

forms for a sufficiently long period to justify considering the person noninfectious. Sulfanilamide has multiplied the technician's work and added greater uncertainty to the value of his results.

DR. WIRT B. DAKIN, Los Angeles: I wish to present a new "believe it or not" incident: The officers on a submerged submarine noticed that one of their sailors was cyanotic. The vessel was promptly brought to the surface. With hatches open they rushed to their base, where the patient was hospitalized. The submarine's oxygen apparatus was overhauled but nothing found wrong. This incident cost the navy (American taxpayers) about \$5,000. The sailor had been treating himself with sulfanilamide. On being discharged from the navy hospital he consulted a civilian urologist and said "Doctor, you must not repeat what I have told you. If the navy officers found this out I should be hung by the heels from the tallest yardarm."

DR. ANSON L. CLARK, Oklahoma City: Dr. Helmholtz has been kind enough to emphasize the infecting organism *Streptococcus faecalis*. In diagnosis when this type of micro-organism is present may I make a plea for closer cooperation between the clinician and the laboratory? Recently I had a report from the laboratory of a large hospital that the urine showed short-chained streptococci. Such a report would lead one to believe that sulfanilamide would be of therapeutic value. In examining the slide carefully myself I found the diamond-shaped streptococci in pairs typical of *Streptococcus faecalis*. This organism apparently is not inhibited in its growth by sulfanilamide. May I again suggest that urologists familiarize themselves with brucellosis because of the important effect this type of infection may have on the urinary tract? Therapeutic measures in the treatment of brucellosis vary widely, from administration of vaccines to fever therapy. In my experience a carefully prepared vaccine, such as the Parke Davis product, has given the most uniformly satisfactory results. It must be remembered that the dose usually suggested is much larger than should be given if one would avoid the unpleasant complications many have encountered in giving undulant fever vaccine.

DR. HENRY F. HELMHOLTZ, Rochester, Minn.: I want to emphasize one thing about the bacteriologic examination of the urine. It is outstanding that *Streptococcus faecalis* is the one organism that apparently grows almost as well in a solution of sulfanilamide as it does in a broth culture, so that it cannot be hoped that sulfanilamide will cure an infection caused by *Streptococcus faecalis*. In cases in which sulfanilamide has been administered, one not infrequently sees *Escherichia coli* disappear from the urine, only to find that a pure culture of *Streptococcus faecalis* remains; in such cases there unquestionably has been a double infection. Owing to the fact that *Escherichia coli* overgrows the various organisms in the urine, it appears to be the only infecting organism. Sulfanilamide therapy eliminates all *Escherichia coli* organisms, leaving merely *Streptococcus faecalis* on culture. In going over some of my old records of treatment with methenamine, the ketogenic diet and mandelic acid, I found when the infection was clearing up that *Escherichia coli* disappeared first and that a few colonies of *Streptococcus faecalis* remained on the plates. Thus *Streptococcus faecalis* is also resistant to these other forms of therapy, which fortunately will end the infection with a few extra days of treatment. Strangely enough, if treatment is discontinued before the urine is sterilized it will be found that within a few days only *Escherichia coli* will be present and it will not be possible to see *Streptococcus faecalis*. This same thing applies to *Escherichia coli* and *Pseudomonas*. At the Mayo Clinic my associates and I have observed two cases now in which after elimination of *Escherichia coli* a pure culture of *Pseudomonas* was obtained. In both cases there were small stones in the kidney and we were never able to clear up the infection. There is one other point I should like to mention, namely that *Staphylococcus aureus* apparently is the organism most susceptible to sulfanilamide therapy, and yet the clinical results are poor in cases in which this organism is present. I think this probably indicates that the infection caused by *Staphylococcus aureus* is not a superficial infection but that the deep tissues are involved and the sulfanilamide does not reach the organism in sufficient concentration to kill it. Certainly staphylococcal septicemia and osteomyelitis do not yield readily to sulfanilamide therapy.

## SURGICAL LIGATION OF A PATENT DUCTUS ARTERIOSUS

REPORT OF FIRST SUCCESSFUL CASE

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The continued patency of a ductus arteriosus for more than the first few years of life has long been known to be a potential source of danger to a patient for two reasons: First, the additional work of the left ventricle in maintaining the peripheral blood pressure in the presence of a large arteriovenous communication may lead eventually to cardiac decompensation of severe degree. Second, the presence of a patent ductus arteriosus makes the possessor peculiarly subject to fatal bacterial endarteritis. While it is true that some persons have been known to live to old age with a patent ductus of Botalli, statistics have shown that the majority die relatively young because of complications arising from this congenital abnormality. Dr. Maude Abbott<sup>1</sup> presented a series of ninety-two cases which came to autopsy in which it was shown that the patient had had a patent ductus arteriosus without any other cardiovascular abnormality. Of these patients, approximately one fourth died of bacterial endarteritis of the pulmonary artery and an additional one half died of slow or rapid cardiac decompensation. The average age of death of patients in this series was 24 years.

The complications arising from the persistence of a patent ductus arteriosus would seem to make surgical ligation of this anomalous vessel a rational procedure, if such a procedure could be completed with promise of a low operative mortality. Dramatic results have previously been obtained in persons with cardiac enlargement and decompensation resulting from a peripheral arteriovenous aneurysm when the short-circuiting vessels have been ligated or excised.<sup>2</sup> On similar theoretical grounds, future cardiac embarrassment should be averted if a shunt between the aorta and the pulmonary artery could be removed. It would also seem plausible to expect that the shutting off of the anomalous stream of blood pouring into the pulmonary artery would lessen the formation of the thickened endothelial plaques within the pulmonary artery, which are so likely to be the seat of later bacterial infection. The surgical approach to the aortic arch and pulmonary conus having been studied previously in animal experimentation,<sup>3</sup> it seemed within reason that a patent ductus could be adequately exposed in man and possibly ligated without undue danger. It was therefore decided to undertake the operation in a child who presented the classic signs of a patent ductus arteriosus. At the age of 7 years she already had cardiac hypertrophy, which developed presumably from the embarrassment resulting from the anomalous communication. It was to be expected, therefore, that she would have increasingly severe disability in the future, aside from the danger of having bacterial endarteritis develop.

From the Surgical and Medical Services of the Children's Hospital and the Departments of Surgery and Pediatrics of the Harvard Medical School.

1. Abbott, Maude E.: *Atlas of Congenital Heart Disease*, New York, American Heart Association, 1936, pp. 60-61.

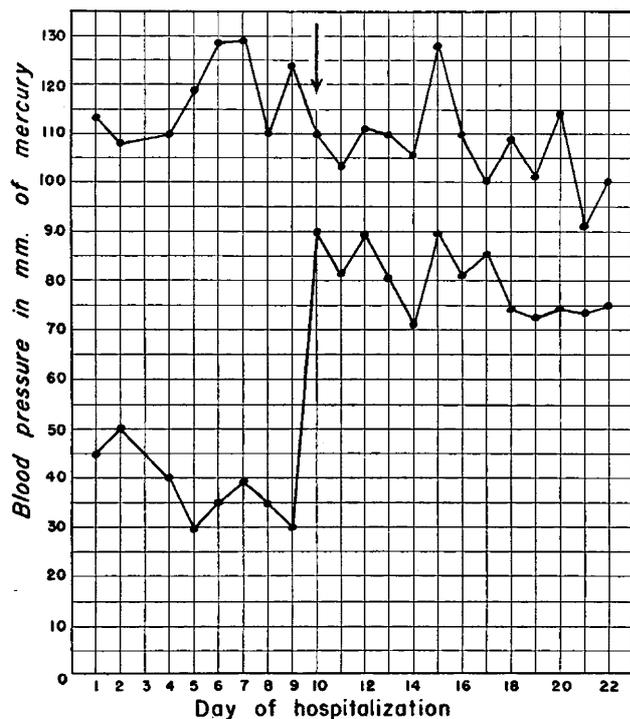
2. Holman, Emile: *Arteriovenous Aneurysm*, New York, Macmillan Company, 1937, pp. 169-178.

3. Gross, R. E.: *A Surgical Approach for Ligation of a Patent Ductus Arteriosus*, *New England J. Med.*, to be published.

## REPORT OF CASE

*History.*—L. S., a girl aged 7½ years, entered the hospital Aug. 17, 1938, for study of her cardiac condition. The family history was irrelevant. She was born normally at full term. No cyanosis was noted at birth or during the postnatal period. The records of the hospital where she was born give no information about an examination of the heart at that time. At the age of 3 years she was seen in the cardiac clinic of another hospital, where it was found that she had physical signs suggesting congenital malformation of the heart. At that time she had a precordial thrill and a loud murmur. The carotid pulsations were abnormally marked, and pistol shot sounds could be heard over the brachial and femoral arteries. The blood pressure was recorded in both arms as 104 mm. of mercury systolic and 0 diastolic. There was definite cardiac enlargement, as shown by teleroentgenograms. The diagnosis made at that time was "congenital malformation of the heart with a patent ductus arteriosus."

During the next four years she was seen in several different hospitals, where the same diagnosis was made. At no time



Daily blood pressure readings of the patient with a patent ductus arteriosus before and after operation. Prior to operation the large ductus opening from the aorta produced a low diastolic pressure. Following operative closure of the ductus, the diastolic pressure rose to twice its former level. The average daily diastolic pressure preoperatively was 38 mm. of mercury. The average diastolic pressure postoperatively was 80 mm. of mercury. The arrow points to the time of operation.

had cyanosis been observed. Dyspnea developed after moderate exercise, and her physical activities had been limited accordingly. She had never had peripheral edema or other evidence of cardiac decompensation. Frequently the child had been conscious of "something wrong in the chest" and her mother spontaneously offered the information that she had heard a "buzzing noise" in her daughter's chest when standing nearby.

*Physical Examination.*—At the time of admission, the patient was slender and undernourished. The pulsations of the carotid arteries were abnormally forceful. The radial pulse was of the Corrigan type, and a capillary pulsation was readily seen. The veins over the chest were somewhat prominent. There was a precordial bulge. The heart was definitely enlarged by percussion, the enlargement being for the most part to the left. Over the entire precordium there was a prominent coarse thrill which was most intense in the third interspace to the left of the sternum. This thrill was continuous but was accentuated during systole. There was a rough "machinery" murmur heard with maximal intensity over the pulmonic area to the left of the sternum in the second and particularly in the

third interspace. It was continuous throughout the cardiac cycle but like the thrill was greatly accentuated during systole. It was transmitted to the left along the third interspace and into the axilla with only slightly diminished intensity. The systolic element was heard faintly over the vessels of the neck and could be heard clearly in the right axilla and over the mid-thoracic region posteriorly. Blood pressure readings were respectively right arm 115/40, left arm 110/50, right leg 150/55, left leg 140/40 mm. of mercury. There was no clubbing of the fingers and no evidence of peripheral edema. The liver edge was palpable at the costal margin. The examination in other respects was negative.

*Laboratory Data.*—A 7-foot x-ray film of the chest showed the transverse diameter of the heart to be 11.7 cm., compared to an internal diameter of the chest of 20 cm. There appeared to be definite enlargement of the left ventricle. There was questionable prominence of the pulmonary artery. A mottled increased density around the lung hili was interpreted as representing circulatory congestion. Fluoroscopic examination showed a "hilar dance." An electrocardiogram was normal, showing no deviation of the axis. The red blood count was 5,080,000 cells per cubic millimeter and the hemoglobin was 85 per cent (Sahli). Circulation time with dehydrocholic acid was 10 and 8 seconds, respectively, on two tests.

*Operation.*—August 26, operation was undertaken (by R. E. G.) under cyclopropane anesthesia. The approach to the mediastinum was made through the left pleural cavity antero-laterally. Incision was made through the left third interspace, cutting the third costal cartilage, and the third rib was retracted upward. As the left lung was allowed to collapse inferiorly, an excellent view was gained of the lateral aspect of the mediastinum. The parietal pleura covering the aortic arch and left pulmonary artery was then incised and these structures were directly exposed. A large patent ductus arteriosus was found, which was from 7 to 8 mm. in diameter and from 5 to 6 mm. in length. A palpating finger placed on the heart disclosed a continuous and very vibrant thrill over the entire organ, which was increasingly prominent as the finger reached up over the pulmonary artery. A sterile stethoscope was employed and an extremely loud continuous murmur was heard over the entire heart. When the stethoscope was placed on the pulmonary artery there was an almost deafening, continuous roar, sounding much like a large volume of steam escaping in a closed room.

A number 8 braided silk tie was placed around the ductus with an aneurysm needle, and the vessel was temporarily occluded for a three minute observation period. During this time the blood pressure rose from 110/35 to 125/90. Since there was no embarrassment of the circulation, it was decided to ligate the ductus permanently. The ductus was too short to tie double and divide, so that ligation alone was resorted to. When the thread was drawn up tight the thrill completely disappeared. The chest was closed, the lung being reexpanded with positive pressure anesthesia just prior to placing the last stitch in the intercostal muscles.

*Postoperative Course.*—The child underwent the operative procedure exceedingly well and showed no signs of shock. Prior to operation blood had been taken from a donor in order to have it ready whenever needed, but the patient's condition was so good that it was not given. There was only mild discomfort on the afternoon of the day of operation, and on the following morning the child was allowed to sit up in a chair. By the third day she was walking about the ward. When the skin sutures were removed on the seventh day the wound was well healed, but because of the interest in the case the child was detained in the hospital until the thirteenth day. After the dressing was removed and the chest could be examined adequately the thrill had completely disappeared, there was a faint systolic murmur in the left third interspace which was not transmitted over the precordium, and no murmur could be heard in the axilla, in the neck or over the back. The daily blood pressures which had been taken prior to operation and subsequent thereto showed a striking change in the diastolic levels, as is shown by the accompanying chart. The average of the daily pressures prior to operation had been 114 systolic and 38 diastolic as contrasted with a postoperative daily average of 108 systolic and 80 diastolic.

## SUMMARY

A girl aged 7½ years had a known patency of the ductus arteriosus and beginning cardiac hypertrophy. In the hope of preventing subsequent bacterial endarteritis and with the immediate purpose of reducing the work of the heart caused by the shunt between the aorta and the pulmonary artery, the patent ductus was surgically explored and ligated. The child stood the operative procedure exceedingly well. The most objective finding, which indicated that the serious loss of blood from the aorta into the pulmonic artery had been arrested by operation, was a comparison of the pre-operative and postoperative levels of the diastolic blood pressure. Prior to operation the daily blood pressure showed an average diastolic level of 38 mm. of mercury as compared with a postoperative diastolic level of 80 mm. of mercury. This is the first patient in whom a patent ductus arteriosus has been successfully ligated.

## Clinical Notes, Suggestions and New Instruments

### SULFANILAMIDE THERAPY IN ACTINOMYCOSIS

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As the experience with sulfanilamide enlarges it becomes increasingly apparent that its usefulness covers a wide field. To the long list of diseases favorably affected by its administration has recently been added actinomycosis. Oliver Walker<sup>1</sup> of Liverpool reported a clinical cure of actinomycosis of the lower part of the abdomen in a man aged 23 in whom the disease developed after an operation for ruptured appendix. Compound solution of iodine and potassium iodide had been given for a brief period, without apparent benefit. Sulfanilamide was then employed in 15 grain (1 Gm.) doses by mouth three times a day for five days, at the end of which time a definite diminution in the discharge was observed and a disappearance of the sulfur granules was noted. So striking was the improvement that after an interval of ten days sulfanilamide therapy was resumed in the same doses for five more days. When the patient was seen at the end of three months the abdominal wound was entirely healed and the general condition excellent.

The experience which we have to report has to do with an 11 year old white boy who was admitted to the children's surgical ward of the Cook County Hospital Oct. 19, 1937. There was a tender inflammatory mass the size of an orange in the middle of the lower part of the abdomen between the umbilicus and the symphysis. The temperature was 101 F. and the white blood cell count 14,100. The urine was normal. At first glance it seemed probable that the process was either an appendical abscess or an infected cyst of the urachus. The swelling had been present for about one week, was associated with a loss of several pounds and had followed a rather prolonged period of difficulty in urination. There was nothing suggestive of an attack of appendicitis. Catheterization did not affect the size or shape of this swelling, although a cystogram seemed to indicate an extramural mass causing pressure on the dome of the bladder. Hot dressings were applied for several days; the skin became more reddened, fluctuation developed and the process pointed at the umbilicus, where spontaneous opening occurred October 29. Eleven days later an incision for better drainage was made over the center of the mass by Dr. Gatewood, and several ounces of thick pus was liberated. The wall was thick and the character of the discharge strongly suggested actinomycosis. After this suspicion had been confirmed by microscopic examination of the granules we were able to elicit from the patient the fact that during the summer months of 1937 he had been in the habit of playing a good deal in the fields and would often chew bits of grass, hay and straw.

1. Walker, Oliver: Sulfanilamide in the Treatment of Actinomycosis, *Lancet* 1: 1219 (May 28) 1938.

All the well known methods of treating actinomycosis were immediately begun. Seven grains (0.45 Gm.) of thymol and potassium iodide were given once each day. To the surface of the wound a 10 per cent solution of thymol in cottonseed oil was applied twice daily. Roentgen therapy was started November 19 and continued for four months, sixteen treatments being given at intervals of four to six days. The potassium iodide was gradually increased to 20 grains (1.3 Gm.) three times a day. During this regimen he became progressively worse. His temperature ranged between 101 and 102 F., he rapidly lost weight and the process in the lower part of the abdomen became larger and extended toward the right, where a new sinus opened just medial to the anterior superior spine. It seemed apparent that if the course of the disease did not change a fatal termination was almost certain. For this reason, purely on an empirical basis, the use of sulfanilamide was begun (Jan. 18, 1938), 10 grains (0.65 Gm.) being used by mouth three times a day, in addition to the other medication. Almost coincident with this change in therapy, in fact within a week's time, an improvement in the boy's condition was observed. The mass in the lower part of the abdomen gradually became smaller and softer, and the amount of discharge diminished. The patient's appetite returned, he began to pick up weight and his general appearance rapidly improved. By March 25, when he was discharged from the hospital (all medication except sulfanilamide having been stopped) he had gained 10 pounds (4.5 Kg.), he was eating well, the mass in the lower part of the abdomen was becoming steadily smaller, and little drainage was present.

The boy has returned frequently to the outpatient clinic for observation. By July 18 the wound at the midline had entirely healed, although a new sinus opening of two weeks' duration in the left lower quadrant was discharging a small amount of pus. August 29 this opening also had closed and on October 1 all wounds were entirely healed. He had gained over 20 pounds (9 Kg.) and was eating normally and going to school. When last seen, Nov. 16, 1938, and shown at a clinic for alumni of the Cook County Hospital, the boy proudly stated that he weighed over 100 pounds (45 Kg.). He was certainly the picture of robust health and showed no ill effects from the continuous taking of sulfanilamide for about ten months.

The evidence in this case leads us to believe that the agent responsible for the improvement and apparent clinical cure of the actinomycosis was the sulfanilamide, because the favorable change in the course of the disease was coincident with its use.

### INEFFECTIVENESS OF SULFANILAMIDE IN RABIES FROM VACCINATED DOGS

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A white man aged 41, seen because of a mild digestive upset with vomiting and a generalized headache of twenty-four hours' duration, strangled when he attempted to drink cold water. He stated that he had been bitten on the upper lip twenty-two days before the onset of symptoms by a neighbor's dog while attempting to retrieve his own dog during a fight in which his dog also was bitten. Since both dogs had been vaccinated against rabies six months previously by the single injection method, he did not consult a physician. The neighbor's dog was reported to have been restless for several days. It was confined but escaped and was struck by an automobile. It died, supposedly from injuries, two days after biting the patient. The patient's dog became ill two weeks after the fight and died three days later. Neither dog's head was submitted to the state laboratory for examination for rabies.

The patient had a temperature of 101 F. and hyperactive reflexes. He was talkative and apprehensive. Although he could swallow warm water without difficulty, cold water caused spasm of the throat muscles. When he was offered a glass of cold water he reached for it but suddenly exclaimed "I can't do it" and buried his face in a pillow. No abnormality of the throat was found. A smear of material from the throat was negative. The urine showed a trace of albumin and a heavy sediment of amorphous urates but was otherwise normal. The red cell count was 4,700,000 and the white cell count 9,300. The Schilling differential count showed a shift to the left in spite