granular mononuclear cells predominating in the blood picture. Some cases in which the cells appear to be more or less equally divided between these two types, and in which many cells are rather indeterminate in character, are called "mixed-cell leukemia." These have been regarded as evidence that the myelogenous and the lymphatic types of leukemia are by no means separate entities, but that the leukemic process represents a disease of all the hematopoietic tissues.

What may be considered as the opposite to this view, is the idea that there are two definite and separate diseases, viz.—lymphatic and myelogenous leukemia. This conception is founded on the view that the lymphocyte and myelocyte are not so closely related in origin as is ordinarily supposed, but arise in definitely different regions, viz., the lymphoid tissue of the lymph nodes, alimentary tract and spleen in the case of the lymphocyte, and the red bone marrow in the case of the myelocyte.

The microscopical examination of the material from a large number of autopsies, inclines the writer strongly to this idea of the separateness of lymphoid and myeloid tissues. The chief cause for confusion seems to be the fact that the undifferentiated cells of both types are large and pale staining, with vesicular nuclei, and are absolutely indistinguishable one from the other by ordinary methods. The myeloblasts, as Naegeli has named the undifferentiated bone marrow cells, are, therefore, often called "bone marrow lymphocytes." When in the course of a myelogenous leukemia such cells appear in the blood, the picture naturally appears "mixed." When they predominate, the disease is considered "lymphatic."

The writer has pointed out in a previous communication¹ the fact that a large proportion of the cases diagnosed as acute lymphatic leukemia are probably myelogenous; that a certain number of them undoubtedly are, and among this latter group are included probably all those cases giving rise to green nodules, known as "chloroma." If, then, the two types of leukemia are separate processes, the mixed cell cases must be in fact myelogenous, and their blood must contain a sufficient proportion of the non-granular myeloblasts ("marrow lymphocytes") to give the appearance of a mixture of myelocytes and lymphocytes.

Since the publication of the article referred to above, another case of chloroma² has come under the writer's observation. In this case, as in the others, the invading cells gave a positive indophenol reaction, and the cytoplasm of a large proportion of them, including many that were actively dividing, was finely granular. The indophenol reaction, which is a test for the presence of an oxydizing ferment, is positive in all cells of the myelocyte series, except the most primitive

undifferentiated forms. It is constantly absent in cells of the lymphocyte series. In this case then, as in other cases of chloroma, the process is myelogenous. The blood picture, however, seen in specimens stained by "Wright's" modification of "Leishman's" stain, showed a very large proportion of cells resembling lymphocytes, both large and small, and the clinical diagnosis of acute lymphatic leukemia was made. Sections of the invaded tissue, on the other hand, when stained with eosin and methylene blue showed that these cells, which were supposed to be lymphocytes, did not possess the characteristic lymphocyte nucleus, and were apparently of the same type as the large granular cells present. Furthermore, even in the specimen stained by "Wright's" stain, many of these cells which resembled small lymphocytes contained a few large and small basophilic granules. It is probable that almost all of them were of myeloblastic origin, as all gradations between them and fully developed myelocytes could apparently be traced.

As to the essential nature of leukemia, the limit of our knowledge is reached when it is said that leukemia is, beyond a doubt, a malignant tumor whose cells invade the blood stream and grow there. The clinical course of the disease, with its invariably fatal issue, and all the histological and anatomical evidence, point to this view. That a tumor arising from the cells which give rise to the polynuclear leucocytes should occur cannot be considered unnatural, in view of the fact that from practically every other tissue in the body neoplasms are known to arise. Viewed in this light, leukemia can be considered as comprising two definite tumors: (1) a tumor arising from the lymphocyte, and (2) a tumor arising from the myelocyte. The terms "lymphoblastoma" and "myeloblastoma" are applied to these two tumors respectively to indicate that each arises from the primitive cell of its type (lymphoblast or myeloblast) and can manifest any stage of cell differentiation.

In other tumors there is marked variation, both in the degree of differentiation reached by the tumor cells, and in the tendency to invade normal tissues and form metastasis. For example, the cells of a fibro-sarcoma may produce a fair number of intercellular fibrils, and may resemble closely an adult connective tissue cell. Such a tumor tends to grow and invade slowly. On the other hand, the cells may be larger and closer together and may produce very little intercellular substance, and thus may resemble the younger less differentiated fibroblast. In such a tumor growth is usually much more rapid, and invasion of the normal tissues more marked. In many rapidly growing tumors a large proportion of the cells differ distinctly from any normal type. (They are often larger than the normal cells and usually contain a relatively increased amount of chromatin. Sometimes, giant cells with one or many nuclei are common.) Thus in general it may be said that the

younger and less differentiated the cells of a given tumor, the greater their tendency to invasion, and conversely, the more they resemble the adult type, the less do they invade.

If we apply this idea to the tumors of myelocyte origin, we expect to find cases in which the cells are, most of them, well developed granular cells, which multiply slowly, and rarely, if ever, leave what may be considered the normal habitat of their type, viz., the bone marrow and blood stream. Such cases are those of ordinary chronic myelogenous leukemia. We expect also to find cases in which the cells are, a large proportion of them, undifferentiated, non-granular and sometimes atypical, their growth rapid, and their tendency to invade normal tissues well marked; cases in which, furthermore, the course of the disease is relatively short. We find these cases are those of acute myelogenous leukemia. In many of them it is evident that invasion of normal tissues has gone on to such an extent that definite tumor masses are present. These masses, when green or greenish in color, as is usually the case, are called "chloroma."

Of the three cases of this acute condition which have come under the writer's personal observation, all showed a "mixed celled" blood picture; a definite infiltration of normal tissues, and a rapidly fatal course. In two of them, greenish masses or nodules were present in various organs, and were found microscopically to consist of fairly rapidly proliferating cells, which were identical with those seen in the blood stream. In the other case, infiltration of normal tissue was present, especially in the kidney, but was relatively small in amount, and nowhere gave rise to a green coloration or definite nodules which could be recognized in gross. This case and one of the two others were diagnosed clinically as acute lymphatic leukemia, while the remaining case was from the beginning, considered myelogenous. In all of them, however, the invading cells gave a positive indophenol-oxydase reaction, and in sections a fairly large proportion of the cells were seen to be granular. These three cases, then, are examples of rapidly growing tumors arising from the myeloblast in the bone marrow, and invading not only blood and bone-marrow generally, but also to a marked degree, the normal tissues outside the blood stream.

No acute cases of leukemia, in which the invading cell was undoubtedly of lymphoblastic origin, have come under the writer's personal observation. In the chronic cases, just as in chronic myelogenous leukemia, normal tissues outside the blood stream are rarely invaded. The tumor cells arise in some part of the lymphoid tissue and invade lymph nodes and the blood stream. The cells are—most of them—mature in type and resemble the adult lymphocyte (small lymphocyte). These are the cases of chronic lymphatic leukemia. In certain other tumors of probable lymphoblastic origin, the blood stream is apparently never invaded, and the tumors

either invade the surrounding normal tissues locally, metastasize into lymphoid tissue only, or show general metastases into various organs. These cases include the conditions ordinarily spoken of as lympho-sarcoma, pseudo-leukemia and malignant lymphoma. The writer has recently studied a tumor whose cells were apparently lymphoblastic which gave rise to multiple metastases in the liver, spleen, kidneys, lymph nodes, bone-marrow and dura. When all are considered, then, we have, arising from the lymphoblast, tumors which invade blood stream and lymphoid tissue more or less exclusively, giving rise to the clinical picture of lymphatic leukemia, as well as certain other tumors which seldom or never, invade the blood stream.

As far as the question of treatment is concerned, leukemia may be regarded in the same light as other inoperable malignant tumors. Certain agents undoubtedly serve to inhibit the proliferation of the tumor cells, and to lengthen the course of the disease. The chief of these are arsenic, benzol, the x-ray and the radio-active substance, thorium-x.

In general, we may summarize our knowledge of leukemia by saying that it represents the invasion of the blood stream by two distinct types of tumor cells, the one derived from the myeloblast and the other from the lymphoblast. The two tumors, therefore, are of separate and distinct origin. The myeloblastoma arises from the myeloblasts of the bone marrow, which are the parent cells of the polynuclear leucocytes; the lymphoblastoma from the undifferentiated cells of lymphoid tissue. The tumors are usually of slow growth and invade only the blood stream and the tissue from which they arise. More or less invasion of other tissues is characteristic of the rarer rapidly growing forms, which constitute the clinical cases of acute leukemia.

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THE OFFICE OF CORONER AND THE MEDICAL SCHOOL AT SYRACUSE.

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THROUGHOUT the United States medical men are lamenting the fact that in this country there is so little opportunity to perform autopsies. It is a recognized fact that advancements in scientific medicine have gone hand in hand with, and have depended upon advancements in pathology. So today they feel that one of the greatest handicaps to the advancement of medicine in this country is the lack of opportunities to per-