W\nHEN ANEMIA is discovered in association with leukopenia and thrombocytopenia, one's first consideration is a possible disturbance of the bone marrow. This may be on the basis of a deficiency in essential materials (such as vitamin B12 or folic acid), or due to hypoplasia or infiltration of the marrow, or perhaps because of hypersplenism. With splenomegaly and pancytopenia occurring together, hypersplenism is often one's first thought. This clinical concept of an overactive spleen having an effect either on circulating blood cells or by remote effects on the bone marrow is bolstered by the finding of a highly cellular marrow, containing, rather paradoxically, the cells deficient in the blood. If then, in a case showing splenomegaly and cytopenia, the marrow is found to be hypocellular, the idea of hypersplenism is considerably vitiated, and other considerations must come to the fore before any serious thought is given to the possibility of splenectomy. This diagnostic situation—splenomegaly, anemia with pancytopenia, and a hypoplastic marrow, is of fairly frequent occurrence in hematologic practice and its management therefore a real problem. A panel consisting of Drs. Jacobson, Moore, and Crosby et al. was asked the following question:

In a case presenting splenomegaly, anemia and pancytopenia and showing a somewhat hypoplastic marrow, what would your further diagnostic and therapeutic program be?

DR. JACOBSON:

My differential diagnosis would include in order of consideration:
1. Banti's syndrome or related hepatic problem.
2. Lymphoma or granuloma such as sarcoid (or even on the basis of a low grade infection).
3. Idiopathic refractory anemia.
4. Disseminated lupus or other related disease type.
5. Myeloid metaplasia.
7. Arsenic intoxication or possibly some other chemical agent such as chloromycetin in a patient being treated for leukemia or infection or having a special sensitivity such as to hair dye preparations, etc.
The diagnostic tests I would perform might be divided into:

1. A study of the peripheral blood for leads on morphologic grounds as well as cell numbers.
2. A study of liver function or related abnormality, including plasma proteins, bilirubin, etc.
3. Study of sectioned sternal bone marrow—microscopically—for presence of lymphoma, granuloma or a replacement phenomenon. Culture of marrow may be indicated.
4. Study of bone marrow function and hemolysis. Pigment excretion, fragility, Coombs' test, platelets and W.B.C. agglutination. Possibly Cr red cell survival and Fe iron turnover and utilization.
5. L.E. preparation.
6. Careful search of the history to rule out the possibility that the patient has taken drug such as arsenic for disease such as chronic myelogenous leukemia with resultant pancytopenia, etc., and possibility that patient might have been on drug such as chloromycetin for treatment of some condition.

If none of these tests uncovered significant leads, I might:

1. Observe patient without therapy if condition not immediately critical, in hope of obtaining leads.
2. If no leads, and state of patient demands therapy, then I would use steroids and observe response in blood, etc., from standpoint of marrow function—possibly going so far as to study Fe uptake, etc.
3. If no leads from (1) and no response from (2), then I might recommend spleen biopsy, if no absolute contraindications, with the idea that if trouble resulted (bleeding, etc.) from procedure, one could proceed with splenectomy.
4. If no leads from spleen biopsy (splenic puncture), then I would probably recommend splenectomy, unless observation suggested that patient could tolerate pancytopenia and still remain in fairly satisfactory clinical state.

**Dr. Moore:**

If the thrombocytopenia is moderate and the patient is not bleeding, we would make the following additional observations:

(a) determine the presence or absence of a hemolytic component to the anemia by measuring erythrocyte survival with either the Ashby or the chromium-tagging technic, and by measuring total urobilinogen excretion over a four day period;
(b) inject a tracer dose of radioiron intravenously so that plasma iron turnover and rate of utilization of iron for hemoglobin synthesis can be determined as an additional index of the production of red blood cells by the marrow; and then
(c) administer 100 mg. of cortisone orally per day for 10 to 14 days to see whether cortisone could stimulate a rise in any of the formed elements. A second tracer dose of radioiron has occasionally been given during the pe-
riod of cortisone administration in order to detect any increase in the utiliza-
tion of radioiron for hemoglobin synthesis.

If practical considerations make it impossible to observe the patient for the long period required for the above studies, “b” is eliminated, “a” and “c” are done concurrently. When thrombocytopenia is severe, the abnormal bleeding invalidates the determination of red cell survival so that observation is also omitted. In the presence of severe granulocytopenia, antibiotics are administered prophylactically during the therapeutic trial with cortisone.

If the data obtained demonstrate no hemolytic component to the anemia and no response to cortisone, the patient is treated with transfusions and supportive care; splenectomy is not done. On the other hand, clear evidence of accelerated red cell destruction and of an increase in reticulocytes, granulocytes or platelets during cortisone administration prompts us to urge that the spleen be removed. Therapeutic results have justified that position. Decision about splenectomy is more difficult when only one of the two above criteria is obtained. But if the rate of hemolysis is so great that frequent transfusions are required, splenectomy is justifiable even though cortisone fails to cause a rise in any of the formed elements. Conversely, when the response to cortisone is definite, particularly if the marrow seems to become more cellular, we feel that splenectomy should be tried even though red cell survival is within normal limits.

In the above discussion, it is assumed that no immuno-hematologic mechanism could be demonstrated and that a thorough search has failed to detect exposure to known marrow toxins.

(DR. CROSBY)

Dr. Crosby's answer came in the form of the minutes of a panel discussion held at Walter Reed Army Medical Center and entitled

DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS IN HYPOPLASTIC PANCYTOPENIA WITH SPLENOMEGALY*

Minutes of a Discussion Held at the Army Medical Service Graduate School, 21 December, 1954


CROSBY: Pancytopenia, where red cells, white cells and platelets all are diminished, may be due to inadequate production or to shortened survival of these elements. The diseases that cause pancytopenia are numerous and diverse; many of them present special problems of therapy. Our present consideration is simplified by two important qualifications: the pancytopenia is associated with splenomegaly and hypoplasia of the bone marrow.

O'BRIEN: I should like to ask what is to be our criterion of hypoplasia. An attempt to aspirate marrow through a needle is not always successful. The

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failure may be due to fibrosis or it may be due to hyperplasia where the cellular elements are so tightly packed that they are able to resist the force applied by the aspirating syringe. I would suggest that when aspirated marrow—or the lack of it—indicates hypoplasia we should take an actual biopsy. Using a needle trephine this can be done with no more effort or discomfort than the ordinary sternal puncture. Conversely it should be remembered that a generally hypoplastic marrow may contain "islands" of active tissue. Aspiration from such an area may give an erroneous impression of hyperplasia.

Crosby: While we are defining terms let us also decide what we mean by pancytopenia. The cells in the blood are diminished, but what is the limit that defines "cytopenia?"

Lange: Any answer to that question would be more or less arbitrary. For the sake of our argument let us say that the hemoglobin is 10 Gm. or less, the white cell count is 4,000 or less and the direct platelet count is 150,000 or less.

Crosby: Agreed? Then let us decide what diseases meet the specifications of our problem: pancytopenia, hypoplasia and splenomegaly. Many causes of pancytopenia can be eliminated. We need not consider panhypopituitarism where the marrow is normal and the spleen is not enlarged. We need not consider aleukemic leukemia where the marrow is hyperplastic or benzol poisoning where there is no splenomegaly.

[Table one, page 761, was then constructed.]

Rheingold: Perhaps it should be made clear that complications of such diseases may alter the usual picture. A patient with leukemia may have his bone marrow made hypoplastic by the effects of treatment, and a patient whose marrow has been damaged by benzol may develop splenomegaly as a result of myeloid metaplasia.

Crosby: I agree, but in general the toxic hypoplasias and indeed the idiopathic hypoplasias are not associated with splenomegaly unless they are somehow complicated.

Dr. Rheingold, you have had experience with hypoplasia following the use of chloramphenicol. Had any of your patients an enlarged spleen?

Rheingold: No, but if chromic hypoplasia or myelofibrosis occurred myeloid metaplasia in the spleen might produce splenomegaly.

Crosby: Dr. Lange, you have described a chromic hypoplasia that developed in some of the survivors of the atomic blast in Nagasaki several years after they had recovered from acute radiation illness. Was splenomegaly a feature of this disease?

Lange: No, in none of the six patients was a large spleen encountered. It is entirely possible, however, for any patient with this sort of hypoplasia of the bone marrow to have a splenomegaly due to some entirely unrelated disease, malaria or portal hypertension for example.

Crosby: In published reports of large series of patients with toxic or idiopathic hypoplasia without metaplasia there are only a few cases where splenomegaly occurred and most of these had obvious signs of hemolytic disease.

That brings up another point. We cannot cleanly separate the pancytopenias into two groups: those due to inadequate production and those due to short
survival of the circulating cells. Even where production is shown to be deficient there may also be some shortening of life span due to a hemolytic or “pancytolytic” effect. From the therapeutic point of view it is especially important to recognize this possibility. There are two ways in which pancytopenia can be corrected; by increasing production of the cellular elements or by prolonging their survival. When cytolytic disease is present some improvement may be gained by therapy that is aimed at prolonging cellular life span even in the presence of a marrow disease which would preclude increased production.

RHEINGOLD: I think that emphasizes the necessity for accurate and adequate diagnosis before any definitive or what might be dangerous therapy is begun.

O'BRIEN: Dangerous?

RHEINGOLD: Yes. Certainly splenectomy in the face of severe thrombocytopenia is not without hazard. In Hodgkin’s disease one would hesitate to give nitrogen mustard if he were aware that his patient’s pancytopenia was due to fibrosis of the marrow. I used cortisone once in a patient of the sort we are discussing here (case 1). There was no evidence of tuberculosis but when splenectomy was subsequently done, it was learned that the spleen showed evidence of this disease. Fortunately no harm was done, but in retrospect when cortisone was used the patient should have had treatment with anti-tuberculous drugs as well. The diagnosis of disseminated tuberculosis as a cause of pancytopenia may be difficult but one should attempt to rule it in or out before cortisone is used, because this is one disease which may be made worse by the incautious use of steroid hormones. Furthermore before splenectomy is performed we would like to see what the treatment of underlying tuberculosis could do for the pancytopenia before undertaking any therapy directed at the secondary hematologic disease.

LANGE: Dr. Rheingold makes a valuable distinction, one which should be a rule in the treatment of this or any other hematologic problem. Pancytopenia is only a symptom of disease. Our first effort should be directed at discovering and, if possible, treating the primary disease. We should always bear in mind that the correction of anemia or the prevention of infection in agranulocytosis or hemorrhage in thrombocytopenia are stop-gap procedures.

O'BRIEN: There are other precautions to remember in using these “secondary” therapeutic agents. The requirement of the patient is the most important of these. Not all patients with 2,000 white cells need antibiotics to control infection, nor does every patient with 20,000 platelets need cortisone. The most common failure to evaluate the requirement of the patient occurs in the treatment of anemia by means of blood transfusion. Too often, in making the decision to transfuse, the physician is guided by the red cell count rather than by physiologic need. Every transfusion carries the risk of a reaction and the possibility of infectious hepatitis. The development of “iron overload” is more than a possibility or a risk. It is a certainty in patients with chronic refractory anemia who require transfusions to sustain them. These patients absorb more than the normal amount of iron from their diet so they develop hemosiderosis even if they are not transfused. In addition every liter of blood carries 0.5 Gm. of iron into their bodies. Iron is not excreted and it cannot be lost except by bleeding. Heavy deposits of iron in vital organs may shorten the life of the anemic patient. For this reason one should give as little blood as possible in chronic
anemia and he should not attempt to maintain the patient's hemoglobin concentration at some arbitrary level.

Crosby: The other end of this argument should also be mentioned: we must not let a patient die of anemia for fear of transfusing him. Patients who receive large numbers of transfusions are apt to become immunized against some of the less antigenic of the blood-group antigens thus making them more susceptible to incompatible transfusion reactions. It may require very careful cross matching to avoid these reactions. This sort of patient may also be prone to develop non-specific transfusion reactions due to some factor in the donor's plasma. To prevent this the plasma may be siphoned off and the red cells washed with sterile saline. The plasma-free red cells can then be transfused with impunity. In neither case should transfusion be withheld when anemia is severe. Furthermore, we should be careful not to underestimate the requirement for transfusion in severe anemia. The requirement may be surprisingly great when pancytopenia is complicated by hemolytic disease. A liter of blood per day or more may be needed to tide a patient over a severe hemolytic crisis.

Dr. Rheingold, how shall we decide if or when to remove the large spleen in our patient with pancytopenia and a hypoplastic marrow?

Rheingold: Splenectomy should not be done when we are fairly sure that it can do no good. If there is some hope that it may help, the operation should be considered and the possible benefit weighed against the risk. Where the primary disease can be controlled, in tuberculosis or Hodgkin's disease, for example, splenectomy may be unnecessary. In general, cortisone should be given a careful trial before splenectomy is done. If the pancytopenia yields to cortisone this may indicate that the bone marrow suppression or the cytolytic effect is malleable and we would then have some basis for hoping that splenectomy would produce a longer-lasting effect. An insidious hemolytic disease may develop in some of the more chronic cases so that the transfusion requirement becomes progressively greater. Here splenectomy should be considered.

Lange: There are even more sensitive tools for the detection of hemolytic disease such as red cell survival measured either by the Ashby technic or by the disappearance of radio-chrome-tagged cells. And the radio-iron uptake curve is characteristically distorted in hemolytic anemia. Radio-iron studies are also of value in establishing the amount of hematopoietic activity that is taking place in the marrow. By the use of red cell survival plus measurement of marrow function we can determine with some precision how much of the anemia is due to hemolysis and how much to inadequate erythropoiesis. One would certainly favor splenectomy if hemolysis played a major role.

Rheingold: The patient with 15,000 platelets may also be a candidate for splenectomy. At that level he is on the edge of disaster. If splenectomy only doubles the platelet count he would be safer.

O'Brien: We have recently removed the spleen from such a patient, a little girl with Fanconi's syndrome (case 2). It was hoped that her need for transfusions would be diminished and that her platelet count would increase to a safer level. The platelets improved only transiently and it is too soon to know if her transfusion requirement is less.

Crosby: Not much more can be hoped for in the congenital hypoplastic
When we recommend splenectomy for these children it is only in the hope of small gains, and we usually defer the recommendation until the small gains will make some difference. This is another example of weighing the requirement of the patient against what is hoped to be gained by therapy.

**Rheingold:** We should also mention those conditions where little or nothing is to be gained by splenectomy. In Hodgkin's disease splenectomy is usually unrewarding. In the acute, self-limited pancytopenias—those represented in the table by aregenerative crisis and iatrogenic hypoplasia—splenectomy is not indicated, at least not with the hope of relieving the crisis. That is not to say that a patient with hereditary spherocytosis in aregenerative crisis is not a candidate for splenectomy. Certainly he is, but my own inclination would be to see him through the crisis before removing his spleen.

**Crosby:** The aregenerative crisis is an interesting and important problem. It was originally described in patients with hereditary spherocytosis and it was suggested that it might represent a form of acute hypersplenism because after splenectomy these patients do not develop anemic crises. The aregenerative crisis occurs because the bone marrow abruptly ceases to produce blood cells and there is an acute hypoplasia. Usually the marrow is reconstituted within two weeks, and the therapeutic problem is to tide the patient over this critical time. After splenectomy the hereditary spherocytes survive normally so that a two-week lapse of erythropoiesis is of little matter. This may explain the absence of the crises after splenectomy in hereditary spherocytosis. The spleen probably is not otherwise involved in the aregenerative crisis. The crisis has been observed in normal children following infections or exposure to certain drugs. It has been observed in sickle cell anemia where the spleen is atrophic, and we have recently reviewed a case resembling thalassemia minor in which an aregenerative crisis occurred several months after splenectomy (case 3). In most of the patients in crisis, anemia is the therapeutic problem and transfusion is the solution, but we have seen severe agranulocytosis where the use of antibiotics was probably life-saving. Purpura has also been described which would justify the use of cortisone. I agree with you, Dr. Rheingold, that splenectomy in the midst of an aregenerative crisis is not indicated.

**O'Brien:** A similar problem is posed by the hypoplasia we sometimes induce with myelosuppressive drugs. We have treated selected cases of systemic Hodgkin's disease with large doses of nitrogen mustard. We have learned that severe temporary leukopenia is the consequence and in anticipation of this we give the patients large doses of penicillin as the white cell count begins to fall and before he develops any signs of infection (case 4). Although the patients also may develop anemia and thrombocytopenia these have not been clinical problems.

**Rheingold:** When thrombocytopenic purpura becomes a problem in these self-limited conditions the use of platelet transfusions is a practical expedient.

**O'Brien:** On several occasions we have used fresh whole blood drawn into plastic equipment. We transfuse it immediately in fairly large amounts and the results have been good (case 3).

**Crosby:** Dr. Lange, what is your opinion regarding splenectomy in myeloid metaplasia when the spleen is filled with hematopoietic tissue?

**Lange:** Metaplasia of the spleen was once thought to be a contraindication...
to splenectomy. It was believed that the spleen under these circumstances represented the body's source of blood cells. Recently this attitude has been convincingly challenged. Some of these patients after splenectomy showed a gratifying improvement. It seemed that their spleens were destroying more cells than they created. In myeloid metaplasia I would consider splenectomy where hemolytic disease has become a problem and also when the size or weight of the spleen has become oppressive.

Crosby: Would you recommend a diagnostic splenic puncture?

Lange: This is one place where the procedure may be of value, but I do not believe it is always necessary to puncture the spleen in order to establish the diagnosis of myeloid metaplasia. The coincidence of a fibrotic or sclerotic bone marrow, anemia with or without pancytopenia, the presence of myelocytes and erythroblasts in the peripheral blood and splenomegaly offer strong presumptive evidence.

Crosby: We have discussed the problem of pancytopenia at considerable length without evolving any formula for a diagnostic or therapeutic program. Do you think, Dr. Lange, that a formulation is possible?

Lange: Our discussion has shown that pancytopenia, even when the problem has been narrowed down by the presence of hypoplasia and splenomegaly, is not a simple situation. We have evolved no formula because none is possible. Each patient must be considered individually first to establish his diagnosis and second to treat him according to his requirements.

Crosby: If you had not said "no formula is possible" I'd say you've given us a good one.

APPENDIX—CASE REPORTS

Case 1: A 57 year old metal inspector, first presented himself to me in May 1953 with a history of onset of easy fatigability about a year previously. He had consulted a physician who treated the anemia he found with anti-anemic therapy without success. In December 1952 a bone-marrow study was reported to the patient as showing “no malignancy” and further anti-anemic therapy was continued. He received four whole-blood transfusions in February 1953 with great benefit. However, by May 1953 he felt markedly fatigued and was having angina with effort. Previous history revealed no toxic agents, although he had contact with lead, cadmium and aluminum ore from 1947 to 1951. Physical examination revealed only pallor without lymphadenopathy, hepatomegaly, splenomegaly, or hemorrhagic signs. There was present a pancytopenia, with R.B.C. 2,000,000, Hb 7 Gm., hematocrit 23, W.B.C. 1900 with 36 per cent segmented neutrophils, 60 per cent lymphocytes, 1 per cent monocytes, and 3 per cent eosinophils. Platelets 13,600. Bone marrow study revealed an aplastic marrow. The patient was unable to maintain an adequate hematocrit, despite 1500 ml. of blood during the last of May, again in June, and in July. He received 300 mg. of cortisone a day for three days in early July, but stopped it because it upset his digestion. He developed furuncles on his neck in late July, which responded promptly to magnamycin. He was restarted on cortisone. On August 5, he developed chills and fever and a recurrence of his furunculosis, which again responded to magnamycin.

Because of the failure to maintain his hematocrit, and the infections, he was admitted to the hospital for further study and possible splenectomy. There his fever ranged between 102 and 103 F. despite antibiotic therapy. Sputa examinations were negative for acid-fast bacilli, and chest X-ray was negative. Blood cultures were negative. On September 9, 1953, a splenectomy was done. Grossly the spleen showed tubercle formation, and on microscopic caseation necrosis and some acid-fast bacilli were found. His blood counts rose and leveled off: hematocrit 38, platelets 250,000; W.B.C. 5-7000 with 40-45% segmented neutrophils. He was treated with anti-tuberculous drugs, and to date has had no further
manifestation of this disease. He needed imo transfusions until December 1953, but since that time requires blood occasionally to keep his hematocrit between 32 and 35, where he is most comfortable. He still has a moderate leukopenia (about 3000) and a considerable thrombopenia (30–40,000) without infection or hemorrhagic manifestations.

Case 2: A six year old white girl with stunted growth (15 Kg.), mental retardation, absent thumb and an 18 months' history of pancytopenia with a hypoplastic bone marrow. Transfusions were of temporary benefit. In the autumn of 1954, it was found that the uptake of Fe by her red cells was impaired and the survival of transfused red cells in her circulation was abnormally short. Hb 4.6 Gm., W.B.C. 1000 to 2500, platelets 15,000 to 30,000, reticulocytes 1 to 2.5 per cent. Cortisone produced a reticulocytosis of 10 per cent with no increase of Hb or cellular elements in the blood. With a septicemia in November her condition deteriorated. Hb 3.5 Gm., W.B.C. 2500, platelets 1500. The spleen (35 Gm.) and several accessories were removed uneventfully on 13 December. Just as splenectomy was begun the patient received a transfusion of blood freshly collected in plastic and later a transfusion of platelet-rich plasma. Immediately after surgery: Hb 14 Gm., W.B.C. 5000, platelets 290,000. One week later: Hb 12 Gm., W.B.C. 4000, platelets 30,000. One month later: Hb 10 Gm., W.B.C. 4800, platelets 37,000, reticulocytes 1 per cent.

Case 3: A 54 year old white male was found in September 1950 to have hypochromic anemia and splenomegaly, R.B.C. 4.0 million, Hb 9.2 Gm., W.B.C. 8700, platelets 450,000, reticulocytes 5 per cent. The red cells showed poikilocytosis and basophilic stippling. Osmotic fragility was less than normal. The bone marrow showed erythroid hyperplasia. The spleen was removed (325 Gm.) but there was no improvement in the anemia. On December 15, 1950, the patient was readmitted with severe anemia and petechiae. Hb 4 Gm., W.B.C. less than 2000, platelets 38,000, reticulocytes 0.65 per cent. The bone marrow was described as aplastic. On December 30 the bone marrow once more showed erythroid hyperplasia. The hemoglobin was 11 Gm. (he had been transfused), W.B.C. 2000, platelets 385,000, reticulocytes 6.5 per cent. In October 1951 the marrow was still hyperplastic. Hb 11 Gm., W.B.C. 11,000, platelets 785,000, reticulocytes 5 per cent.

Case 4: A 25 year old white male with a history of oral ulcers, cervical adenopathy and fatigue dating from April 1952. Repeated biopsies were not diagnostic until September 1954 when a cervical lymph node revealed Hodgkin's disease. Hb 12 Gm., W.B.C. 4300, platelets 263,000, reticulocytes 2 per cent. Only cervical adenopathy was evident, and the patient was treated with x-ray: 2400 r to the neck and 2400 r to the mediastinum. W.B.C. fell to 1750. After 30 days' leave he returned with fever and a palpable spleen. Hb 11 Gm., W.B.C. 2000, platelets "adequate." It was decided to use chemotherapy, and from 23 to 25 November the patient received 50 mg. of methyl-his mustard. 26 November Hb 9.8 Gm., W.B.C. 750. 30 November Hb 8.7 Gm., W.B.C. 250, platelets 50,000. 1 December Hb 8.9 Gm., W.B.C. 150, platelets 38,000. Bone marrow aplastic. 10 December Hb 6.6 Gm., W.B.C. 1000, platelets 9000. 17 December Hb 6.7 Gm., W.B.C. 3000, platelets 114,000. 5 January Hb 10 Gm., W.B.C. 3500, platelets 227,000. Spleen not palpable. During the period of leukopenia the patient received large doses of penicillin by mouth. He developed no evidence of infection other than a moderate pharyngitis, and there were no signs of purpura. He received no transfusions or steroids.

**TABLE I. HYPOPLASTIC PANCYTOPENIA WITH SPLENOMEGALY**

Conditions in which hypoplasia and splenomegaly are related:
- Hodgkin's disease and lymphosarcoma
- Myeloid metaplasia
- Fanconi's syndrome and similar diseases
- Disseminated tuberculosis

Conditions in which hypoplasia and splenomegaly are not related:
- Aregenerative crisis
- Iatrogenic hypoplasia
- Coincidence
REFERENCES


Moderator's Comment:

The working out of a case such as those presented in Crosby's panel has indeed considerable fascination and there is no hard and fast rule as to therapy.
until the diagnosis has been “nailed down.” The necessity in some cases of carrying out a large variety of laboratory procedures, some of them quite technical, is brought out particularly in Jacobson’s comments. Curiously none of Crosby’s panel has recommended the diagnostic value of splenic puncture, which we rely upon in these cases as often having considerable value. Jacobson suggests it, but he uses a Silverman needle and we use a simple 21 gauge needle affixed to a syringe. With this technique, we have made the diagnosis of lymphosarcoma or reticulum cell sarcoma of the spleen on a number of occasions, and of course the diagnosis of myeloid metaplasia of the spleen is readily confirmed. Whether or not to do splenectomy in a given case is often a matter for long-term consideration, but when no other therapeutic opening seems possible and the patient’s condition is getting worse, splenectomy may have to be done on the basis of a “gamble.” Not infrequently the gamble “pays off” in the form of a remarkable, even an incredible result. Thus, no patient having a similar situation and who is in reasonably good condition should be denied the benefit of splenectomy unless there is some impelling reason why the operation should not be done. With modern surgical methods and the availability of plastic bag blood transfusions, antibiotics and the like, few contraindications to splenectomy remain, even in the older age group.—W. D.
Panels in Therapy. IV. The Therapeutic Management of a Case Presenting Splenomegaly, Pancytopenia, and a Hypocellular Marrow

LEON O. JACOBSON, CARL V. MOORE and WILLIAM H. CROSBY