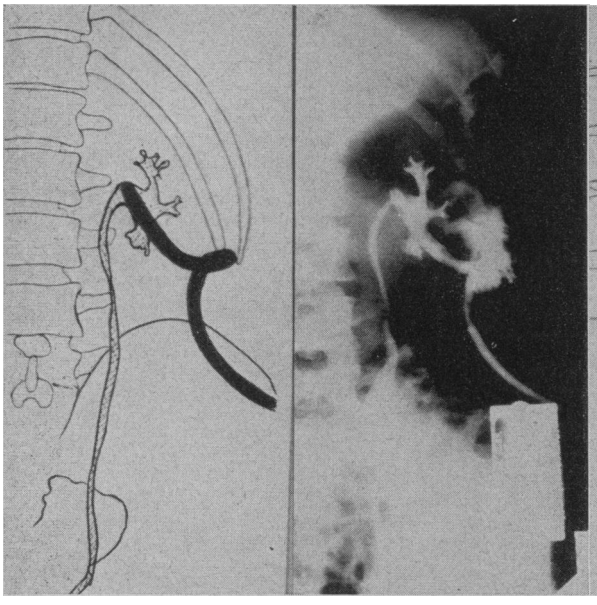

Fig. 10.—This is the same as Figures 8 and 9 showing the pyeloureterogram made by injecting sodium iodine solution through the nephrostomy tube.

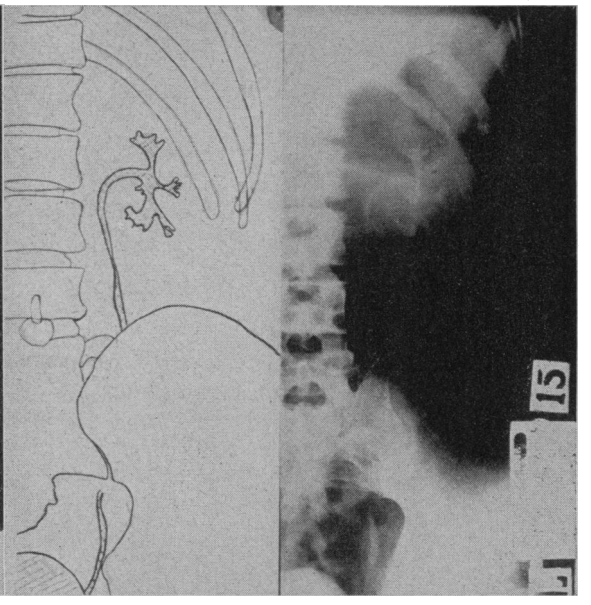

Fig. 11.—This is an intravenous urography of Fig. 8, showing normal functioning kidney and ureter.

tion of the ureter to the pelvis, stenosis of the pelvo-ureteral junction, and strictures of the ureter, must be corrected. In other words, anything that interferes with the free drainage of urine from kidney to the bladder must be corrected before the splint is applied.

It is my opinion that the ureteral splint should be an x-ray ureteral catheter, the diameter of which should not be larger than the caliber of the ureter; that, when possible, it should be inserted through the nephrostomy opening and anchored at its upper end, and that it should extend well down the ureter.

For additional comment, I refer you to Thomas Gibson's original article "The Ureteral Splint," which he presented before the Western Section Meeting of the American Urological Association in April, 1939.

CONCLUSIONS

1. Cases are presented showing faulty application of the ureteral splint.
2. An x-ray ureteral catheter is used, and should not be larger in diameter than the lumen of the ureter.
3. The ureteral catheter should extend well down the ureter.
4. The ureteral splint can be successful only when all obstructions to the outflow of urine from the kidney to the bladder have been corrected.

400 Twenty-ninth Street

MACROCYTIC ANEMIA IN LIVER DISEASE*

EDGAR WAYBURN, M. D.
San Francisco

DURING the past several years the work of a number of investigators has made it obvious that the so-called pernicious anemia blood picture is not a pathognomonic sign of one disease, but a type of faulty blood formation. Whatever disease process is able to produce, the disturbance in hematopoeisis will produce the blood picture. Among the diseases in which this condition has been described are pernicious anemia itself, sprue, tropical macrocytic anemia, macrocytic anemia of pregnant women, nutritional deficiency, various lesions of the G-I tract, certain cases of hemolytic jaundice, and certain diseases of the liver. These conditions all result in the same type of underlying process; defective blood formation, in which there is a failure of maturation of the cells of the red corpuscle series. In pernicious anemia this is often carried out to an extreme extent. In liver disease it is usually much more mild. However, with the same degree of anemia it is extremely difficult, if not impossible, to distinguish between the two blood pictures.

There is general agreement among investigators[1, 2, 3, 4, 5] on several aspects of the anemia of liver disease. The macrocytosis affects the great majority of the red corpuscles, which show relatively little variation in size or shape. This appearance is strikingly like that of mild pernicious anemia. Nucleated red cells are uncommon. The

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From the Department of Medicine, Stanford University Medical School.

fragility of the erythrocytes is normal. Spontaneous remissions and relapses of the anemia may occur. There is no relationship between the concentration of the bilirubin in the serum and the size of the red blood cells. On the whole the degree of macrocytosis seems to vary with the degree of anemia.

There is considerable disagreement about the percentage of patients with liver disease who have macrocytosis. Part of this is due to the criteria and classification of the conditions involved, and part to the methods used. On one condition alone, Laennec's cirrhosis, the more recent figures vary from 41 per cent [3] to 90 per cent.[4]

In his entire series of 132 patients, Wintrobe [3] classified 23 per cent without anemia, 33 per cent with macrocytic anemia, 30 per cent with normocytic anemia, 2 per cent with simple microcytic anemia and 12 per cent with hypochromic, microcytic anemia. The last named type of anemia was attributed, in most instances, to chronic loss of blood, (being found in cirrhosis only, when there was associated hemorrhage).

Spontaneous remissions in the anemia, and return of the size of the cells toward the normal may occur during the course of liver disease. This may not be necessarily correlated with the trend of the rest of the condition. Some cases of macrocytic anemia, particularly those with a low red-blood count, respond well to the injection of the pernicious anemia fraction of liver extract. Some respond to therapy with preparations of yeast. Others do not seem to yield to either type of treatment.

DETERMINATION OF KINDS OF ANAEMIA

The methods which may be used for the determination of the kind of anemia present include: (1) The determination of the color index. In macrocytic anemia this is near, or over 1. (2) The direct measurement of the cells by the method of Price-Jones, or by refraction.[1, 5] By definition [6] a macrocytic anemia may be said to be one in which there is an increase in the number of red-blood cells of the circulating blood having a diameter greater than 7.5 microns. (3) The determination of the mean corpuscular volume (MCV)[7, 8] which is found by dividing the hematocrit or packed red-cell volume by the number of red cells. The normal MCV ranges between 86 and 94 cubic microns. An MCV of 96 or greater may be said to be macrocytosis.

The methods used in this study were the determination of hemoglobin, red-blood cells, color index, packed cell volume, mean corpuscular volume, mean corpuscular hemoglobin content and mean corpuscular hemoglobin concentration, with occasional checking of the results by means of Price-Jones curves.

The use of volume determinations is superior to other methods of measurement for our purposes. They magnify the differences between the

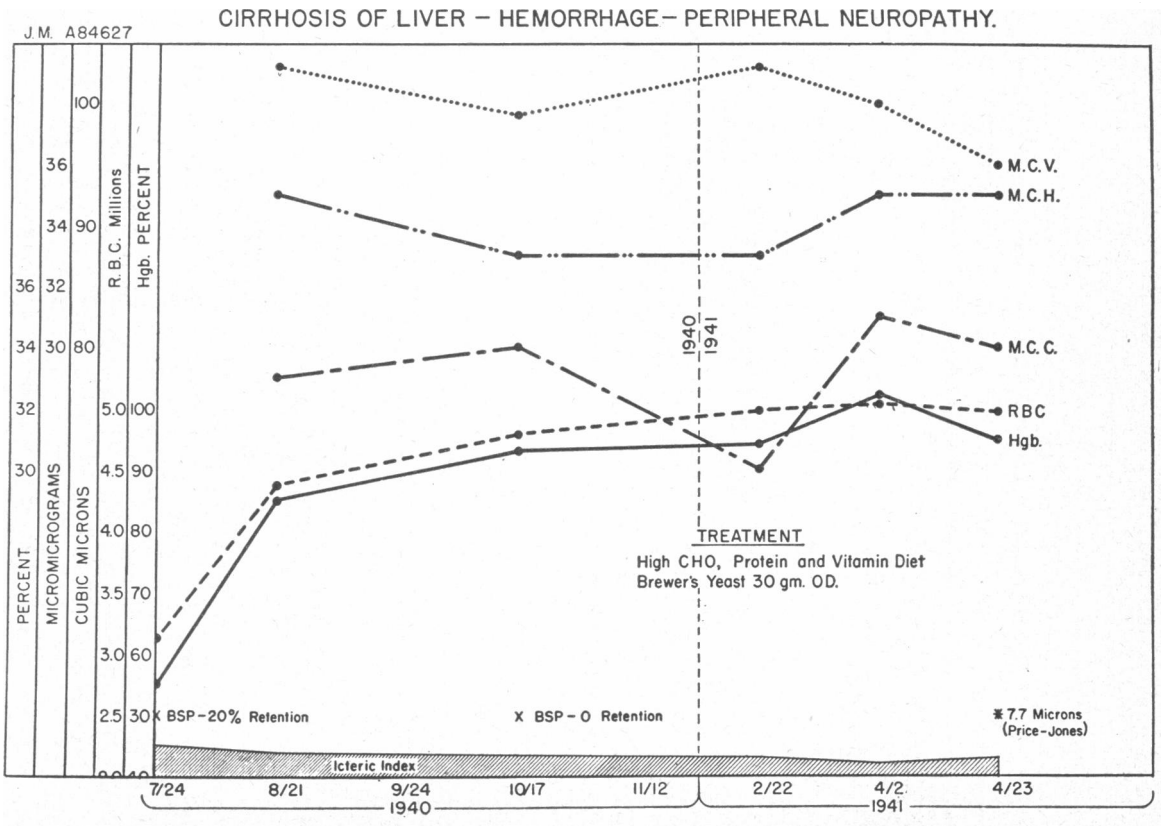

Fig. 1.—Blood values in a case of cirrhosis of the liver under treatment.

abnormal and the normal cells, and give figures which seem quite accurate and which check closely with measurements obtained by the Price-Jones method on the same blood. They are made particularly valuable in liver disease by the fact that the cells show comparatively little variation in size or shape, but are uniformly moderately large. These lesser degrees of cell enlargement are most readily detected by volumetric measurements.

CLINICAL MATERIAL FOR THIS STUDY

A selected group of cases with liver disease have been followed at the Stanford University Out-Patient Department during the past two years. (*Table I.*) Included in this group were sixteen patients with Laennec's cirrhosis, and eleven patients who had had acute hepatitis of varying degrees of severity. Practically all of them had been in the hospital (San Francisco Hospital or Stanford) prior to being seen in the clinic.

None of these cases had hemoglobin determinations under 70 per cent. The lowest was 74 per cent (12.5 gm.) in a case of cirrhosis, the highest 102 per cent (17.5 gm.) in a patient with convalescent hepatitis. All had received some degree of treatment, in a few no more than a well-balanced diet, in most a high carbohydrate, protein and vitamin diet, and twenty to forty grams of brewers' yeast daily, with additional liver extract and vitamins in some. The values obtained in this series, then, represent to a certain extent values obtained in cases with liver disease while under treatment, rather than initial values.

Only one of the eleven patients who had had acute hepatitis had cells within the limits of normal, while four of the sixteen with cirrhosis showed this phenomenon. This makes a total of 22 out of the 27 cases, or 82 per cent with macrocytosis.

The range of values for the mean corpuscular volume was 86 to 111 cubic microns in the acute hepatitis patients, and 80 to 115 in the cirrhosis cases, an average of 101.9 cubic microns in the former, and 97.8 in the latter. The average mean corpuscular volume for the entire group was 99 cubic microns. Most of the individual values were consistently near this average value, and most of the cells in the cases measured by the Price-Jones procedure were remarkable for their lack of variation. The mean hemoglobin content of the red corpuscles was 34 micromicrograms in the hepatitis cases and 32 in those with cirrhosis, averaging 33 micromicrograms for the entire group. The concentration of hemoglobin in the cells averaged 33 per cent which is within the range of normal values. The blood values, then, consistently reveal cells larger than normal and well filled with hemoglobin.

These patients have been treated by rest, abstinence from alcohol, diet high in carbohydrate, protein and vitamin content and low in fat (Carbohydrate 500 grams, Protein 100 grams, Fat 25 grams) and brewers' yeast, 20 to 30 grams daily. A few received liver extract or a syrup rich in Vitamin B complex. In most of those with symptoms there has been continued clinical improvement. In general the values for hemoglobin and erythrocytes have increased towards higher normal figures. In some there has been a regression in the size of the cells towards normocytosis, but in others this has not occurred, while the patient was improving clinically. In others there has been a change from normocytosis to macrocytosis. One patient, whose blood was obtained two years after an attack of catarrhal jaundice, had a mean corpuscular volume of 110 cubic microns without any other laboratory or clinical evidence of disease. The number of observations recorded is very small as yet, but it would appear that macrocytosis may remain long after other evidence of liver disease has disappeared.

One case is cited as an example (*Figure* 2):

REPORT OF CASE

J. M. is a 35-year-old white woman, who had been addicted to large amounts of alcohol for several years. Hematemesis during a drinking bout resulted in her hospitalization. She had a large, hard, slightly tender liver, spider hemangiomata, peripheral neuropathy and anemia. The hemoglobin was 55 per cent (S), the red-blood count 3,130,000 with a color index of .9. There was abnormal retention of bromsulphalein (20 per cent at the end of an hour, 5 mg. per kilogram of body weight being injected). She was first seen in the clinic a month later, having shown considerable improvement. The hemoglobin had risen to 85 per cent (14.6 gm.), the red-blood cells to 4,360,000. The color index had risen to .97. The mean corpuscular volume was 103 cubic microns, the mean corpuscular hemoglobin content 35 micromicrograms, and the concentration 33 per cent. Since that time she has continued to do well. For the past six months she has been in excellent general condition clinically. She

TABLE 1.—*Incidence of Macrocytosis and Hyperchromia in 27 Cases of Liver Disease.*

	Hgb gms.	RBC Mill.	Normocytosis	MCV Range	MCV Cu. Mic. Average	MCH Mic. Mic. Average	MCC % Average
Acute Hepatitis, Average of 11, (2 mos. 2 yrs. after)	13.4 to 17.5	3.56 to 5.36	1 of 11	86-111	101.9	34	34
Cirrhosis of Liver, average of 16 (treated)	12.5 to 16.1	3.88 to 5.04	4 of 16	80-115	97.8	32	33
Total Liver Disease, average of 27 cases			5 of 27	80-115	99.0	33	33

has slight residual numbness and impaired vibration sense in the right foot. Her liver is still palpable; she still exhibits hemangiomata. Her hemoglobin and red-blood count have been maintained at high normal values. She has no retention of bromsulphalein dye. Her corpuscular volume and hemoglobin content reveal persistent nacrocytosis and hyperchromia.

ETIOLOGY

There is general acceptance of the primary etiologic factors which may lead to macrocytic anemia. According to Castle,[9] an as yet unidentified substance, called the "extrinsic factor," is ingested in the food; this reacts in the stomach with the "intrinsic factor" which is contained in the gastric secretion. The product so formed is absorbed from the intestine; it passes through and is modified by and stored in the liver. It then is utilized by the bone marrow as it is needed. This is the substance which is necessary for the maturation of normal red-blood cells. Any interference in this chain of events results in macrocytic anemia.

It has usually been assumed that when damage to the liver becomes extensive, there is interference with the storage process; when this goes on sufficiently long, so that there is exhaustion of the hematopoietic principle already present, macrocytic anemia results. Two conditions seem necessary in this regard: first, that the damage be widespread, and second, that it persist for some time. It does not necessarily have to be severe according to my personal experience, although Wintrobe[9] states it occurred in those cases in which "damage was particularly great and extensively distributed."

Extracts from the livers of patients dying of cirrhosis of the liver, and exhibiting macrocytic anemia, have been injected into patients with pernicious anemia. The results have been at variance. By some investigators[10] no evidence of the hematopoietic substance was found. By others[11] good reticulocytosis and response in the hemoglobin and red-blood count were demonstrated. These studies indicate that macrocytic anemia in liver disease must, in some instances at least, be due to causes other than an inability of the liver to store the hematopoietic principle.

The classical type of anemia produced by faulty nutrition is the hypochromic microcytic anemia of iron deficiency. It has been repeatedly demonstrated that macrocytic anemia may be produced by defective diet over a prolonged period.[12, 13] Remissions may be sustained in such patients by means of diet alone.

RELATION TO DISEASES OF NUTRITIONAL ORIGIN

Macrocytic anemia has recently been reported in a number of different types of disease of nutritional origin. Wills and Evans[14] described a pernicious anemia-like blood picture in a disease which they termed tropical macrocytic anemia; treatment with crude yeast and liver extracts produced remission, but the highly-purified fractions effective in pernicious anemia did not. They postulated the existence of another hematopoietic factor besides the extrinsic pernicious anemia principle. They were able to produce anemia in monkeys fed a deficient diet, and to obtain similar results in the therapy of this condition.[15] Macrocytic anemia has been reported in pregnancy.[16, 17, 18] Elsom and Sample[16] produced it in pregnant women by a diet insufficient in Vitamin B, finding that other clinical evidence of Vitamin B deficiency appeared coincident with the advent of macrocytic anemia. When yeast or liver extract was given, all symptoms disappeared and the blood values returned to normal. Bianco and Jolliffe[19] studied the blood of alcoholic addicts with and without complications which included peripheral neuropathy, pellagra, encephalopathy and cirrhosis. No anemia was noted in the cases without complications, while anemia was found in 61 per cent of those with other diseases. However, in 50 per cent of both groups macrocytosis occurred. Sydenstricker and his collaborators[20] found that commercial liver extract improved patients with both pernicious anemia and pellagra, (although it did not raise the blood count in the latter disease). A similarly-prepared extract from the liver of a patient who had died with severe untreated pellagra was administered to a patient with pernicious anemia, with satisfactory results. However, it did not affect two pellagrins who were later brought into a remission by the use of commercial liver extract. Cirrhosis of the liver[21] very often, and other diseases of the liver not infrequently, are associated with deficiency diseases. It may be that the mechanism of the macrocytosis, as well as that of the anemia, are related in the two conditions. In both the difficulty may lie in the failure to obtain sufficient amount of an extrinsic substance separate from the antipernicious anemia principle or in the inability to utilize it or both. The irregularity of response to aparently adequate doses of liver extract is further evidence that the macrocytic anemia of liver disease may not be caused by a simple lack of storage of the antipernicious anemia substance.

The observations presented here, that macrocytosis may persist long after a patient is clinically well and the blood is otherwise normal, are against the view that it is due entirely to an extrinsic deficiency,[19] and indicate that it may be the result of a defect in the ability of a once damaged liver to synthesize the substance necessary for maturation of blood.

SUMMARY

In liver disease there is generally a macrocytic type of anemia which is mild in degree.

The macrocytosis frequently persists in spite of treatment, and in spite of the return to normal of the general well being, the hemoglobin and the red-blood count of the patient. The cells remain consistently large and well-filled with hemoglobin.

The explanation of the macrocytic anemia as a simple failure of storage in the diseased liver of the hematopoietic substance seems inadequate. It is suggested that the phenomenon is partly the result of an extrinsic deficiency, partly the result of

an inability of the liver to synthesize the maturation factor.

490 Post Street.

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FEMORAL HERNIA: A MODIFIED POSITION FOR ITS REPAIR*

CLARENCE E. REES, M. D.
San Diego

THE femoral vein in the usual operating position encroaches upon the operative field in the repair of femoral hernia. The purpose of this paper is to describe a modified position which displaces the femoral vein laterally, and thereby facilitates the procedure.

Femoral hernia occurs much less frequently than does inguinal hernia. Reported series of comparative statistics vary from 1:17[1] to 1:50.[2] This low incidence may prevent the casual operator from contacting a sufficient number of cases to become familiar with the surgical anatomy of the region, and with the accepted procedures for the repair of the defect. Therefore, a preliminary brief consideration of some of the anatomical and diagnostic problems involved, and of the application of the different surgical approaches to the problem may be in order.

ANATOMICAL PROBLEMS

Anatomically, the structures to be considered may be divided into three groups: (1) the inguinal and lacunar ligaments, which form the roof and medial border of the ring; (2) the ligament of Cooper and the pectineal fascia which form the floor of the ring and the canal; and (3) the process of fascia, which separates the femoral vein from the canal and forms the indefinite lateral boundary of the latter. These are the structures involved in both the reduction and the repair of the hernial defect. It is the approximation of the first to the second, without injury to or constriction of the third, after the ligation, reduction, and transplantation of the sac, that constitutes an accepted operation.

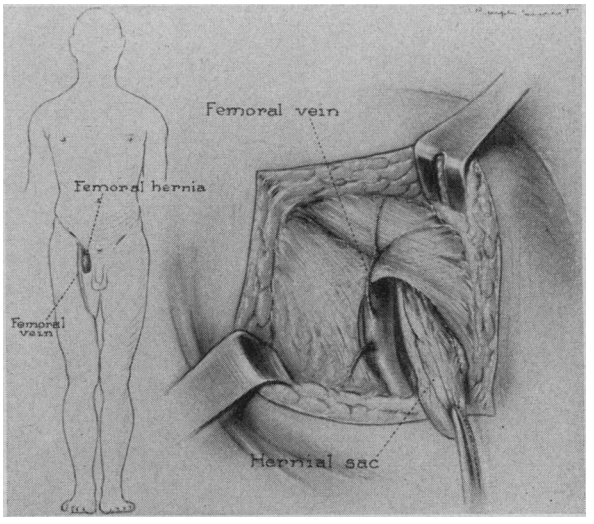

Fig. 1.—Modified position in the repair of femoral hernia. Relationship of femoral vein to sac in usual operating position.

The lacunar ligament is of particular importance, since its sectioning offers a method of enlarging the ring, when this is necessary, without cutting the main fibres of the inguinal ligament. In sectioning of the lacunar ligament there is less likelihood of damage to important structures, and a firmer closure of the ring is obtained. Anatomical studies[3] have shown that in 28 per cent of all individuals an anomalous obturator artery arises from the deep epigastric artery. In 3 per cent of these cases the obturator artery descends to the obturator foramen medial to the femoral ring; in 25 per cent it descends medial to the vein, but lateral to the ring. This means that the lacunar ligament can be sectioned with less chance of vascular injury than can the inguinal ligament. Furthermore, sectioning of the lacunar ligament does not weaken the closure of the femoral ring, as does sectioning of the inguinal ligament. In the first instance repair of the ligament entails only a continuation of the closure medially over the sec-

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From the Rees-Stealy Clinic, San Diego.