

Education is not concerned primarily with intellectual luxuries, but with elements which make the individual a valuable member of society. —William Mather Lewis

# BULLETIN

of the  
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SOCIETY**

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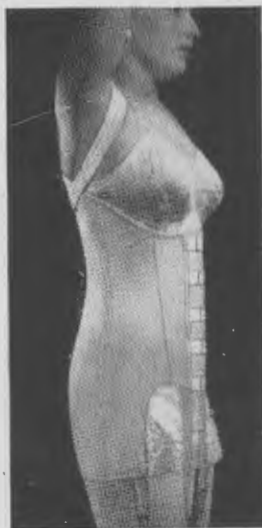
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## PRESIDENT'S PAGE

●

Our Annual Postgraduate Assembly, held on April 17th, is now history. The Postgraduate Chairman, Dr. S. R. Zoss; the Program Chairman, Dr. E. J. Wenaas; and the Social Chairman, Dr. J. K. Herald, are greatly commended by the Society for successful management of this affair. Much effort and planning was necessary to bring this event to a successful conclusion.

The attendance was far beyond our expectations. Our registration shows attendance from 15 different cities and towns in Pennsylvania and from 35 in Ohio. Looks are though our Publicity Committee was surely on the job.

### Cancer Clinic

There is under way at this time a National Campaign for the early detection of cancer, under the auspices of the American Cancer Society. What has the Mahoning County Medical Society done about this pertinent matter?

1. Two clinics have been set up. One at the South Side Unit of the Youngstown Hospital and one at St. Elizabeth's Hospital. These clinics are now being staffed by the respective hospital staffs and will be in operation in the near future. Both clinics will be listed in the telephone directory which will be in circulation about July first.

2. Functions of these Clinics. Dr. Heberding and his committee have worked long and hard to make these worth while clinics not only a success but an example for other communities to emulate. They are, as the name implies, for detection only and not for treatment. Patients will be sent back to their own physician and a complete report sent to him, thereby retaining that patient-physician relationship that is paramount in bringing these conditions under control.

EDWARD J. REILLY, M. D., *President*

●

## LABORATORY AIDS IN ANEMIA

By ARTHUR E. RAPPOPORT, M. D.

*Department of Laboratories, Youngstown Hospital Association*

Following the publication of a short paper on "A Study of Anemia" in the April issue of the Mahoning County Medical Bulletin, we were requested to amplify the scope of that article by pointing out specific diagnostic laboratory procedures which would aid in analyzing cases of anemia.

The basic initial examination is the enumeration of the red and white blood corpuscles, the quantitative determination of the hemoglobin in grams and of the packed cell volume, as well as an examination of a stained smear for morphologic characteristics of the red blood corpuscles and the determination of the differential white count. On the basis of this information the anemia may be classified according to size of the cell, its hemoglobin content and the morphologic changes from the normal size and shape.

If the anemia proves to be of a *macrocytic type*, a *deficiency of anti-anemic principle* should be suspected. The diseases caused by such a deficiency are: pernicious anemia, sprue, idiopathic steatorrhea, some cases of intestinal stricture or resection, gastrocolic fistula, celiac disease, pellagra, other forms of chronic diarrhea, "tropical" nutritional macrocytic anemia, rare cases of carcinoma of the stomach following total gastrectomy, macrocytic anemia of pregnancy, diphyllobothrium latum infestation, chronic and extensive liver disease, macrocytic anemia of hypothyroidism and "Achromic" anemia. Additional causes would be conditions usually associated with normocytic anemia, particularly sickle cell anemia, macrocytic hemolytic anemia of obscure etiology, acute hemolytic anemia and possibly anemias due to internal radiation.

Of course, a complete history and physical examination should be carried out with particular reference to signs and symptoms which are frequently characteristic, but whose enumeration is not within the scope of this paper. Further tests which are necessary are: Gastric analysis, Icterus Index and Van den Bergh reaction, Urobilinogen and Bone Marrow Aspiration. Stools should be examined for blood, ova and parasites, increased fat content and, in the presence of diarrhea, bacteriological examinations and studies for possible malignancy should be performed. A blood NPN and serologic test for syphilis should not be omitted. In the presence of neurologic changes a spinal fluid may frequently be necessary.

History and physical examination in order to prove the presence or absence of nutritional defects such as pellagra are necessary. Diseases of the liver, particularly cirrhosis, may lead to a macrocytic anemia; thus requiring complete liver studies including several Liver Function Tests. The fish tapeworm may lead to a clinical syndrome and blood picture resembling that of pernicious anemia, while hypothyroidism has also been responsible for pernicious anemia-like symptom complexes. These syndromes are listed in order that definitive differential diagnostic procedures be carried out to exclude them from the classical picture of pernicious anemia.

A very valuable clinical procedure is the administration of liver as a thera-



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peutic test. The giving of a potent liver extract for several days should be followed by a characteristic reticulocyte response and rapid relief of symptoms, as well as a rise in the red cell count. Material containing liver, iron and other substances should not be utilized for this test, and should not be used as a "shot-gun" prescription in therapy at any time.

If on the basis of the original classification, the anemia proves to be of normocytic variety the causes may be due to the following: A. *Sudden loss of blood* as in acute posthemorrhagic anemia including scurvy, hemophilia, purpura. B. *Destruction of blood* (1) *Acute* due to protozoa or bacteria, chemical, vegetable or animal poisons, hemolysins of incompatible blood, paroxysmal "cold" hemoglobinuria, acute exacerbation of chronic hemolytic anemia. (2) *Chronic* due to congenital hemolytic jaundice, sickle cell anemia, chronic hemolytic anemia, nocturnal hemoglobinuria, chronic "acquired" hemolytic jaundice. C. *Lack of blood formations* as in *aplastic anemia* due to organic arsenicals, benzol, gold compounds, mustard gas, Bi, Hg, Ag, dinitrophenol, hair dyes and exposure to radioactive substances. D. *Simple chronic anemia* associated with various inflammatory and non-inflammatory disease—especially renal disease, malignancy and chronic infections. E. *Myelophthisic anemia* due to metastatic carcinoma in bone marrow, Hodgkin's disease, leukemia, multiple myeloma, myelosclerosis, marble bone disease. F. *Hydremia* due to "physiologic" anemia of pregnancy.

To classify diseases of the first group (A. above), blood and urine Vitamin C levels, platelet count, bleeding and clotting time, clot retraction time, prothrombin time, tourniquet test, and examinations of stools and urine for occult blood are necessary.

In the study of the second group (B. above), causes for hemolysis should be sought which are obvious from the listing. Tests necessary would be blood typing, determination of Rh factor, serological examination for "cold" antibodies, bacteriological examinations for hemolytic organisms and determination of possible exposure to hemolytic agents. For the chronic hemolytic type, blood fragility test, sickle cell test and the examination of urine for blood cells and hemoglobin should be carried out. For all possible hemolytic anemias, liver studies should include at least the determination of Icterus Index, Van den Bergh, Urobilinogen and Bromsulphalein Excretion. The blood smears usually show marked anisocytosis but little poikilocytosis, and evidence of red cell regeneration as evidenced by increased numbers of reticulocytes, appreciable polychromatophilia and numerous normoblasts. Microcytes (Spherocytes) are characteristic of familial hemolytic jaundice. The white cells usually show a leucocytosis including myelocytosis and thrombocytosis. Bone marrow examination is extremely important in the diagnosis inasmuch as it is very characteristic.

In *aplastic anemias*, the red cells are usually normal in appearance and polychromatophilia, stippling and nucleated red cells are usually not found. The reticulocyte count is low. Occasionally the anemia is macrocytic probably due to the presence of immature forms. The anemia is usually associated with leucopenia and thrombocytopenia, the granulocytes being particularly reduced while only occasionally is there a true absolute lymphocytopenia. The bleeding time is prolonged and blood clot retracts poorly while the coagulation time is generally normal. Gastric secretion is not affected and no evidence of blood destruction is found in plasma, urine or stools. The bone marrow



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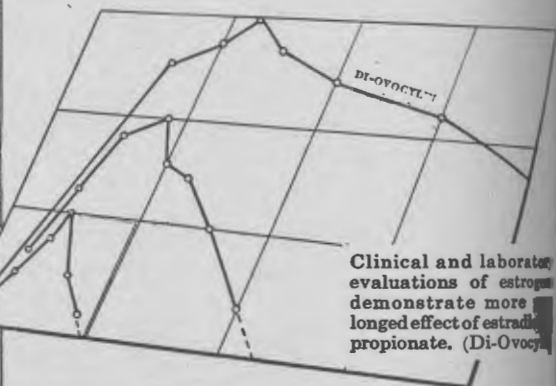
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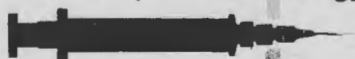
\*Greene, R. R.; Int. Abst. Surg. 74: 595, 1942

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usually is specific although in some cases it may show normal cellularity or even hyperplasia.

The groups of *microcytic* and *hypochromic anemias* may be combined for practical purposes. As pointed out in the previous article this group is usually due to Iron deficiency. This may arise from: (A) Deficiency of foods containing iron. (B) Defective absorption of Iron in association with achlorhydria following gastrectomy, sprue, idiopathic steatorrhea, celiac disease or chronic diarrhea. (C) Continued loss of blood due to chronic alimentary or genitourinary tract bleeding, multiple hereditary telangiectasia. (D) Excessive demands for iron due to requirements for growth or repeated pregnancies. (E) Above causes in various degrees and combinations due to chlorosis, chronic hypochromic anemia of women. (F) Deficient antenatal storage or postnatal supply due to hypochromic anemia of infants.

The laboratory tests required for analysis of this group should include the gastric analysis in order to rule out the very large group of *chronic hypochromic anemia* (idiopathic hypochromic anemia) which usually affects women in the third to fifth decades. Here *achlorhydria* is a leading characteristic and its presence requires the differentiation of this syndrome from that of pernicious anemia. Stools should be examined for hookworm as well as for evidence of dysentery and sprue. The diet must be analyzed for its content of meat, liver and other foods containing iron particularly in infants up to three years of age and from poorer classes. The red cells here show extreme poverty of hemoglobin indicated by exaggeration of their central pallor. Fragility is usually normal but there may be some increased resistance to destruction.

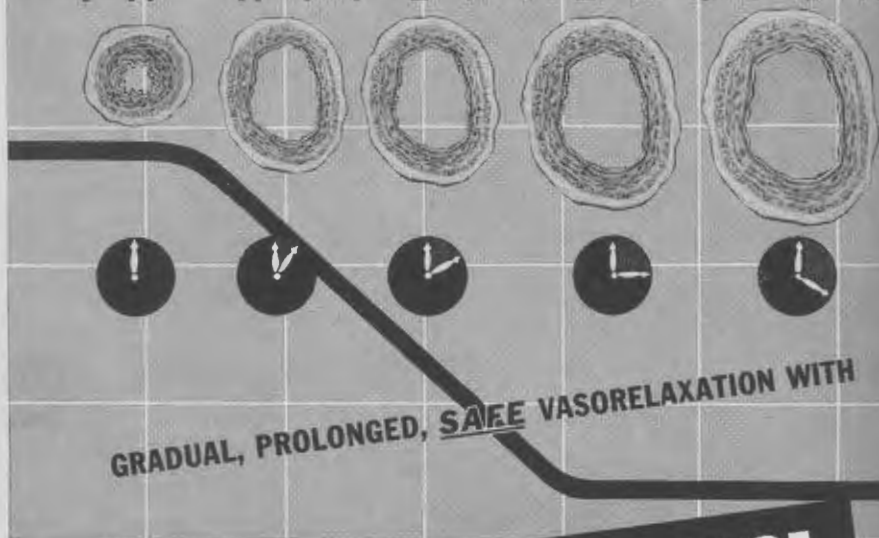
For completeness sake, one must include a group of ill-defined anemias seen in infancy and childhood. In erythroblastosis fetalis, examination of the Rh factor in father, mother and infant, the analysis of the blood smear for erythroblasts and the determination of the Icterus Index will suffice to make a diagnosis although it must be differentiated from simple icterus neonatorum, congenital obliteration of the bile ducts, congenital syphilis, sepsis and hemorrhagic disease of the newborn.

Chronic congenital anemia differs from the above in that it resembles aplastic anemia. Nutritional anemia may be due not only to absence of iron but also to elements of Vitamin B complex. Anemia in infants raised on goat's milk have been reported. Premature or multiple births frequently show anemia of the infants.

A hemolytic anemia of infants (Mediterranean or Cooley's anemia) is a disease complex which shows erythroblastosis splenomegaly and familial incidence as well as characteristic changes in the skeletal system. The red cells on smear show marked anisocytosis and poikilocytosis as well as the characteristic "target cells". Stippled cells and Howell-Jolly bodies are found and the reticulocytes are increased. The fragility of the red corpuscles is usually decreased. The icterus index is slightly or moderately increased while the urine contains increased quantities of urobilinogen. Many of these cases resemble Baucher's, Niemann-Pick's or Schuller-Christian's disease.

Anemias associated with splenomegaly deserve special consideration. Under this group one must consider the so-called Banti syndrome, Felty's anemia, portal or splenic vein thrombosis and the so-called splenic anemia. A test of

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value in this group, in addition to those already described, is the Adrenalin Test.

While most anemic syndromes may thus be satisfactorily classified and treated on a rational basis, some may pose difficult diagnostic problems. In such cases, close co-operation between the attending physician and the hematologist is necessary, in order fully to exploit all aspects of these interesting, yet at times, vague disease complexes. It is hoped that the attention of the clinical pathologist will be called to the existence of such cases in the hospital and private practice, in order promptly to arrive at a precise analysis of the disease.

## SERVICE RECORDS

### LT. W. E. SOVIK

Dr. Sovik entered the Navy in 1944 and 10 days afterwards was on his way overseas. He saw service in Wales, England, France and Belgium. On D-Day, when the hospital landing ships were taking in troops and taking out the wounded, he was one of those present and probably the only Mahoning County physician on duty there with the naval forces on that day. He will ever have the memory of those 60 hours under the terrific battle strain of D-Day.

### MILTON M. KENDALL

Dr. Kendall served in England with the Eighth Air Force. He was in charge of the medical care of all flying and ground crew personnel at a fighter base. During May and June of 1944 he was attached to the Royal Air Force and went through the Normandy Invasion. He also participated in a number of air-sea rescue missions in the English Channel. Again in December of 1944 he was with an RAF unit that fought through the Rhineland campaign. While in England, Dr. Kendall received a British license to practice medicine in the United Kingdom, and was also elected a fellow of the Royal Society of Medicine.

### MAJOR JOSEPH J. SOFRANEC, JR.

Dr. Sofranec entered the armed forces in August of 1942. After brief Army training at Walter Reed General Hospital, Washington, and Camp Pickett, Virginia, he was sent to England with the 110th Station Hospital. He was there when the D-Day casualties came in. In May of 1945 he was sent to France and remained there until assigned back to the States in September. His outfit was awarded a meritorious service plaque.

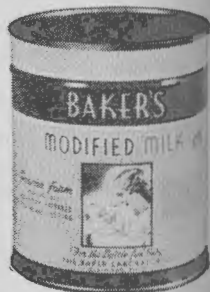
### MAJOR H. E. CHALKER

Entered the service August 8, 1942 and was assigned to the Station Hospital at Camp Crowder, Missouri. Nine months later he was transferred to the 179th Station Hospital in the Aleutians. In November 1944 he was transferred to the 183rd Station Hospital at Anchorage, Alaska. He served as chief of surgery at the 179th and 183rd Station Hospitals. His terminal leave expired January 21st, 1946.



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## NEWS

Dr. L. K. Reed has returned from serving with the 307th General Hospital for three and a half years, and is practicing internal medicine at his old location, 634 Market Street.

Dr. and Mrs. V. L. Goodwin have returned from Roanoke, Va., where Dr. Goodwin attended the Spring lectures at the Gill Memorial Eye and Ear Hospital. Before returning, they spent some time at Virginia Beach and Atlantic City.

Dr. and Mrs. F. J. Bierkamp and Dr. and Mrs. F. W. McNamara arrived home after a month's vacation in Florida. They were guests at the Indian Queen Hotel at Miami Beach, and were also guests for a week at the home of Mr. and Mrs. John T. Watters, former Youngstowners now living in Coral Gables.

Dr. and Mrs. C. D. Hauser have returned from a trip by motor to Buffalo where they were guests at the Statler for a short time while Dr. Hauser attended a reunion of his class at University of Buffalo.

Dr. and Mrs. Howard E. Possner, Waterfield, Conn., have concluded a few days' visit in the home of Dr. and Mrs. Olin W. Haulman, Sampson Road.

Dr. and Mrs. J. B. Birch and Mr. and Mrs. Bert M. Summers recently returned from a sojourn to Atlantic City.

Dr. and Mrs. John Renner have moved into their new home at 262 Granada Avenue.

Dr. and Mrs. F. F. Piercy have returned from New York City where they spent a week.

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### *May Meeting*

**Speaker: ELMER L. DeGOWIN, M. D.**  
University of Iowa

**Subject: "ANURIA, DIFFERENTIAL,  
DIAGNOSIS AND TREATMENT"**

### DINNER - DANCE

The Ladies' Auxiliary to the Mahoning County Medical Society will hold a Dinner-Dance on Thursday, June 6th, at Tippecanoe Country Club. A fine program has been arranged. In addition to dancing, there will be bridge, prizes and an old fashioned get-together. Dinner will be served at 6:30 P. M., and an evening of dancing and entertainment from 9 to 12. Herbert MacPherson's Orchestra will furnish the music. Mail reservations to Mrs. W. O. Mermis, 105 Overhill Road, Youngstown 7, Ohio.

*Committee in Charge:* Mrs. W. O. Mermis, Social Chairman; Mrs. Brack Bowman, Co-Chairman; Mrs. E. E. Kirkwood, Mrs. Raymond Hall, Mrs. W. H. Evans, Mrs. J. R. Buchanan, Mrs. W. E. Maine. Mrs. John S. Goldcamp, Program Chairman; Mrs. E. H. Nagel, Mrs. Paul Fuzy.

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**Mrs. C. A. Gustafson**, Vice President

**Mrs. John Rogers**, Secretary

**Mrs. W. K. Allsop**, President-Elect

**Mrs. M. M. Kendall**, Treasurer

The Woman's Auxiliary to the Mahoning County Medical Society held a meeting Monday, March 25th, at 1.30 P. M. at the South Side Hospital Nurses' Home.

Dr. Eugene E. Elder, Superintendent of Youngstown Receiving Hospital, was the principal speaker. He emphasized the unique status of the institution, it being the first of its kind in the State of Ohio.

The Public Welfare Department of the State of Ohio, under whose supervision the Receiving Hospital is conducted, is keenly interested both in its activities and in the public response to such an institution.

Primarily the hospital was designed to care for borderline cases; a place where mentally disturbed and confused individuals could take their problems for consultation, advice and treatment, if required. The Receiving Hospital is not to be known as a hospital for the insane.

Dr. Elder pointed out the fact that admission to the hospital is voluntary, upon recommendation of the family physician and not by compulsion of the court, as is the case in the State hospitals. He strongly emphasized that the public must be made to understand that admission to or treatment in an institution of this kind is in no way different from that afforded in a general hospital. There is no stigma upon the patient. There should be no reluctance to seek consultation or advice, or in being admitted for treatment.

The hospital was opened four months ago and has admitted 200 patients, of which 130 have been discharged, 100 as improved and 30 have been transferred to veterans hospitals. (Most patients have been ex-servicemen.)

At present the cost per day to care for a patient is \$6.03 as compared with \$6.45 in the city hospitals. This figure will, in time, be cut appreciably.

Dr. Elder paid tribute to the untiring efforts and far-sightedness of Judge Woodside, who for many years, has advocated the establishment of such a hospital. Having witnessed and decried the incarceration of mental cases in the county jail pending action in the Probate Court, and realizing the inadequacy and inhumanity of such a situation, practically made it a personal crusade. The action of the State Welfare Department in opening its first Receiving Hospital in Youngstown is a tribute to Judge Woodside's effort.

A business meeting preceded Dr. Elder's talk.

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## Case Presentation at the Clinical-Pathological Conference at the Youngstown Hospital, April 12, 1946

Dr. Patrick presented the following case history: A thirty-eight year old Para iii was admitted November 30, 1945, in labor. There was a history of two previous miscarriages, one at 7 months and one at 6½ months. Twelve hours after admission a low forceps delivery of a living infant girl was performed; birth weight was eight pounds, twelve ounces. The birth was three weeks premature.

The condition of the infant was poor at birth, and in spite of CO<sub>2</sub> inhalations, aspiration, and injection of alphalobelin she died 25 minutes later.

Laboratory work showed the cord blood to have a negative Kline. The mother was tested for Rh factor and found to be Rh negative.

At autopsy the weight of the baby was 3513 gms. The placenta weighed 820 gms., showing a 1:4.2 ratio to the weight of the fetus. The normal ratio of placental weight to fetal weight is 1:6.3 to 7.9. The spleen and liver were both enlarged, the spleen weighing 65 gms. (normal fetal weight 9-13 gms.) and the liver 328 gms. (normal weight 135-160 gms.). 500 cc. of free fluid was found in the peritoneal cavity.

Microscopic findings showed marked erythropoiesis in the liver and spleen with distortion of the liver structure. In the placenta the structure conformed to one type of change seen in erythroblastosis.

Dr. Lupse discussed erythroblastosis as a problem in Obstetrics. It was his conviction that many of the abortions and premature births can be explained by the Rh factor, whereas previously the condition had no known cause.

Dr. Jensen gave the statistical incidence and types of erythroblastosis with the mortality data.

Dr. Altdoerffer reported a case of erythroblastosis with the classical picture of Rh positive father, Rh positive fetus, and Rh negative mother. When severe jaundice developed shortly after birth the infant was immediately transfused with 200 cc. of type 0, Rh negative blood, and eight hours later was given another 100 cc. Between transfusions 400 cc. of saline was given in order to keep the canula open—making a total of 700 cc. fluid given in nine hours, of which 300 cc. was whole blood. The infant's red cell count rose from 2,500,000 to 5,000,000 and the jaundice gradually subsided. Complete recovery followed.

During the discussion it was noticed that Weiner believes all females from childhood through child bearing period should be checked for Rh before accepting blood transfusions. Apparently even in childhood there is risk in giving Rh positive blood to an Rh negative girl. Levine has calculated that only 0.13 cc. of fetal blood is required to sensitize an Rh negative mother. Concerning this transfusion problem Dr. Rogers said that there are now a few professional donors available with type 0, Rh negative blood. The question arises as to whether a higher price should be paid for this fortunate combination.

It was also noted that the titre of Anti-Rh serum in mothers' blood changes little during pregnancy, indicating that there is slight leak of red cells through the placental barrier. This may suggest that the greatest hazard is at the time of labor when there may be appreciable leak through the placenta both ways.

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## POSTGRADUATE NOTES

Big assignment, this postgraduate reporting. A beautiful, bright, sunny day—just our kind of weather. Committee is sure on the job—what happened? Must have had some training since I was Chairman. Zoss! Imagine him working! Oh! There are Lowendorf, Dulick, Steinberg and last, but not least, Banninga, eager to take in the money.

“Quit pushing”. These colleagues of mine are sure rough. Can’t wait to register. No, it doesn’t cost you a cent, paid in your dues. Tell same ones, same thing, year after year. I wonder what they would really do if this eager committee tried to get the five they are displaying?

Registration is only \$5.00 this year. Wonder what he means by that? Oh, well, I won’t worry about next year. Lecture starts in five minutes. Projector, loud speaker, everything ready to go. Bowman from Canton, first man to register. Oh! There comes Rutledge from Alliance, 6th District Councilor, believe that is Elliott with him. W. J. Brown, from Conneaut, with that broad smile. Long way to come to be with us. He appreciates our good programs. A. W. Conkey from Canton and Phil Linsey from Cleveland. Howdy, boys. Biggins from Sharpsville, never misses. King and Bennett from Alliance. They really sneaked out; I can tell by their expressions. Chalker from Girard—glad to see you, doggone it! Proletti from New Castle with that big cigar; sure, nuff, it’s a boy! Doc Thomas from Niles, Martin and Biggs from Wadsworth.

Going in to see what is going on. “Low Back Pain”, by Dr. Lenhart. Sure have heard that many times; so has he, the way he goes about it.

Displays. Oh! Not in the hall? Oh, times have changed. Fred Lyons with a truck load of equipment; sure is nice. Immediate delivery? Oh, yes! Some new customers. Wilfred Howard, Breon & Co., Buffington’s, Pitman-Moore, “Zane Gray” representative. That isn’t the guy that used to write those novels? Lloyd Stillson and Lamar Donahay, “Insurance”, oh, yes, that’s a good company he represents. No Treudley samples? Ralph White, beaming. No wonder, Ralph, Jr., is home from the Pacific. Good looking chap. Doesn’t look a bit like Ralph. Cassaday, Merrell, Ciba, Endo, Lester, Mead-Johnson, Similac, Zemmer, all passing out samples. No Beil-Rempes? Something happened. Professional Pharmacy; that’s a new one. My pockets are bulging. Wish I had one of those A & P bags to put my samples in. They will sure come in handy. My shelves are empty. I had such a good time visiting those booths I forgot the time and missed some of those problems in treatment of rheumatism. Did get a Klondike on the way out—one of Isaly’s—nice folks—prescribe homogenized milk for the kiddies. Wainwright! He’s right about that rheumatism all right.

Back to those displays. I have her figured out now, Helen Mantle, that’s it. She’s what I call a sure fit—any size. More samples this year than last, they tell me. What! Something wrong over there! I see the *Bulletin* com-

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mittee in conference with someone. Oh, yes, sir, one of those floorwalkers. Have to give our Society credit. They sure protect our advertisers.

Back to the desk. They are still registering. Nice crowd, Sam. How many? 200 now, and we are just starting. You don't say. I'll relieve, so some of you boys can hear that man Polvogt. There go Wenaas and Goodwin. Smart man that Polvogt. They'll catch on. Let's see the visitors' register. What do you know. From all around—New Castle, Beaver Falls, Warren, Massillon, Newton Falls, Sharon, Kent, Canton, Salem, Columbiana, ~~Seentown~~—where is that? Publicity sure gets around, or I'll bet it's our *Bulletin*? It sure gets around, and takes too.

Harrison from East Liverpool, Snyder from New Kensington, Shaw from Springdale, and here is Buckwalter from Columbiana. He is a faithful attendant. Ken Camp, what do you know? I wondered where he was. The Krupko's from McDonald, Elizabeth Veach from New Wilmington, another never-misser; Glass, Copeland; I did not get that other fellow's name; good looking chap; suit on something like mine. Lot of boys from New Castle—Snyder, Beaver, Pop—I knew he wouldn't miss it—Biggins from Sharpsville, Hackett from Canton. Nice fellow just registered from Dover. I've seen him here before. He's with that good-looking Allen from Dover. Newman and Boyce from Fremont, Smith from Bristolville. Gee whiz, where are all these places? Here comes Lonaker from Conneaut; too much business; I can't handle it. Six from Salem at one time!

Afternoon program over. Won't be long 'til dinner; tables look nice, flags, flowers, and everything. What! No tux! Council looks so comfortable. Been a good joke on some of them if our guests came prepared for a dressup! A few extra bulges there that are not provided for in a two or three year old tux. That man Paul Mahar promised me roast beef. Here it comes—what! Turkey! There must be a mistake! It was supposed to be roast beef. There ain't no justice. I got writer's cramp, and surely thought I would be compensated with roast beef. There comes Sam out of the kitchen! If you know him like I do, you know he isn't eating roast beef. Oh, well! Professor Reinhoff will be on next and he is sure good. Not long since he was here. Peptic ulcer, good subject on a full stomach.

Our Program Committee sure finds the good speakers, and, co-operating with the Social and Postgraduate Committees, no wonder we have a big time.

Space does not permit mentioning all our guests, but we are happy to welcome all of you and hope you will all come back next year.

—X Y Z.

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## COUNCIL MEETING

The regular monthly Council Meeting was held at the office of the Secretary on the 8th of April. The following doctors were present: E. J. Reilly, G. M. McKelvey, J. N. McCann, J. J. McDonough, P. J. McOwen, E. J. Wenaas, E. C. Baker, C. A. Gustafson, E. H. Nagel and W. M. Skipp.

The following letter was read from the Ohio State Nurses' Association:

March 18th, 1946.

Mahoning County Medical Society,  
Edw. J. Reilly, M. D., President,  
125 W. Commerce Street, Youngstown, Ohio.

Dear Sir:

In order to promote good understanding and co-operation among medical, nursing and allied professions dealing with the health of the community, District No. 3, Ohio State Nurses' Association, voted to establish a Special Committee on Professional Relationships.

We are particularly desirous of having a member of the Medical Society serve on this committee. Would you be good enough to appoint one of your members who is interested in our common problems and who would be willing to serve. The number of meetings will be determined by the Committee.

May we hear from you as soon as convenient?

Yours very truly,

EMMA S. MODELAND, R. N.

*President of District No. 3, Ohio State Nurses' Association*

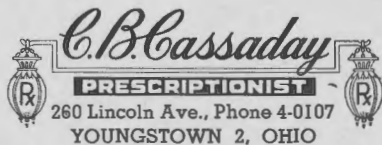
Dr. W. J. Tims was appointed by Dr. Reilly to serve.

Dr. Skipp submitted a report on the recent survey conducted by Dr. Gregg, relative to a full-time Public Health Commissioner. Survey and report were turned over to the Public Health Committee for study and report back to Council.

V. L. GOODWIN, M. D., *Secretary.*

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## THE TREATMENT OF URINARY INFECTIONS WITH SULFASUXIDINE (SUCCINYLSULFATHIAZOLE)

By HOUSTON S. EVERETT, M. D.

### The Problem

Urinary infections are frequent and often serious complications of gynecological and obstetrical conditions. The etiological agent in the production of such infections may be any one of a variety of microorganisms, but in the majority of them some member of the coliform group of bacilli is the responsible agent. Of this group *Escherichia coli* is the most frequent offender. These facts are especially true with regard to those infections occurring during pregnancy and the puerperium.

By careful attention to eradication of such contributing factors as lesions productive of urinary stasis and distant foci of infection, much progress has been made in the prevention and treatment of these infections. The therapy of the infections, once established, has been greatly augmented by modern chemotherapeutic methods, especially the use of sulfonamide drugs. Chemotherapy, however, has proved generally more effective in the acute forms of urinary infections than in the chronic varieties. So long as such complicating factors as stasis or calculus are permitted to exist, even the most efficient means of chemotherapy will usually fail to eradicate the infection. In some other cases, even though no such factors have existed, or if they have existed have been thoroughly eradicated, infection will persist in a chronic state in spite of the most efficient known methods of chemotherapy. In other cases, it is found that the infection will subside temporarily in response to chemotherapy, but will quickly recur after withdrawal of the drugs. Such chronic or frequently recurring infections generally result in slowly progressive damage to the kidneys, and furthermore, constitute an additional hazard in that should such stasis-producing factors as the physiological dilation of the renal pelvis and ureters occurring during pregnancy or postoperative or postpartum urinary retention intervene, acute febrile episodes of pyelonephritis are very apt to result. It is most important, therefore, that use be made of every available means to accomplish complete and permanent eradication of urinary infections of this type.

Urinary infection by all types of organisms is generally considered to be secondary, in that the organisms reach the urinary tract from some source elsewhere in the body. The possible routes by which access to the urinary organs is attained have for many years been the subject of much contention, and a vast literature has grown out of these discussions. The question is not entirely settled, and for the present discussion it is of no great importance. It has been thoroughly reviewed in most textbooks of urology as well as in many independent articles.

For coccal infections, elimination of the source depends upon a thorough search for, and eradication when found, of focal infections in distant parts of the body. In the case of coliform infections, however, the normal flora of the intestinal tract constitutes a permanent massive reservoir of the offending organisms. If this reservoir can in some way be depleted even temporarily, and the constant source of infection thus removed, the normally high resistance of the tissues of the urinary tract to infection, may be given a chance to recover,

so that chronic infection may subside, and frequent recurrences will be less apt to occur in the future.

### The Drug

Since about 1940, considerable investigation has been carried out in attempts to find a drug of the sulfonamide group locally effective in the intestinal tract. Such work is still in progress and has already met with considerable success. It is desirable that such a drug should be poorly absorbed from the intestine, so that it may remain to exert its effect upon the bacterial flora of the large bowel, and so that possible toxic effects resulting from its absorption into the blood stream may be reduced to a minimum. To date, the most efficient drug fulfilling these criteria is Succinylsulfathiazole, manufactured by Sharp and Dohme under the trade name of Sulfasuxidine, and first thoroughly studied both experimentally and clinically by Poth and his collaborators in the surgical department of the Johns Hopkins University. The chief clinical uses of the drug so far reported are preparation of the bowel for operation upon it, the treatment of bacillary dysentery, and the treatment of ulcerative colitis. Although Poth's first preliminary report appeared in October, 1941, already considerable literature regarding the use of the drug for these purposes has appeared.

In dogs the drug was found to be nontoxic and harmless when administered in doses of 1 gm. per kilogram of body weight daily for as long as five weeks. This dosage resulted in a fecal content of the drug of 5 to 10 per cent, and only about 5 per cent of the ingested drug was excreted in the urine. Crystalluria did not occur, and the observed blood levels were never more than 1.5 mg. per cent of sulfathiazole and 2 mg. per cent of succinylsulfathiazole. The dosage for human beings recommended by Poth and his associates was an initial dose of 0.25 gm. per kilogram of body weight, and 0.25 gm. per kilogram in six divided doses daily thereafter. With this dosage, the blood level of free sulfathiazole reported by Poth rarely exceeded 1.5 mg. per cent, although occasionally, higher levels were found for one or two days during the administration of the drug. The highest level recorded was 2.9 mg. per cent, and this was for only one day. The average of 77 determinations in 10 human subjects was 0.95 mg. per cent. The blood levels of succinylsulfathiazole ranged from 0.5 to 8 mg. per cent, the average being 2.11 mg. per cent. In general, the higher blood levels of both substances were obtained on the earlier days of administration following the initial massive dose. The average daily urine excretion in the same cases was found to be 0.34 gm. of free sulfathiazole and 0.38 gm. of succinylsulfathiazole.

No toxic reactions to the drug were encountered in the earlier observations of Poth, but subsequently an occasional case with skin rash or febrile reaction has been reported. The subjects in whom these reactions occurred usually have been shown to be highly sensitive to sulfathiazole, as similar reactions were precipitated by single small doses of this drug. One case of fatal agranulocytosis following administration of the drug was reported by Johnson. Clay and Pickrell have reported the only case yet recorded of hematuria and crystalluria resulting from administration of the drug.

According to the work of Poth and his associates, the purpose accomplished by this drug is to reduce greatly the concentration of the intestinal bacterial flora, especially the coliform bacilli. It was found that when the suggested dosage was administered the count of *E. coli* in the stools was reduced in from

one to seven days from the normal of 10,000,000 or more to less than 1,000 per gm. of wet stool. In some cases after administration of the drug no *E. coli* could be grown in stool cultures. The drug has the additional effects of overcoming any tendency to constipation and of rendering the stools soft and odorless.

#### Conclusions

Succinylsulfathiazole has been found effective in the treatment of urinary infections due to *E. coli*.

When administered in daily doses of 0.25 gm. per kilogram of body weight the urine is usually rendered sterile in less than one week.

Continuation of the drug in daily doses of 0.125 gm. per kilogram of body weight for two more weeks seems to protect the patient against recurrence of infection.

The drug has proved effective against infections which had proved resistant to other sulfonamides and to mandelic acid.

The drug is not effective against infections due to organisms other than *E. coli*.

Because of its scant absorption and low toxicity, it is well tolerated by patients with impaired renal function, or severe anemia who would tolerate other sulfonamides poorly.

Theories of the possible mode of action of the drug are discussed. The most probable mode of action seems to be that elimination of the source of infection from the bowel permits the tissues of the urinary tract to throw off infection by means of their own resistant powers.

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#### Discussion

DR. FRANKLIN L. PAYNE, Philadelphia, Pa.—As we review the titles of the papers that have been presented before this body during the past few years, we are struck by the scarcity of topics in female urology. It was the teaching of Dr. Clark and of Dr. Keene, my preceptors at the University of Pennsylvania, that female urology constitutes an indispensable part of the gynecologic specialty. I subscribe to this teaching. Therefore, it is particularly pleasing to me to be granted the opportunity to discuss this work that has been done so ably by a gynecologist.

Having had no personal experience with the use of succinylsulfathiazole in the treatment of urinary tract infections, my discussion consists of certain observations that are based upon a review of the literature, including Dr. Everett's manuscript and a limited experience in the management of urinary tract infections by other measures. As Cook stated recently, in simple uncomplicated infections of the urinary tract almost any of the sulfonamide compounds are effective in more than 90 per cent of the cases. We can



state further that most acute uncomplicated urinary tract infections clear up within a short time whether treated by means of alkalinization, acidification, alternation of the two, the older so-called urinary antiseptics, simple water diuresis, or by sulfonamides.

The few who do not respond and those with the tendency to recur, such as the ten cases referred to in Dr. Everett's Table II, offer a real opportunity for clinical investigation. His originality in thought and his success in the treatment of the *E. Coli* infections deserve commendation. It is unfortunate that a greater number of the recurrent or intractable cases do not result from this organism. Our experience indicates that *E. Coli* infections occur far less frequently than do those from other types of invaders, which appear not to respond to succinylsulfathiazole.

In the experimental investigation of succinylsulfathiazole, this drug has been shown not to remain entirely within the intestinal canal. Welch, by administering 5 milligrams per kg. per day of each drug to monkeys by gavage, found the average concentration in the blood of succinylsulfathiazole to be 3 mg. per cent, and of sulfathiazole to be 0.8 mg. per cent. Apparently, the latter is formed by hydrolysis.

Poth detected an average of 2 mg. per cent of succinylsulfathiazole and 0.95 mg. per cent of sulfathiazole in the blood stream, following his routine dosage in the human being. While such concentrations are desirable in the treatment of urinary tract infections, by the same token, they may be distinctly harmful to the patient. Poth, Clay and Pickrell, and Johnson have reported a total of four unfavorable constitutional reactions to succinylsulfathiazole—one of which was fatal. These reactions were ascribed to either sensitivity or idiosyncrasy to sulfathiazole and emphasis was laid upon the danger of prolonged administration or intermittent application of sulfonamide therapy. Each of those writers recognized that the ingestion of succinylsulfathiazole is attended by the risk of an untoward response.

Patients who receive this drug—as is true of all sulfonamides—should be kept under careful observation, for it cannot be administered without fear of unfavorable reactions.

In considering the mode of action of succinylsulfathiazole, the essayist pictures the most likely effect to be that of alimentary bacterial depletion with subsequent or concomitant assertion of the natural resistant and recuperative powers of the urinary tract. The chronology of events gives reason to question this conclusion. Poth found that the intestinal flora is about depleted in 93 per cent of the cases at the end of a week. Of 41 cases treated by Everett, 91 per cent of the urines were rendered sterile—usually in less than a week. It is doubtful, that this round the corner therapy could produce simultaneous results in both the intestinal and the urinary tracts, if the latter result is dependent upon completion of the former. The time relationship suggests a dual action, and this suggestion is supported by investigative studies. Poth found the urinary excretion of sulfathiazole to average 0.34 mg. per cent, and that of succinylsulfathiazole to average 0.38 per cent following his routine dosage. Everett found the urinary concentration of sulfathiazole to vary from 1.75 mg. per cent to 12 mg. per cent. He did not report the urinary concentration of succinylsulfathiazole. The remarkable susceptibility of *B. coli* organisms in the intestinal canal to this type of therapy has been demonstrated repeatedly and these organisms should react similarly in the urinary tract. Many writers have emphasized the low dosage requirements in other forms of sulfonamide therapy for urinary infections. It seems reasonable, therefore, that Dr. Everett's results are due first, to local action of these drugs as they are excreted by the kidneys and second, to intestinal bacterial depletion.

DR. J. MASON HUNDLEY, JR., Baltimore, Md.—For many years considerable interest has been centered upon the subject of urinary antiseptics, initiated in some measure by the work of Shohl and Janney in 1917, who showed that the growth of *Escherichia coli* was inhibited by changing the hydrogen-ion concentration of the urine. Some years later Clark and Helmholtz introduced the ketogenic diet, its essential factor being the high fat content in relation to the carbohydrate component. Due to the incomplete metabolism of the fats, a condition of acidosis is produced with the outpouring of ketone bodies in the urine, chiefly beta-hydroxy-butyric acid. It has been shown by Fuller that it is this ketone body in the presence of markedly acid urine that produces the desired bactericidal effect. This diet, as will be remembered, was difficult to carry out as it frequently produced severe gastrointestinal disturbances.

Another advance was the introduction of mandelic acid. This substance, which is



secreted unchanged, is efficacious only in a markedly acid urine, the acidity being accomplished by the administration of ammonium chloride. Ammonium mandelate, as it is now produced, is of use in patients in whom sulfa therapy is not tolerated and continues to be used in selected cases.

No real success was attained, however, in the treatment of urinary tract infections until the introduction of sulfanilamide and its closely related substances. The most popular urinary antiseptics today, I believe, are sulfathiazole, sulfadiazine and sulfamerazine, and probably the latter evokes fewer untoward reactions than any of its associated compounds. As is well known, after continued use of the sulfanilamides, organisms originally susceptible may become fast and the drug be ineffective. The use of sulfasuxidine for persistent urinary tract infections, particularly those due to the *Escherichia coli*, seems to be a distinct advance and well worthy of trial. In this relation I have had no personal experience, having employed it only with intestinal operations and especially in the preoperative treatment of complete prinal lacerations.

Sulfasuxidin therapy will be of inestimable value in treating pyelitis with pregnancy when the usual infecting *Escherichia coli* is not susceptible to the sulfa group.

In using any type of chemotherapy for urinary infections, it is first obligatory to relieve any obstructive lesion. If such a condition is not removed, there is no permanency of urinary sterilization, for with cessation of therapy there is soon a return of the infection.

I agree with the essayist that permanent cures are difficult to explain when they are initiated by only a temporary sterilization of the bowel content, this being complete or more frequently incomplete.

When one reviews some of the opinions in regard to the lymphatic relationship between the bladder and kidney and especially between the large bowel and kidney, it is more difficult to understand how a permanent cure could be produced. Franke has demonstrated that lymphatics from the large intestine pass over the capsule of the kidney, that the kidney has a rich network of lymphatics that emerge at the hilum, and that there is a connection between these lymphatics and those of the capsule. Mayer is of the opinion that the lymphatic connection only occurs between the colon and the right kidney and that pathologic changes of the intestinal wall are necessary before a transmigration of organisms can take place, probably explaining, if he is correct, the intermittency of kidney infections. Regardless of these anatomic findings, which may not be constant, sulfasuxidine would appear to be of great value in eradicating persistent urinary infections due to the *Escherichia coli*.

DR. EVERETT (closing).—Dr. Payne spoke of the possible dual action of this drug, and he is quite right in emphasizing this point. I emphasized the mode of action through the intestinal tract particularly because some of these cases had not completely cleared up with the administration of sulfathiazole alone. It is possible that the two modes of action together may be the final answer, but I do believe that the elimination or reduction of the intestinal flora is a least partly responsible for the results obtained.

Dr. Hundley stressed the eradication of urinary obstructions, and I have mentioned that point in the paper also. Our clinic under the leadership of Dr. Hunner has for years stressed the importance of establishing adequate renal drainage in the treatment of infections as well as many other diseases of the urinary tracts. Every possible effort was made to eliminate any discoverable obstructive lesion in each of these cases.



## THE LIBRARY CORNER

**Charles K. Petter, M. D.: Diseases of the Chest; 11:419, 1945. "Chemotherapy of Tuberculosis."**

In the search of a sulfonamide compound which would be more effective than sulfapyridine in combating pneumonia, there was developed a group of compounds known as the sulfones. The first of these, diamino-piphenyl-sulfone, demonstrated a striking ability to control tuberculous disease in laboratory animals, but was extremely toxic. Derivatives from this compound were less toxic, but some of them were less effective. Promin (p, p'-diamino-diphenyl-sulfone-n, n'-dextrose sodium solfonate) has been employed clinically and has been reported to have favorably influenced human tuberculosis.

The author investigated clinically another sulfone, diasone (disodium-formaldehyde-sulfoxylate-diamino-diphenyl-sulfone), which has been shown by Feldman to be less toxic experimentally than diamino-diphenyl-sulfone and by Callomon to be only slightly less effective than promin.

Over a period of 18 months the author treated 170 persons with diasone and from data so obtained makes the following pertinent statements:

1. Reactions to the compound usually are not severe, have not been observed to have caused any permanent damage to tissues or organs, and are controlled by withholding the drug.

2. Dermatitis of severe proportions is the only reaction reported by other investigators. Six serious cases have been reported. The author has seen 2 cases with less severe dermatitis.

3. Pulmonary tuberculous lesions of the exudative type have shown favorable response for the most part, exceeding the obtainable without the administration of diasone. Lesions predominantly fibrotic or fibrocavernous either have not been favorably in-

fluenced or were so affected only slightly. Large, thick-walled cavities must be attacked surgically.

4. Acute exacerbation of the disease while receiving diasone occurred in only 1 case. This after the woman had been improving for 60 days.

5. Symptomatic, radiographic and laboratory evidence of improvement was secured in 80 per cent of a small group with genito-urinary and occeous tuberculosis (all but 2 patients).

6. Favorable results were also obtained in a few cases of tuberculosis and mixed infection empyema.

"Predominantly exudative pulmonary lesions, particularly earlier and less extensive disease, have shown resolution and become sputum negative, in the majority of cases. These changes have occurred sooner than would have been anticipated with conventional therapy. Patients with large unilateral cavitation and clear contralateral lung have been carried through thoracoplasty without 'spill over' into good lung. Likewise, those who had fresh bronchogenic spreads in contralateral lung were carried through thoracoplasty and progressively improved the fresh lesion.

"A number of advanced cases and a few of those less involved showed either no change or became worse while receiving diasone."

"Rapid and pronounced decrease in urinary tract symptoms, disappearance of tubercle bacilli from the urine and an increase in general well being have followed the administration of diasone to patients with unilateral and/or bilateral renal involvement as well as bladder involvement."

Sanatorium stay was 25 to 50 per cent less in the diasone treated patients, and most of the discharged patients were able to resume active work and half of them have continued to take diasone at work.

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