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PROCEEDINGS OF THE TWENTY-FOURTH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CLINICAL INVESTIGATION HELD IN ATLANTIC CITY, N. J., MAY 2, 1932

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Research Article

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A Method of Studying Fresh Blood by Dark Field Illumination. By O. C. HANSEN (introduced by H. L. Amoss), Durham, N. Carolina.

The result of five years experience of studying normal and abnormal blood by dark field illumination is given. Comparison is made of this method with that which employs supra-vital stains. Mature and immature leukocytes, as well as red blood cells, are described as viewed by dark field illumination. We believe most, if not all, circulating blood cells can be recognized in the dark field and that an accurate impression of haematological disturbances can be arrived at by studying fresh blood in the dark field. It is also a great help in recognizing malaria parasites with ease. The simplicity of this method, as well as the fact that it is not dependent upon dyes and staining technique, should make it available for office practice. Slides of dark field drawings are shown.

Iron Metabolism Studies. By PAUL REZNIKOFF, New York, N. Y.

The intake and output of iron were studied by the Elvehjem-Kennedy method in two subjects, one normal and one suffering from polycythemia vera, over a period of 8 months and blood counts were followed.

Both subjects approached balance on diets ranging from 10 to 20 mgm. iron daily. The normal individual stored iron when given parenteral liver extract, when fed a "secondary" extract, and when given 60 mgm. iron as iron ammonium citrate (the equivalent of the iron content of the latter extract). Later in the study neither high iron intake, parenteral liver, nor copper sulphate caused any storing of iron. No definite correlation was found between red blood count, hemoglobin and iron balance in this normal individual.

The polycythemic patient showed little response to Fowler's solution or x-ray therapy. Phenylhydrazine caused a fall of erythocyte count from six to three million and of hemoglobin from one hundred to fifty-five per cent, but very little coincident excretion of iron.

These studies, therefore, indicate that the body can store iron for long periods (382.8 mgm. in 7 months) without use by the hematopoietic system, or, in case of erythrocyte depression (852.4 mgm. in 7 months), without excretion, and this work also suggests that iron metabolism should be studied by tissue analysis.

Treatment of Polycythemia Vera with Solution of Potassium Arsenite. By CLAUDE E. FORKNER (introduced by C. S. Keefer), Boston, Mass.

Arsenic has been used for many years in the treatment of anemia and has been considered an agent favoring regeneration of erythrocytes and hemoglobin. The use of arsenic in polycythemia vera has been reported as either contraindicated or of no value. Türk in 1904, from the result of treating one case with Fowler's solution, concluded the drug was of value. In his case the erythrocyte count was reduced from 9,000,000 to 7,000,000 cells per cu. mm.

Five patients with typical polycythemia vera have been treated by means of oral administration of solution of potassium arsenite. Some of these patients had been followed for several years prior to this treatment. The use of phenylhydrazine hydrochloride and of roentgen rays, applied over the long bones, had been ineffective in one case. The administration of large doses of the pulp of raw spleen had been of no value in two other cases.

Prompt remissions occurred following administration of solution of potassium arsenite in each of these five cases manifested by: (1) Lowering of erythrocyte and hemoglobin values to normal or near normal levels, (2) reduction of the leucocyte count to normal or subnormal values, (3) reduction of the hematocrit cell volume, (4) decrease in the size of the spleen and liver, (5) increase in strength and weight, (6) marked subjective improvement.

Remissions may thus be induced and maintained, at least for many months, by continuous administration of the drug.

Purified Liver Extract Intravenously in the Treatment of Pernicious Anemia. By RAPHAEL ISAACS, CYRUS C. STURGIS and (by invitation) S. M. GOLDHAMER and F. H. BETHELL, Ann Arbor, Mich.

It has been possible to remove from commercial liver extract by a very simple method, substances which cause headache, lowering of the blood pressure, chills, fever and vasomotor disturbances. Liver extract so prepared has been given intravenously to 80 patients (400 injections) and the blood counts brought to normal. The extract made from about 100 grams of fresh liver, intravenously, produces a maximum reticulocyte response ten per cent higher than that produced by the extract from 4200 grams given by mouth. Four to six injections of this extract at weekly intervals are sufficient to bring the erythrocyte count to normal, and the maintenance dose is one injection every four to six weeks.

The Interrelation of Pernicious and Idiopathic Hypochromic Anemia. The Study of a Family in Which Both Conditions Occurred Singly and Combined. By CLARK W. HEATH (introduced by Dr. George R. Minot), Boston, Mass.

The medical literature reveals evidence to prove an interrelationship between pernicious anemia and idiopathic hypochromic anemia. This is illustrated, not only by reports of hypochromic anemia in families in which pernicious anemia also occurs, but also by reports of hypochromic anemia preceding the onset and during the remission of pernicious anemia.

A family has been studied in which three sisters each had both hypochromic anemia and pernicious anemia with combined system disease. Iron medication in two of these sisters changed an initial microcytosis and low color index to a macrocytosis and high color index. Two brothers had pernicious anemia, one with chronic intermittent diarrhea as the chief symptom, the other with early combined system disease. Another sister died of a progressive anemia resembling pernicious anemia. Two sons of one of the sisters had a macrocytosis without definite anemia and with normal gastric acidity. A daughter of one of the sisters had chronic menorrhagia and hypochromic anemia with hypochlorhydria. Her condition was completely restored to normal by iron. The red blood cells in the anemic members of the family showed an increased resistance span to hypotonic solutions of sodium chloride which became normal as the anemia lessened. There was a high incidence of menorrhagia, migraine and enlargement of the thyroid gland in this family.

The interrelationship of pernicious anemia and idiopathic hypochromic anemia leads to a hypothesis of the etiology of the latter condition. It is believed that in this family there is a hereditary tendency to reduced gastric function. The relationship of pernicious anemia to gastro-intestinal disorders has been shown by Castle, who has found that pernicious anemia is secondary to the absence of a specific factor in the stomach secretions. In idiopathic hypochromic anemia there is typically an absence of gastric free hydrochloric acid which may be related to the etiology. It is therefore believed that idiopathic hypochromic anemia is primarily the result of a deficiency, conditioned by a disorder of the gastro-intestinal tract, leading to an inability to absorb or utilize hemoglobin-building material from the food.

Observations on the Etiology and Treatment of the Anemia of Hookworm Disease in Porto Rico. By C. P. RHOADS (by invitation) and WILLIAM B. CASTLE, Boston, Mass.

Study of over 150 cases of hypochromic anemia associated with hookworm infestation demonstrated that the morphological and physiological characteristics of this anemia are similar to those of other hypochromic anemias without hookworm infection encountered both in Porto Rico and elsewhere, and regarded as mainly due to defective blood formation. No evidence for the presence of substances due to the activity of the hookworm capable of acting either as depressors of blood production or as hemolytic agents was found. Since it was demonstrated that the intramuscular injection of red blood cells into these patients produced increased blood formation, it is logical to assume that the effect of blood loss produced by the hookworm may be significant as a loss of potential hematopoietic factors leading to defective blood formation.

No significant effect upon the anemia was produced during periods of from 2 to 3 weeks and frequently for longer periods either by the elimination of the hookworms or by the administration of a diet enriched by 300 grams of meat and 1500 cc. of milk daily or by a combination of these. On the other hand, the daily administration of 6 grams of iron ammonium citrate was almost invariably followed by promptly increased blood formation indicated by reticulocyte crises followed by rapid increases of red blood cell and hemoglobin values and general clinical improvement, despite the persistence of heavy hookworm infestation and the original deficient diet. Substances containing the extract of liver described by Whipple and his associates as of value in hemorrhagic-dietary anemias in the dog were somewhat effective but never as effective as iron in the dosage employed; the liver extract described by Cohn, Minot and their associates as effective in pernicious anemia was found to be without effect. Since in studying these cases of hookworm anemia deficient diets were found to be the rule and gastric anacidity a frequent finding, as is the case in hypochromic anemias not associated with the hookworm, it is suggested that dietary deficiency and gastro-intestinal changes are of major etiological significance.

Observations on the Etiology and Treatment of Anemia in Pregnancy. By MAURICE B. STAUSS (introduced by Henry Jackson, Jr.), Boston, Mass.

The "physiologic" anemia of pregnancy was investigated by studying the blood, the gastric secretions and the dietary histories of a group of normal women throughout pregnancy. More than half of these women showed a marked decrease or absence of free hydrochloric acid in the gastric juice during pregnancy, with a return to normal following parturition. These women, and those with poor diets, had an average loss of 12 per cent hemoglobin during

pregnancy, whereas women who showed a less marked decrease in free hydrochloric acid and who ate satisfactorily during pregnancy lost an average of only 5 per cent hemoglobin. Three women with permanent post-histamine gastric anacidity had an average loss of 18 per cent hemoglobin in spite of their satisfactory dietary intake during pregnancy. These observations indicate the importance of direct dietary deficiency and deficiency conditioned by changes in the gastric juice in the etiology of the "physiologic" anemia of pregnancy.

Thirty-five women who had less than 45 per cent hemoglobin during the latter half of pregnancy or following parturition were studied. Nineteen of these were found to have post-histamine gastric anacidity and 12 more had little or no free HCl following alcohol test meals.

In addition to this striking incidence of disturbed gastric function, over two-thirds of these patients were found to have had diets which were definitely deficient in iron and other mineral elements and in protein.

None of the 35 patients made any significant improvement during control periods without therapy. Thirty had anemia of the hypochromic type. Liver extract produced no improvement in these cases; but all treated with large doses of iron improved rapidly, gaining an average of 0.65 per cent hemoglobin per day, *whether treated during or after pregnancy.*

The observations on the hypochromic anemia of pregnancy correspond to similar studies on idiopathic hypochromic anemia and indicate that the etiologic factors of direct dietary deficiency and deficiency conditioned by gastric anacidity are common to both. Furthermore, an analogy may be made between the blood requirements of the foetus and the chronic blood loss associated with certain cases of idiopathic hypochromic anemia. In addition, the therapeutic value of iron is shown to be as great in the hypochromic anemia of pregnancy as in other hypochromic anemia.

Five patients had anemia of the hyperchromic type (pernicious anemia of pregnancy). Two of these became well under therapy with iron and two under therapy with liver extract. In view of the observations previously made upon Addisonian pernicious anemia, the effect of beefsteak and gastric juice was studied. Beefsteak alone was found to have no effect upon blood formation upon one patient with macrocytic anemia during pregnancy and to have distinct effect after parturition. Immediately thereafter beefsteak plus normal human gastric juice was found to have a markedly positive effect. Since patients with "pernicious anemia of pregnancy" remain well once cured, it is reasonable to believe in the light of these observations that the anemia is due to the temporary loss of the intrinsic factor of the gastric juice during pregnancy with an ultimate return occurring sooner or later after delivery.

The observations on the hyperchromic anemia of pregnancy indicate that in addition to an iron deficiency in most cases, there is a temporary absence from the gastric secretions of the specific intrinsic factor, the complete absence of which has been invariably observed in Addisonian pernicious anemia in relapse.

Hence, the same etiologic mechanisms hold for the anemias of pregnancy as for similar anemias in nonpregnant individuals, and like therapy is equally efficacious.

Non-Specific Serological Reactions in Acute Bacterial Infections. By WILLIAM S. TILLETT and (by invitation) T. J. ABERNETHY and A. MURRAY FISHER, Baltimore, Md.

The results embodied in this report indicate that sera derived from patients acutely ill with many different acute bacterial infections are capable of reacting with certain strains of *Streptococcus hemolyticus.* Although a mixture of

suitable cultures and reactive sera results in the formation of coarse clumps of bacteria, the phenomenon exhibits certain unique characteristics which differ from the usual specific anti-bacterial serological reactions. The unusual features may be summarized as follows:

1. Absence of specificity. Sera from patients suffering from infection with pneumococcus, meningococcus, *B. typhosus,* or other bacteria agglutinated in equally high titre the test cultures of hemolytic streptococci. 2. The capacity of a patient's serum to react was demonstrable early after abrupt onset of disease, persisted during the active phase, and disappeared rapidly a few days after recovery. 3. Agglutinable cultures were rendered inert by heating to the thermal death point. 4. The fraction of serum containing the streptococcus reacting factor may be chemically separated from that containing agglutinins specific for the etiological agent.

The results indicate that the phenomenon is a broad reaction to infection induced by different causes and that sera from cases of diverse etiology possess a common, and apparently identical, property. Investigation has therefore been directed toward attempting to identify this property of blood which is acquired and lost so rapidly. The occurrence and general characteristics of the reaction indicate that it may be based upon a mechanism materially different from specific antigen-antibody reactions.

Although normal serum fails to react with the cultures, normal plasma causes a coarse clumping of hemolytic streptococci. Plasma from patients acutely ill clump the organisms in higher titre than normal plasma. By mixing organisms contained in several hundred cc. of culture with 1 to 2 cc. of plasma, an actual clot is sometimes formed. There is abundant evidence in the literature that fibrinogen of the blood is increased markedly in acute infections. The results of Maltaner and Johnston and others indicate that "secondary" clots obtained from sera are due to unchanged fibrinogen in the serum. It seems possible, therefore, that the explanation of the hemolytic streptococcus agglutination described depends upon a relationship between the organisms and the excess fibrinogen present in the blood of patients with acute bacterial infections.

Further Studies on Rheumatoid Arthritis. By M. H. DAWSON and (by invitation) R. H. BOOTS, New York, N. Y.

The studies on rheumatoid arthritis which were presented last year have been continued.

The agglutination phenomenon with *Streptococcus hemolyticus* which was shown to be present in the serum of patients suffering from rheumatoid arthritis has been further analyzed. These studies have revealed that the reaction is highly characteristic both for the bacterial species *Streptococcus hemolyticus* and the disease rheumatoid arthritis. It has been found, however, that certain attributes of the reaction distinguish it from ordinary agglutination reactions occurring during the course of specific infectious diseases.

Studies on the relationship between rheumatoid arthritis and rheumatic fever have been continued. In this connection comparative data on the age and sex incidences of these two diseases will be presented.

The determination of the sedimentation rate of the erythrocytes has been found to be a procedure of great clinical value in the study of cases of rheumatoid arthritis. It has been found that the simple procedure gives a reliable index of the state of activity of the disease and affords an accurate method of determining the results of therapeutic methods instituted.

A large series of patients suffering from rheumatoid arthritis have been treated by the following procedures: (*a*) Intravenous inoculation with *Streptococcus hemolyticus* vaccines. (*b*) Transfusions.

The rationale underlying these procedures will be discussed and the results presented.

A Laboratory Method for the Diagnosis of Psittacosis in Man. By T. M. RIVERS and (by invitation) G. P. BERRY, New York, N. Y.

The continued appearance of disease in human beings who have been in contact with parrots and parrakeets has created the necessity for a safe and reliable method for the diagnosis of psittacosis. The following laboratory procedure has, in our experience, met the necessary requirements of safety and accuracy.

The patient's sputum, to which 20–50 volumes of meat infusion broth, pH 7.8, and a small amount of alundum have been added, is thoroughly ground in a mortar. The emulsion is centrifuged for 10 minutes at a speed of 3,000 r.p.m. Then the supernatant fluid is filtered through a Berkefeld V candle at a pressure of 15–30 cm. of mercury. Each of 6 mice receive intraperitoneally on 3 successive days 2 cc. of the filtrate. The animals are housed in screened battery jars placed in shallow baths of lysol solution in order to prevent the mechanical spread of the infection by insects. All animals are observed for a period of 30 days.

The criteria by which the presence of psittacosis in the inoculated mice is established are: (1) the development of illness in some or all of the animals which is usually fatal within 10 days, but occasionally not before 30; (2) the characteristic pathological picture which in mice consists of focal necrotic lesions in the liver and spleen; (3) the absence of ordinary bacterial infections as determined by means of necropsy cultures; (4) the presence in liver and spleen impression smears of the "minute bodies" of psittacosis; (5) the establishment of serial passages of the virus in mice by means of liver and spleen emulsions from the animals receiving the sputum filtrates; and (6) the demonstration in mice surviving the inoculations of sputum for 30 days of an active immunity against a potent strain of psittacosis virus. All of these conditions obviously need not be fulfilled in each instance: sometimes one, sometimes another serves to establish the diagnosis.

The results obtained by the use of this method in 10 cases of psittacosis are: unequivocal demonstration of the virus in 8, probable demonstration in 1, failure of demonstration in 1. Sputa collected from the 5th to the 24th day of disease have been positive. From human autopsy material, *e.g.*, lung, liver, and spleen, the virus of psittacosis has been obtained by means of a similar procedure.

The Isolation of a New Type of Spotted Fever Virus and Report of a Case. By HOBART A. REIMANN and (by invitation) HENRY L. ULRICH and LUTHER C. FISHER, Minneapolis, Minn.

The occasion for differential diagnosis between typhus and spotted fever has only recently developed. The widespread distribution of both diseases, render the development of simple methods for differentiation necessary.

A patient in Minnesota presented a clinical picture indistinguishable between typhus and spotted fever. The virus was established by inoculating blood into guinea pigs. The reaction in 140 animals was observed. After intraperitoneal inoculation, fever developed after 5 or 6 days and lasted from 2 to 7 days. Brain virus was less potent. Scrotal swelling appeared in 50

per cent of males. None of the animals died. Rickettsia were found intracellularly in the scrotal exudate. No other important histological changes were noted.

Identification was made by cross immunity tests. Animals immune to Minnesota strain were immune to reinfection with eastern spotted fever but not always to the more virulent Bitterroot strain. Conversely, animals immune to both eastern and Bitterroot strains were immune to Minnesota strain. Animals immune to Minnesota strain were not immune to endemic typhus. Curiously, animals immune to typhus were not regularly non-immune to Minnesota strain. Spotted fever vaccine protected against Minnesota strain. The Minnesota strain is apparently one of exceptionally mild spotted fever.

The Effect of Giving Digitalis on the Volume Output of the Heart and its Size in Heart Failure. By HAROLD J. STEWART, New York, N. Y.

It appears to be a fact that the giving of digitalis decreases the cardiac output (Burwell, Neighbors and Regen, and Stewart) and cardiac size (Stewart) in normal human beings. This report concerns the effect of its administration when hearts are diseased. In addition to estimations of cardiac output by the acetylene method introduced by Grollman, the size of the heart was measured from x-ray photographs taken at a distance of 2 meters. All observations were made with patients in a basal metabolic state immediately before digitalis was given and at frequent intervals afterward. In all instances digitan (Merck) 1.0 gram was given within 24 hours.

We have found that in the presence of *heart failure of the congestive type* (1) the cardiac output *diminishes.* (2) With the administration of digitalis, if *diuresis* occurs, (*a*) the cardiac output *increases;* (*b*) the cardiac size *diminishes;* (*c*) the ventricular rate *decreases;* and (*d*) alterations in the form of the T wave of the electrocardiogram occur. (3) Results like these occur both when the rhythm of the heart is normal and in the presence of auricular fibrillation. (4) Even when the only sign of heart failure is dyspnoea, the effects on output and cardiac size like those described, appear. (5) As the effect of digitalis wears off these functions change in the reverse direction.

It appears, therefore, that in heart failure the effect of giving digitalis differs from that in normal persons for instead of diminishing, the cardiac output *increases.*

Inequality of Blood Pressure in the Brachial Arteries, with Especial Reference to Disease of the Arch of the Aorta. By HORACE M. KORNS and (by invitation) P. H. GUINAND, Iowa City, Iowa.

It has been tacitly assumed that in normal persons the blood pressure and the volume of the pulse are equal in the right and left brachial and carotid arteries, and as a corollary, that sphygmic inequality in these arteries is evidence of disease of the aorta, provided that peripheral causes of partial arterial occlusion, such as encroachment of the clavicle on the subclavian artery, cervical ribs, thrombosis, embolism, and arteriosclerosis, as well as developmental anomalies of the aorta and its main branches, can be excluded. For example, a man aged 45 had syphilitic aortitis and aortic regurgitation, no enlargement of the aorta, dilatation of the innominate artery, and equal carotid pulses, but a much smaller pulse and lower blood pressure in the right subclavian and its branches than in the left. Extension of the mesarteritis into the innominate and right subclavian, with consequent narrowing of the orifice of the latter, was diagnosed clinically and confirmed postmortem.

Unfortunately, not all cases are so satisfactory. Manifest aneurysm of the aorta is here excluded from consideration, and attention directed to cases which present genuine diagnostic difficulties with respect to etiology and pathological physiology and anatomy. The following case serves as an example. A man, aged 49, presented the usual signs of aortic regurgitation, except that his pulse, although possessed of the requisite volume, exhibited a prominent anacrotic interruption which effectively obscured whatever celerity it might have had. The ascending and transverse portions of the aorta were enlarged. The carotid pulses were equal, but the pulse in the left subclavian and its branches was much smaller than in the right, and the brachial pressure was correspondingly low. After two months of anti-syphilitic treatment the disparity of pulse and pressure was much less pronounced, which seemed to fortify the diagnosis of syphilitic aortitis. Six months later, however, in spite of continued treatment, the disparity had returned to its original magnitude.

The next case which came under observation was even more puzzling. The patient was a man of 33 years who presented the cardinal signs of aortic regurgitation, without dynamic evidence of aortic stenosis, but with an aortic systolic murmur. With the possible exception of this murmur, there was nothing to indicate dilatation or elongation of the aorta. At first, with equal carotid pulses, the left brachial pressure was considerably lower than the right, which suggested syphilitic aortitis at the orifice of the left subclavian artery, and, by inference, a syphilitic etiology for the aortic regurgitation. However, it soon became apparent that the pressure and pulse inequality varied in degree from day to day, and was often wanting entirely. Such variability could not be harmonized with any organic lesion, and because of it a large number of normal persons were examined with the idea of determining the normal incidence of significant inequalities in brachial pressure.

The brachial pressures of 1000 healthy young students were measured with mercury manometers simultaneously in both arms. The results are summarized in the accompanying table (Table 1).

TABLE I

Inequalities in pressure levels

	Maximum systolic		Minimum diastolic		Both levels	
	$R > L$	$L > R$	$R > L$	$L > R$	$R > L$	$L > R$
	per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
10 mm.	6.6	1.6	4.8	3.9	0.5	0.2
11 mm. or more	11.8	1.2	7.8	4.2	1.9	0.3
Totals	18.4	2.8	12.6	8.1	2.4	0.5

What we have arbitrarily designated as a significant inequality in brachial systolic or diastolic pressures occurred 419 times, and 310 of these inequalities were occasioned by a higher pressure on the right side. These figures challenge the validity of the old assumption of sphygmic equality in the brachial arteries of normal persons. They also warn against attaching too much significance to inequality of pulse volume and arterial pressure in patients suspected of having disease of the aorta, unless the inequality can be shown to be permanent.

Direct Stimulation of the Vagus Nerves in Man. A Case Report. By HENRY FIELD, JR., and PAUL S. BARKER, Ann Arbor, Mich.

A man, 40 years of age, presented extreme congestive cardiac failure, apparently due to paroxysmal auricular tachycardia. The heart rate, approximately 190, was not influenced by digitalis, quinidine, or ocular or carotid pressure. Quinine intravenously caused slight transient slowing. The patient became moribund. In a last desperate attempt to stop the tachycardia, the vagus nerves in the neck were exposed surgically and stimulated directly with faradic current. This produced no change in heart rate, although other vagus effects were observed.

Four days later partial atrioventricular block developed, without slowing of the auricles, probably caused by digitalis and quinidine. Rapid improvement followed the ventricular slowing. Now for the first time, ocular pressure and atropine administration revealed evidence of vagal action upon the heart. Later the auricles slowed gradually and sinus arrhythmia appeared, suggesting that the rhythm had been sinus tachycardia throughout. For the following six months digitalis was necessary to keep the heart rate below 100.

The case is remarkable for the extreme sinus tachycardia causing failure of an otherwise normal heart, the tachycardia apparently due to complete loss of the cardiac action of the vagi. Furthermore, it is unique as regards the direct electrical stimulation of the vagi.

An Electrocardiographic Study of Experimental Coronary Occlusion: The Inadequacy of the Three Conventional Leads in Recording Certain Characteristic Changes in Action Currents. By FRANCIS CLARK WOOD (by invitation) and CHARLES C. WOLFERTH, Philadelphia, Pa.

In dogs, occlusion of the posterior circumflex branch of the left coronary artery regularly produces a deviation of the R–T interval from the iso-electric line in two of the three conventional limb leads of the electrocardiogram. Occlusion of the anterior descending branch produces no such results.

However, if the chest is filled with normal salt solution to insure satisfactory conduction from all parts of the heart, and if a fourth lead is used (electrodes attached to the front and back of the chest), R–T interval changes can be recorded regularly within two minutes after clamping the anterior descending, as well as after clamping the posterior circumflex coronary artery.

When direct heart leads are used, infarctions which are quite small, regularly produce changes in the R–T interval.

These findings suggest that acute myocardial infarction regularly produces a change in the action current of the heart. A deviation of the R–T interval from the iso-electric line is recordable in all instances if the electrodes are suitably placed.

It has been shown in man as well as in the dog that myocardial infarction can occur in such a position in the heart that the characteristic R–T interval deviation will not appear in the routine electrocardiogram, but will appear in the anteroposterior chest lead.

The Heart in Myxoedema. Roentgen Ray Measurements and Electrocardiograms Before and After Therapy. By J. LERMAN and R. J. CLARK (by invitation) and J. H. MEANS, Boston, Mass.

Zondek, later Fahr, have described "myxoedema heart." The condition is one of enlargement which diminishes under thyroid. Coincident changes in electrocardiogram and improvement in cardiac symptoms take place.

We have studied thirty such cases roentgenographically and twenty-four electrocardiographically. Twenty-three showed transverse enlargement varying from 0.5 to 6.3 cm. After thyroid medication the diameter diminished in twenty-seven from 0.3 to 6.9 cm. The shrinkage was gradual and reached its limit in 2 to 5 months. The area of the roentgen heart shadow showed a greater shrinkage than that suggested by the diameter decrease.

The electrocardiograms were all abnormal before thyroid. The most common abnormality was flattening or inversion of the T waves. After treatment most of the electrocardiograms returned to or towards normal. The cases showing the greatest improvement in the electrocardiogram were the ones that showed the greatest shrinkage in the heart shadow.

Under thyroid, high blood pressures tended to drop and low ones to rise. Pulse pressure tended to rise.

Only one patient showed evidence of congestive failure. He died eight months after treatment was begun.

The pathology of the heart in myxoedema in relation to the clinical findings is discussed. The question of pericardial effusion causing these changes is raised.

Studies on the Function of the Suprarenal Cortex. By G. A. HARROP, JR., and (by invitation) ALBERT WEINSTEIN, Baltimore, Md.

Extensive work has already been reported dealing with the picture of adrenal insufficiency in the dog. The objective physical signs are characteristic as is the rise in the blood nonprotein nitrogen and the diminished excretion of nitrogen and urea in the urine.

The relationship between lipoid metabolism and the cortical hormone was studied and it was found that the feeding of certain oils, particularly cotton seed oil, by mouth, enabled suprarenalectomized dogs to carry on normal physiological activities even though the extract supply was only one-third of the minimal maintenance dosage as previously determined. Cholesterol administered alone could not produce this effect. The cholesterol content of the intact adrenal cortex may be increased by the feeding of cholesterol by mouth and is depleted during infections. Injections of large amounts of extract to the intact animal cause a fall within three hours of the blood cholesterol, suggesting some type of inter-reaction between the cholesterol esters and the hormone.

Experiments are in progress in which an attempt is being made to identify this hormone-sparing factor with some particular lipoid. The hypothesis is advanced that certain lipoids may serve either as conveyors of the hormone to the cells within which it acts or that they have a specific interaction with it.

A Case of Generalized Osteitis Fibrosa Cystica (Hyperparathyroidism?) Showing Metabolic Evidence of Spontaneous Healing. By SAMUEL H. BASSETT (introduced by Wm. S. McCann), Rochester, N. Y.

The nitrogen, calcium and phosphorus metabolism has been studied in a woman aged 21 years who presented roentgenological evidence of generalized osteitis fibrosa cystica (hyperparathyroidism?).

The experiment was continued through ten periods of six days each. During the initial thirty-six days, with the patient taking only a constant diet, consisting chiefly of milk, eggs, cheese and orange juice, and containing approximately 1.11 gram calcium, 1.41 gram phosphorus, and 10 grams nitrogen per diem, there was a retention of 14.34 grams calcium, 6.96 grams phosphorus and a loss of 7.18 grams nitrogen.

If the assumption be permitted that the calcium stored was deposited in bone as tertiary calcium phosphate, and that a loss of 1 gram of phosphorus occurs with a loss of 17 grams of nitrogen, calculation of the theoretical phosphorus balance from the above data shows the expected retention of phosphorus to be 6.98 grams. This figure agrees almost exactly with the phosphorus retention demonstrated in this portion of the experiment.

In the seventh and ninth periods, the diet phosphorus was supplemented by the ingestion of a solution of monosodium phosphate. This resulted in a lowering of serum calcium, elevation of serum phosphorus and a marked though temporary increase in retention of both calcium and phosphorus.

The Action of the Parathyroid Hormone on the Renal Threshold for Phosphorus. By READ ELLSWORTH, Baltimore, Md.

Previous observations of Albright and Ellsworth are confirmed that following the administration of parathormone there is an immediate pouring out of phosphorus in the urine and a fall of serum inorganic phosphorus.

In the present communication the following additional points are made: 1. The phosphorus diuresis following parathormone is quantitively sufficient to account for the fall of serum phosphorus. 2. Both urine and serum phosphorus changes occur in some experiments at a considerable interval before any observable alteration in serum calcium. 3. By ultrafiltration it is shown that before parathormone is given, the serum inorganic phosphorus is 97 to 100 per cent filtrable. 4. This strongly suggests that one primary action of the parathyroid hormone is to produce a specific lowering of the renal threshold for phosphorus.

Rickets and Hyperparathyroidism. By BENGT HAMILTON and (by invitation) CHARLES SCHWARTZ, Chicago, Ill.

In a preliminary communication it has been reported that the administration of calcium chloride or calcium gluconate by mouth to rachitic rabbits usually results in death from hypercalcemia, while in normal rabbits a corresponding dose of calcium increases the serum calcium only to a slight degree. It was thought possible that this effect was due to the presence of abnormally large amounts of parathyroid hormone in the blood of rachitic rabbits. A method was devised by which small amounts of parathormone may be demonstrated, using rabbits as test animals. By using this method it was found that the blood of rachitic rabbits is rich in parathormone or some other substance with identical effect on the serum calcium. This finding agrees well with the fact that several investigators have found a hyperplasia of the parathyroid glands in rickets. Our findings indicate that this hyperplasia is accompanied by an increased secretion of hormone. Probably the hyperparathyroidism is secondary to a low calcium absorption which, in the absence of hyperparathyroidism, would lead to a low serum calcium and tetany.

The Concentration of Electrolytes and Non-Electrolytes in the Serum Following Insulin Administration in Diabetic Patients. By F. W. SUNDERMAN (introduced by J. H. Austin), Philadelphia, Pa.

This study was designed to measure in the diabetic patient the change not only in sugar concentration but also of the other components of serum following the administration of a large dose of insulin. Insulin was withheld in 15 patients suffering with severe diabetes mellitus for a period sufficient to induce marked elevation of the blood sugar. After an overnight fast, blood was re-

moved for analyses and the patients were given from 50 to 150 units of insulin, still fasting. At intervals of 20 minutes, finger prick blood sugar values were followed with a technique which gave us measurements within 18 minutes. When the concentration of blood sugar had fallen to within normal limits or upon the appearance of any symptoms of an insulin reaction, a second specimen of blood was removed by vein for analyses and the patient was returned to his usual regimen.

After the administration of insulin coincident with the fall in serum sugar, cholesterol, and phosphate, the concentration of total base, sodium, and chloride in the serum increased toward normal values. The total osmolar concentration, as measured by the freezing point, decreased somewhat but not below normal. There was no consistent change in the total dry substance. The final picture represents a restoration in general toward normal values.

The Blood Lactic Acid in Hepatic Disease. By ALBERT M. SNELL and (by invitation) GRACE M. ROTH, Rochester, Minn.

Bollman and Mann have demonstrated elevations of blood lactic acid after experimental liver injury and in hepatectomized animals. The levels of lactic acid in human subjects show comparable changes in the presence of hepatic disease. High values are found in patients with portal cirrhosis in its terminal stages as well as in postoperative hepatic insufficiency. Following surgical procedures on the bile passages, transitory rises are noted. Following hepatic injury from arsphenamine, there was a definite parallelism between the levels of serum bilirubin and those of lactic acid. The relation of these changes in lactic acid values to other laboratory and clinical data is discussed.

Hypoglycemic Reactions Following Glucose Ingestion. By WALTER S. MCCLELLAN and (by invitation) H. D. HALCRO WARDLAW, New York, N. Y.

Symptoms associated with hypoglycemia following the ingestion of glucose have been reported in the literature in 8 patients. During a study of the influence of the previous diet on the metabolism after the ingestion of 100 grams of glucose in the Sage calorimeter, one subject developed symptoms 4½ hours after taking the glucose on three different occasions. This is the first time, as far as we have found, when the data have been available for analyzing the metabolism preceding an attack.

In the first two observations, when he had been on a high carbohydrate diet, 43 grams of glucose were oxidized showing rapid oxidation before the attack. In the last experiment, preceding which he had received only 25 grams of carbohydrate daily, he utilized only 23 grams for the same period. In this instance the depletion of his blood sugar to 40.8 mgm. was apparently due to a rapid storing of glucose.

Wide variations in the blood sugar time curves of 5 normal controls demonstrated that the previous diet definitely influenced carbohydrate metabolism. In spite of variations in these curves the blood sugar fell to or below its fasting level in all subjects by the end of 4½ hours. In the patient described above the blood sugar was 40.8 mgm. when he had symptoms. In another man it reached 34.0 mgm. without producing symptoms.

Thyroid Hyperplasia Produced in Chickens by Ultraviolet Deficiency. By KENNETH B. TURNER and ETHEL M. BENEDICT (by invitation) and ROBERT F. LOEB, New York, N. Y.

Marked thyroid hyperplasia was consistently produced in chickens raised in an environment from which ultraviolet light was excluded by means of an

amber glass filter. Rickets was prevented by the daily administration of cod liver oil.

In the hyperplastic glands the epithelium was higher, the follicles smaller and more numerous, and the colloid diminished when compared with normal thyroids from control birds. Macroscopically the thyroids of the ultraviolet deficient chickens were greatly enlarged and congested. The average weight of the thyroids from 30 of these chickens was 102 mgm. as compared to an average thyroid weight of 46 mgm. for 28 controls, although the average body weights for each group was the same.

In spite of the evidence of greatly increased activity in the hyperplastic glands, the metabolism as measured by oxygen consumption per minute per gram of chicken determined in four of the group receiving no ultraviolet light was the same as that of four control chickens. The iodine content of the hyperplastic gland was reduced.

The daily administration of potassium iodide to chickens raised in the absence of ultraviolet light effectively prevented thyroid hyperplasia. The thyroids of such birds resembled those of the controls in all details.

The Excretion of Inorganic Sulphates in Man. By J. M. HAYMAN, JR., Cleveland, Ohio.

Inorganic sulphates were estimated in the blood by Power's and Wakefield's method, and the urine by Fiske's benzidine method. Inorganic sulphates are less concentrated by the human kidney than creatinine, and usually less concentrated than urea. In accordance with the belief in filtration and reabsorption, this is regarded as evidence that some sulphate diffuses back through the tubule cells. After intravenous injection of sodium sulphate, the concentration ratio approaches that of creatinine. In nephritis with elevated serum sulphate, the excretion resembles that in a normal individual after injection of sulphate.

Complement Fixation in Smallpox and Vaccinia. By R. F. PARKER and R. S. MUCKENFUSS (by invitation) and D. P. BARR, St. Louis, Mo.

Complement fixation has been positive in twenty-six cases of smallpox in which the fluid was obtained before the ninth day of the eruption, using serum of rabbits hyper-immunized to vaccinia, and three hour ice box fixation with a capillary drop of vesicle fluid as antigen. After this time some negative reactions were observed. Fluid from the pustules of primary vaccinations gave positive reactions in all cases studied.

The blood of patients was studied by this technique, using ether extracted testicular vaccinia virus as antigen. The reaction became positive about the seventh day of smallpox.

Studies on Histamine in the Gastric Juice. By CHARLES L. BROWN (introduced by Cyrus C. Sturgis), Ann Arbor, Mich.

This study is an investigation of one phase of the fate of histamine in the body, namely, whether histamine is secreted by the stomach. Histamine has been isolated from the gastric mucosa, but report of previous work to investigate its possible presence in the gastric secretion has not been found.

The methods of extraction of histamine used by Best in the study of tissues were applied to gastric juice. The gastric juice extracts were assayed by the blood pressure method, using cats, as recommended by Best.

Twenty-seven samples of gastric juice, representing juice obtained with and without histamine stimulation, in normal and diseased individuals, were studied. Twenty-five of these showed a measureable amount (by assay) of a

blood pressure depressing substance which resembled histamine in its evanescent effect. Normals without histamine stimulation assayed from "not potent" to 0.0535 mgm. (in terms of histamine base) histamine activity per 100 cc. gastric juice; normals with histamine stimulation assayed from 0.0023 to 0.0411 mgm. (in terms of histamine base) histamine activity per 100 cc. gastric juice.

These gastric juice extracts in very great dilution caused violent contraction of virgin guinea pig uterus.

Two samples, each made up of two liters of gastric juice, were processed to isolate histamine in the form of dipicrate, but no crystals were obtained which conformed to the melting point and crystallographic characteristics of histamine dipicrate. However, the final extracts were potent by the assay method. The very small possible quantity of histamine may account for the inability to obtain the crystals.

Conclusion. A histamine-like substance, having an evanescent blood pressure depressing effect and causing violent contraction of the virgin guinea pig uterus, is found in the gastric juice, when the juice is obtained without or with histamine stimulation.

The Electrocardiographic Changes Following Ligation of the Smaller Branches of the Coronary Arteries in the Dog. By W. M. FOWLER and H. W. RATHE (by invitation) and FRED M. SMITH, Iowa City, Iowa.

The object of this investigation was to determine the effect of ligation of the smaller subdivisions of the coronary arteries on the electrocardiogram and to correlate these electrocardiographic changes with the location and character of the myocardial lesion.

Thirty-seven experiments were performed upon twenty-four dogs. Two of the dogs died from pneumonia, the remaining animals were sacrificed at varying intervals following the operation, and pathological studies made of the myocardial lesion.

The dogs were anaesthetized with ether, a tracheal canula introduced, and the anaesthetic continued under positive pressure. An incision was made through the chest wall on either the right or left side of the sternum, depending on the ventricle to be exposed. A control electrocardiogram was taken prior to the anaesthetic. Subsequent curves were taken eighteen hours following the operation and at daily intervals thereafter. In the first experiments, curves were taken at frequent intervals immediately after the operation, but this was discontinued, since in every instance the significant electrocardiographic alterations persisted for more than eighteen hours. Furthermore, premature contractions were often so numerous during the early post-operative period that the character of the T deflection was obscured.

A negative T deflection in one or more leads was the most distinctive finding. This was not necessarily accompanied by alterations in the R–T segment. In the subsequent course, the T wave became less negative and in from three to five days, returned to a positive phase. This was followed in many instances by an increase in the amplitude of this deflection and a later return to the original level. When the heart was examined after the electrocardiogram had gone through the successive alterations, a small fibrotic area was found in the myocardium below the ligature. If, however, the heart was examined during the early electrocardiographic alterations, a small area of degeneration with round cell infiltration was noted.

Vessels were ligated on the anterior and posterior surfaces of the left ventricle. Electrocardiographic changes occurred in most instances although no

correlation could be found between these alterations and the location of the occlusion. A vessel of the right ventricle was ligated in seven dogs. In six instances the ligation was followed by an alteration in the electrocardiogram.

In seven dogs, the pericardium was opened and sutured without disturbing the myocardium. The electrocardiographic changes were identical with those following ligation of the smaller vessels. When the hearts were examined at necropsy there were either adhesions between the epicardium and pericardium at the site of the incision or a discoloration of the underlying epicardium. The superficial vessels were patent, but on microscopic examination, degenerative changes of the muscle fibers immediately under the epicardium with a slight degree of round cell infiltration was found.

These experiments indicate that minute myocardial damage is sufficient to produce significant alterations in the T deflection of the electrocardiogram. The early changes are associated with an acute degenerative process in the myocardium. A return of the electrocardiogram to normal is accompanied by a replacement of the areas of degeneration by fibrous tissue.

The Effect of Thyroxin upon the Metabolism of Isolated, Normal and Malignant Tissue. By OVID O. MEYER and CLAIRE MCTIERNAN (by invitation) and JOSEPH C. AUB, Boston, Mass.

By the method of Warburg, micro-respiration measurements were made on isolated tissues. Mouse sarcoma C. R. 180 served as the neoplastic tissue and liver from the same mouse was used as the normal tissue control in each experiment. It was found that after daily subcutaneous injections of thyroxin for periods of three to thirty-three days the metabolism of the liver was appreciably elevated, whereas the oxygen consumption of the tumor in the majority of cases decreased to a significant degree when compared with control animals. The tumors from mice that had received thyroxin were similar microscopically to the controls.

To eliminate the possibility that the failure to obtain the usual thyroxin effect was due to the tumor's lack of innervation, thyroxin was administered to dogs in 28 to 44 mgm. doses over periods ranging from nine to thirteen days. At the end of the given period, the dogs were killed and the metabolism of the cortex of the denervated and normal kidneys was measured and found to be similar.

Conclusion. Thyroxin failed to elevate the tumor metabolism in a manner similar to that of normal tissue. This is probably due to some factor within the tumor tissue rather than a lack of nerve supply.

The effects of pancreatectomy on normal and tumor metabolism was also briefly discussed.

The Effects of Temperature and of Tissue Turgor on the Movement of Fluid through the Human Capillary Wall. By EUGENE M. LANDIS and (by invitation) JOHN H. GIBBON, JR., Philadelphia, Pa.

A plethysmograph measuring the volume of a segment of forearm under a pressure of 200 mm. Hg was used to study certain factors concerned in the movement of fluid through the capillary wall. Measurements made by means of the pressure plethysmograph are relatively independent of the variations in arm volume produced by vasomotor changes. The temperature of the apparatus was kept constant to within one degree Centigrade by circulating water through the space between the double wall of the instrument. The subjects were recumbent, with one arm abducted and the forearm extending vertically.

Tissue fluid accumulates at very low venous pressures, the rate of accumulation being proportional to venous pressures at least up to 60 cm. water. The temperature of the forearm conspicuously influences the movement of fluid. The rate of filtration produced by a venous pressure of 60 cm. water with a forearm temperature of 44.5° C. is over twice as great as the rate observed at the same venous pressure and a forearm temperature of 14.5° C.

When volume determinations are repeated over an extended period the rate of filtration produced by any given venous pressure gradually decreases as fluid accumulates in the tissue spaces. This occurs at low and high venous pressures indicating that tissue turgor is a factor in preventing the loss of large amounts of fluid from the blood stream.

The Rates of Utilization of Thyroxin and of Desiccated Thyroid in Man: Relation Between Iodine in Desiccated Thyroid and Thyroxin. By WILLARD OWEN THOMPSON and (by invitation) LAWRENCE L. MCLELLAN, Chicago, Ill.

These observations were made to determine the rate of production of the thyroid hormone in man. We have found that the minimum amount of thyroxin which must be injected intravenously or subcutaneously *every day* in order to maintain the basal metabolism of patients with marked myxedema at the standard normal level is 0.3 mgm. to 0.4 mgm. (This figure has not been determined before by daily injections.) The basal metabolism in these patients before treatment was minus 40 to minus 45 per cent and, therefore, they had little or no functioning thyroid tissue. The following observations suggest that most of the thyroxin was utilized by the body to increase its caloric expenditure and not excreted unused:

1. Injecting 1.5 mgm. every fifth day had the same effect as injecting 0.3 mgm. every day.

2. The intravenous injection of a single dose of 10 mgm. of thyroxin in a patient with marked myxedema produced roughly the same number of excess calories per milligram of thyroxin as injecting the same amount of thyroxin in divided doses of 0.3 mgm. per day.

Observations have been made which make it appear probable that when thyroxin is injected into an individual whose thyroid function is normal to begin with, much of it is promptly excreted unused. However, it would seem that a dose of thyroxin which is just adequate to supply a deficiency in the body may be used almost completely.

In patients with myxedema the calorigenic effects of thyroxin injected intravenously and desiccated thyroid administered by mouth are the same on the basis of their iodine contents. In a patient who required 0.3 mgm. of thyroxin injected intravenously every day to maintain the basal metabolism at the standard normal level, it was necessary to administer 1.5 grains (100 mgm.) of desiccated thyroid daily by mouth to accomplish the same result. This amount of desiccated thyroid contained approximately 0.2 mgm. of iodine, the amount contained in 0.3 mgm. of thyroxin. It would thus appear that all the iodine in desiccated thyroid is in a form equivalent to thyroxin from the standpoint of its physiological effects, and that, when the dose is just adequate to replace a deficiency in the body, it is absorbed almost completely from the gastro-intestinal tract.

Proof of Direct Communication Between Coronary Arteries and the Chambers of the Heart. By JOSEPH T. WEARN and (by invitation) T. G. KLUMPP and L. J. ZSCHIESCHE, Cleveland, Ohio.

It was pointed out in 1928, as a result of perfusion experiments, that perfusate introduced into the coronary arteries escaped into the chambers of the heart without passage through the capillaries. The existence of these channels has been denied by Anrep, Grant and Viko and Stella. Recent injection experiments, which consisted of injecting a substance into the coronary arteries too thick to pass through the capillaries and finding the same substance emerging from the Thebesian vessels, give further evidence of the existence of Thebesian communications with the arteries. Serial sections through one of these openings prove conclusively that there is direct connection between coronary arteries and the chambers of the heart. The importance of these communications is obvious when one considers the frequent obstruction of the coronary arteries without coronary infarction.

These vessels have not been described heretofore.

High Calcium Low Phosphorus Diets for the Rat. Long Time Metabolism Studies. By ALFRED T. SHOHL and (by invitation) HELEN B. BROWN, EDNA E. CHAPMAN, CATHERINE S. ROSE, and ESTHER SAUERWEIN.

Short time metabolism studies have shown that retentions high in calcium and low in phosphorus result from these diets. Does this type of retention continue? If so, is the body composition altered? When cod-liver oil is added to the rickets producing diet of Steenbock, rats continue in good nutrition for a long time. Their growth is restricted by the phosphorus (law of the minimum) and the high calcium, low phosphorus retentions are still present after 20 weeks on the diet. The body composition is not altered and the bones are of normal composition.

The Rôle of the Pulmonary Circulation in the Dyspnoea of Circulatory Failure and of Hyperthyroidism. By GEORGE P. ROBB (by invitation) and SOMA WEISS, Boston, Mass.

Although the velocity and volume of blood flow are increased in hyperthyroidism and decreased in circulatory failure, yet in both conditions the patients exhibit weakness, a tendency to dyspnoea, orthopnoea and a low vital capacity. This similar clinical behavior of patients with opposite disturbances of the blood flow has not so far received satisfactory and detailed explanation. Simultaneous quantitative study of the pulmonary circulation and of the ventilatory function of the lungs has, however, thrown light on the mechanism underlying this clinical paradox.

A group of patients suffering from hypertensive and luetic heart disease had dyspnoea and orthopnoea and a retarded pulmonary blood flow but gave no evidence of congestive failure in the periphery, the velocity and volume of the blood flow and the peripheral venous pressure being normal. However, although the amount of blood in the lungs was normal or slightly increased, the residual air was absolutely or relatively increased and the vital capacity was low. The index between the vital capacity and the residual air was particularly decreased. In the more severe cases of dyspnoea and orthopnoea, the amount of blood in the lungs was often considerably increased during periods when the peripheral circulation still showed no signs of congestive failure. The ratio between the vital capacity and the residual air was considerably disturbed in such cases. With clinical improvement due to rest or

digitalis both the pulmonary circulation and the dynamics of the lungs approached the normal state.

In a group of patients suffering from hyperthyroidism it was also observed that the actual amount of blood in the lungs was normal or increased and the velocity and volume of the blood flow in the pulmonary circuit was increased. The residual air space in these, as in the cardiac patients, was increased and the vital capacity was decreased. The ratio between the vital capacity and the residual air was decreased. Following the administration of Lugol's solution, and after thyroidectomy, the circulation and ventilation of the lungs returned to normal.

From these observations we have concluded that in both the cardiac and hyperthyroid patients, an increased capillary pressure with or without engorgement within the pulmonary circuit produces a functional emphysema of the lungs with a stiffening of the alveoli and a resulting low vital capacity. In heart disease, this increased capillary pressure is the result of back pressure from the impaired heart; in hyperthyroidism, it may develop either from active dilatation of the arterioles or from a passive dilatation due, again, to back pressure from the heart. Gross encroachment on the alveolar space by blood is not an essential factor in the development of the functional emphysema or low vital capacity in circulatory failure or in hyperthyroidism. The response of the lungs with increased capillary pressure and secondary functional emphysema in both conditions is to a large extent the explanation of the identical clinical manifestations discussed.

This study demonstrates the clinical significance of a quantitative, correlated observation of the pulmonary circulation and the ventilatory function of the lungs. It also demonstrates that disturbances in the pulmonary circulation and ventilatory mechanism of the lungs may develop independently of the state of the peripheral circulation.

The Equilibrium between Cerebrospinal Fluid and Blood Plasma. VII. The Distribution of Sodium and of Chloride Ions between Cerebrospinal Fluid and Blood Plasma and the Donnan Membrane Equilibrium. By FRANK FREMONT-SMITH and (by invitation) MARY ELIZABETH DAILEY, Boston, Mass.

We have previously shown that the human cerebrospinal fluid is in osmotic equilibrium with the blood plasma. Since the cerebrospinal fluid is almost protein-free, it is of interest to study the distribution of electrolytes between this fluid and plasma to determine to what extent this distribution may be explained by the laws of thermodynamics. During the past eight years we have studied the distribution of protein and of chloride between human blood plasma and cerebrospinal fluid in over 360 instances. In over 100 of these cases the distribution of sodium has also been determined. The total osmotic pressure has been determined by the freezing point method, and the water content by drying to constant weight.

In 25 instances in which the plasma and cerebrospinal fluid were shown to be in equilibrium by freezing point determinations, and in which the cerebrospinal fluid was essentially normal in composition, the ratio of spinal fluid sodium to serum sodium averaged 1.03 while the ratio of serum chloride to spinal fluid chloride averaged 0.82. If the Donnan membrane equilibrium governs the distribution of ions between these two fluids, the sodium in the water of serum should be greater than the sodium in the water of cerebrospinal fluid, whereas the chloride in water of the cerebrospinal fluid should be greater than that in the water of serum. This is shown to be the case when the con-

centration of these ions in water content of serum and cerebrospinal fluid is calculated. The average sodium content of serum water is 337 mgm. per 100 cc.; in spinal fluid water 324 mgm. per 100 cc.; the chloride in serum water 386 mgm. per 100 cc., and in cerebrospinal fluid water 438 mgm. per 100 cc.

If sodium and chloride is all present as diffusible ions, the distribution ratios for sodium and chloride in the water of these two fluids should be identical according to the formula:

$$r = \frac{[Na]_{C.S.F.}}{[Na]_s} = \frac{[CL]_s}{[CL]_{C.S.F.}}$$

The ratios, determined in water content, average:

$$\frac{\text{cerebrospinal fluid sodium}}{\text{serum sodium}} = 0.96$$

and

$$\frac{\text{serum chloride}}{\text{cerebrospinal fluid chloride}} = 0.88$$

By means of the formula derived by Van Slyke, Wu and McLean (J. Biol. Chem., 1923, lvi, 765)

$$r = \frac{[BP]_f + \sqrt{[BP]_f^2 + 4[A]_s([A]_s + [BP]_s)}}{2([A]_s + [BP]_s)} = 0.93$$

we have calculated the theoretical value for the Donnan ratio to be 0.93. It will be seen that this value is almost midway between the determined ratios for sodium and for chloride in water content. It is possible that some of the water of serum is bound to protein or to other colloids, and is therefore not available for the solution of ions. If it is assumed that an average of 4.3 cc. of water per 100 cc. of plasma is so bound leaving 89.3 cc. of " free water " per 100 cc. of plasma, the distribution ratio for sodium now becomes identical with that for chloride and equals 0.92.

The agreement between this value and the theoretical ratio (0.93) is extraordinarily good considering the complexities of the two fluids studied and the necessary assumptions involved. Moreover slight variations in the composition of the plasma are constantly taking place which would tend to disturb the equilibrium.

Conclusion. From a study of the distribution of sodium and chloride between human blood plasma and cerebrospinal fluid it has been shown that the distribution of these ions is in general in agreement with the Donnan membrane equilibrium although quantitative identity between the observed and calculated ratios has not been obtained.

The Circulation of the Brain and of the Leg in Man as Effected by Alterations in the Gaseous Content of Arterial Blood. By WILLIAM G. LENNOX and (by invitation) ERNA LEONHARDT, Boston, Mass.

Fifty experiments were conducted in which patients breathed various mixtures of CO_2 and of O_2. Before and during the procedure blood was drawn from an internal jugular and a femoral vein and from an artery. The CO_2 content and the O_2 content and capacity of these samples was measured.

For the brain, an increase in the CO_2 content of the arterial blood resulted in a marked decrease, and a loss of CO_2 in a marked increase, in the A–V difference. Alteration of the O_2 saturation of arterial blood produced less distinct

changes in the opposite direction. An increased saturation was associated with an increased, and anoxemia with a decreased A–V difference. These observations are believed to indicate that an increase of CO_2 or a decrease of O_2 in the arterial blood causes a dilatation of cerebral vessels, and the opposite conditions a constriction. These conclusions are consistent with the direct observations of pial vessels of the cat reported by Wolff and Lennox.

Circulatory changes in the leg did not parallel those in the brain.

The Effect of Rattlesnake Venom on Blood Sugar. By G. O. BROUN, St. Louis, Mo.

Lethal doses of the venom of *Crotalus atrox* gives rise to an antemortem hyperglycemia. Sublethal doses at times show the same effect, although not so regularly as the lethal doses. The causation of this hyperglycemia is considered together with the effect of insulin and antivenom on the increased level of blood sugar.

Two Mechanisms in the Production of Duroziez's Sign, their Diagnostic Significance and a Clinical Test for Differentiating between Them. By HERRMAN L. BLUMGART and A. CARLTON ERNSTENE, Boston, Mass.

The Mechanism of Vomiting Induced by Quinidine. By A. CARLTON ERNSTENE and (by invitation) SAMUEL LOWIS, Boston, Mass.

Since knowledge of the mechanism of the toxic symptoms of a drug is of importance in clinical therapeutics, we have studied the mechanism of emesis induced by quinidine. Contrary to expectation, the results of the investigation indicate that quinidine does not cause vomiting reflexly by stimulating afferent fibres from the heart. Quinidine emesis is mainly of peripheral origin, however, the afferent impulses reaching the medulla chiefly by way of the sympathetic division of the autonomic nervous system. We have been led to this conclusion by the following facts established in experiments on cats in which the effective vomiting dose of quinidine had been determined previously by intramuscular injection.

Denervation of the heart according to the technique of Cannon, Lewis and Britton failed to prevent nausea or vomiting in eleven of thirteen instances. Solutions of quinidine sulphate did not cause emesis when applied to the region of the vomiting center in the medulla. Removal of the stomach and intestinal tract did not prevent emesis, if the animals were in good postoperative condition. Paralysis of the vagus nerves by atropine sulphate did not prevent vomiting, although somewhat larger doses of quinidine frequently were necessary to induce emesis after atropine. Nicotine invariably prevented vomiting, and ergotoxine usually did so. Section of the spinal cord at the level of the second thoracic vertebra prevented emesis except at times after greatly increased amounts of quinidine.

The results of the investigation indicate that the chief sites of the therapeutic and toxic actions of quinidine are entirely different.

The Effect of Experimentally Produced Liver Damage on the Blood Fat Curve Following Epinephrine. By CHESTER M. JONES and (by invitation) JOSEPHINE W. FISH, Boston, Mass.

Elsewhere proof has been given of variations in the blood fat curve occurring in individuals suffering from various forms of liver disease. We have tried to reproduce these findings in animals with experimentally produced liver damage.

Chloroform and coal tar have been used in different doses to produce varying degrees of liver necrosis in rabbits. As in human beings the blood fats in normal rabbits rise abruptly following the subcutaneous injection of epinephrine. Following the use of chloroform or coal tar, with the resulting hepatic necrosis, the shape of the fat curve has been substantially modified in these animals. In animals with seriously damaged livers the curve goes progressively downwards. Apparently with somewhat less severe damage the fat curve tends to be absolutely level.

These variations from the normal rise and fall are identical with curves observed in human beings with very serious degrees of liver damage and strengthen our conviction that marked variations from normal in the behavior of the blood fats after the injection of epinephrine are of distinct prognostic value.

The Postoperative Disturbance in the Respiratory Mechanism. By W. J. MERLE SCOTT, Rochester, N. Y.

After operation there often is a marked disturbance in the respiratory mechanism as shown by the volume of the lung and particularly by a reduction in the vital capacity. A general parallelism is found between the latter and the incidence of postoperative pulmonary complications for the different areas of the body. The factors responsible for the diminution in vital capacity have been studied. Mechanical factors such as the alteration in intra-abdominal tension are relatively unimportant. Afferent stimuli from the wound appear to be chiefly responsible for it. After the reduced vital capacity is established, hyperventilation causes little change in it but interruption of pain from the wound results in a considerable increase. If the wound can be made entirely anesthetic for forty-eight hours after operation, most of the decrease in vital capacity can probably be prevented and a coincident reduction in the incidence of postoperative pulmonary complications achieved.

Parathyroid Poisoning as a Complication of Hyperparathyroidism in Man. By FULLER ALBRIGHT, Boston, Mass.

Simple hyperparathyroidism leads to skeletal decalcification, and even death from insufficiency of a bony skeleton. Collip has shown that very large doses of parathyroid extract in animals lead to a very different and sudden type of death. Hueper has shown that this death is associated with calcium deposits in certain abnormal places. Evidence is here presented that there is an increased calcium deposit in tissues where calcium is normally deposited. This strengthens the hypothesis that the calcium deposits are the result of an oversaturation of the blood with calcium phosphate.

Over fifty cases of hyperparathyroidism are now in the literature. One of three cases is cited where the manner of death and the autopsy findings not only make the diagnosis of hyperparathyroidism, but also that of parathyroid poisoning. The importance of recognizing the existence of this fatal complication is in its possible prevention. The series of events which lead up to it is discussed.

The Blood Iodine in Thyroid Disease. By GEORGE M. CURTIS and (by invitation) CHESTER B. DAVIS, Chicago, Ill.

The constant occurrence of iodine in human blood is now established. Our studies indicate a relationship between thyroid activity and the blood iodine level. There is thus opened up a new approach to studies of thyroid function in health and disease.

The normal iodine content of human blood in this region is 12.3 gamma per cent. One gamma equals 0.001 mgm. This is elevated in patients with toxic goiter to over twice the normal value, and more so in toxicity associated with diffuse hyperplastic than with nodular goiters. It rises sharply following preoperative iodinization, and falls following the thyroidectomy. After adequate thyroidectomy, it remains at a low normal level.

In hypothyroid states the blood iodine is lower than normal. This is true for cretinism, diffuse juvenile goiter with hypothyroidism, and postoperative myxedema of varying degree. The administration of desiccated thyroid, to patients with postoperative hypothyroidism, results in a definite and early rise of the blood iodine, which subsequently falls. Patients maintained upon desiccated thyroid over long periods maintain a high normal blood iodine. Members of the same family with varying manifestations of thyroid disease show striking variations in the blood iodine level, although living under similar conditions and on the same food and water.

The Nature of the Cardiac Enlargement Resulting from the Administration of Active Thyroid Material. By FRANCIS M. SMITH (by invitation) and EATON M. MACKAY, San Diego, Calif.

The increase in the weight of the heart which follows the administration of desiccated thyroid to the albino rat bears a linear relationship to the basal metabolic rate and the heart weight as varied in this manner is directly proportional to the total metabolism as measured indirectly by the food intake. In light of the relationship known to exist between the work of the heart as expressed by the cardiac output and the basal and total metabolism it is suggested that the cardiac enlargement which follows thyroid intoxication is in the nature of a simple work hypertrophy. The chief objection to this view is the accumulation of lactic acid in such a myocardium. The possibility exists that this is akin to the accumulation of lactic acid during a given effort stimulus in untrained skeletal muscle. If so it might be expected to disappear after long continued maintenance of a given thyrotoxic level or possibly through the breathing of oxygen rich air.

The Relationship between Oxygen Consumption and Nitrogenous Metabolism. By C. W. BALDRIDGE, Iowa City, Iowa.

As previously demonstrated, the rapid production of erythrocytes during induced remissions in pernicious anemia is associated with a decreased oxygen consumption. We also confirmed the work of Riddle and Sturgis and of Krantz and Riddle, who found increases in total oxygen consumption coincident with the destruction of leukemic leucocytes by roentgen ray.

Further investigations have revealed the following relations: 1. Increased blood destruction in polycythemia occasioned by phenylhydrazine is associated with increased oxygen consumption. 2. Rapid erythropoiesis following hemorrhage in dogs is associated with a slightly decreased total oxygen consumption. 3. Transfusion of compatible blood in dogs is followed by a rise in oxygen consumption which is delayed and coincides with the disappearance of the transfused blood. 4. Subcutaneous injection of hemolyzed blood in dogs is associated with an immediate rise in oxygen consumption. 5. In phlorhizin diabetes and in the period of nitrogen retention which follows it, the oxygen consumption curve is approximately a mirror image of the nitrogen balance curve. This corresponds with the findings in blood dyscrasias but the changes are of greater magnitude.

From these and other observations the following tentative generalizations are drawn. 1. Nitrogen retention (cell formation) is associated with a decreased oxygen consumption. 2. Nitrogen loss (cell destruction) is associated with an increased oxygen consumption.

The Significance of the Mercury Combining Power of Blood. By P. S. HENCH, Rochester, Minn.

The mercury combining power of blood is an index of its urea content, and the amount of urea in the blood can be determined simply by an estimation of its mercury combining power. The technic of the test is so simple that it can be carried out with a minimum of laboratory equipment, and it can be completed in fifteen minutes. This test is an extension of the work done some years ago on the salivary index (the mercury combining power of saliva), and a review of the recent work by the author and others, confirming the accuracy and value of the test, is presented.

Basal Metabolism Changes During the Dietary Correction of Under-Nutrition. By FRANK A. EVANS and (by invitation) JAMES M. STRANG, Pittsburgh, Pa.

Studies of the basal metabolism have been made on 11 patients with severe under-nutrition. These patients, who were treated by dietary measures alone, gained on the average 1070 grams per person per week for 5.4 weeks. The average total weight gain was 5.8 kilograms, which was equivalent to 14 per cent of the average initial weight.

During the dietary periods, the consistently low levels of basal heat output rose from an average of 49.1 calories per hour to 53.5 calories per hour or 9 per cent. In view of the average increase of body surface of 6 per cent which accompanied the weight gain, the average basal metabolic rate changed only 2 per cent.

An increase of weight of 14 per cent is therefore accompanied by an increase in basal heat production of 9 per cent although this fact is obscured if heat production is expressed solely in terms of basal metabolic rate.

Successful Orchidectomy in Addison's Disease. By CARL H. GREENE and L. G. ROWNTREE and (by invitation) WALTMAN WALTERS, Rochester, Minn.

Our experience has shown that any surgical operation on a patient with untreated bilateral renal tuberculosis or Addison's disease usually serves to initiate a crisis of acute adrenal insufficiency, with death within one to sixteen days. A case is reported of a man of thirty-four, with frank Addison's disease, in whom a successful orchidectomy was performed in consequence of the preoperative and postoperative use of adrenal cortical hormone, prepared by the method of Swingle and Pfiffner. The relation of this type of treatment to surgical practice in general is discussed.

The Effect of Ingested Fat and of Acidosis upon the Hyperlipemia of Diabetes Mellitus. By ARTHUR C. CURTIS and (by invitation) JOHN SHELDON, Ann Arbor, Mich.

Three cases of diabetes mellitus with hyperlipemia were studied. The first case showed a decrease in the blood fat although large amounts of fat and a high caloric diet were ingested. When glycosuria and acetonuria were induced by removing insulin, a slight increase in blood fat occurred. The second case had a lipemia of 11.6 per cent. This rapidly fell to 0.7 per cent on a high fat and high caloric diet with insulin. The insulin was then slowly decreased and

finally omitted. No change in the blood fat was evident until acidosis developed. With acidosis the blood fat rose to 3.65 per cent. The third case had a lipemia of 14.16 per cent. This rapidly fell as the diabetes was controlled to 1.40 per cent although the patient was ingesting large amounts of fat. The subsequent removal of insulin was then accompanied by a gradually increasing glycosuria until it became as great as 206 grams in 24 hours. At this time no change in the CO_2 combining power was present and little change in the blood fat had occurred. The acidosis subsequently increased until the CO_2 combining power was 30 mgm. per cent and the acetone bodies in the urine rose from 0.002 gram per 100 cc. of urine to 0.323 gram per 100 cc. of urine. Accompanying the mounting acidosis there was a steady increase in blood fat until at the height of acidosis it was 6.40 per cent. The addition of insulin alone to the previous regimen caused a fall in blood fat from 6.40 per cent to 0.95 per cent in 12 days.

Conclusions:

1. Lipemia has been reproduced in patients having diabetes mellitus.
2. The return of the lipemia is not directly related to ingested fat or to caloric intake.
3. It occurs when the carbohydrate combustion is so diminished that acidosis is produced.
4. The inability to oxidize fat causes its increase in the blood. By addition of insulin, carbohydrate is oxidized and lipemia disappears.

Influence of Hormones on a Glycogen-splitting Enzyme in Malignant Tissue. By FREDERICK H. SCHARLES (by invitation) and WILLIAM T. SALTER, Boston, Mass.

In work directed toward the enzymic activity of cancer cells (summarized for this society in 1931) we found no production of lactic acid by mouse sarcoma (number 180) from mouse glycogen. Barr et al. had previously reported a similar result. The reasons for this finding are two: first, although tumor cells contain an enzyme which does split glycogen, lactic acid is not produced by this tumor amylase; secondly, the intracellular amylase will not effect extracellular glycogen.

This enzyme, which is extractable from tumor by water, differs from other tissue amylases. Its optimum temperature, in vitro, is 48° C. rather than 37° C. The optimum pH for activity is 6.2. Glycogen is hydrolyzed, not into lactic acid, but into what are probably several compounds which yield a net reducing value of about one-third that of the inherent glucose. The glycogenolytic power of the enzyme under suitable conditions in vitro varies directly as the logarithm of its concentration. Of more fundamental import, however, is the fact that hormones can change the effective concentration of the enzyme in the tumor. Insulin causes an increase of 35 per cent and thyroxin of 150 per cent. Adrenalin and starvation cause no demonstrable change. It is not poisoned by cyanide nor iodo-acetate in vitro, nor does radiation with high voltage x-ray diminish its activity.

The Consumption of Blood Sugar by Muscle in the Non-Diabetic and Diabetic State. By WALLACE M. YATER and (by invitation) J. MARKOWITZ and RUSSELL F. CAHOON, Washington, D. C.

1. Heart muscle of a normal heart-lung perfusion consumes 4.0 mgm. of glucose per gram per hour, as was previously shown by Knowlton and Starling and Cruikshank.

2. Heart muscle of a diabetic heart-lung perfusion consumes less than one-fourth this quantity. This figure corresponds to the requirement of resting skeletal muscle of liverless dogs.

3. The decline in blood sugar following removal of the liver in dogs is the same in both the non-diabetic and the diabetic state.

4. The injection of 0.25 gram glucose intravenously per kilo per hour in liverless dogs suffices to maintain a normal level of blood sugar, as was previously shown by Mann and Magath.

5. When liverless dogs are subjected to severe strychnine spasms the continuous injection of glucose at this rate is insufficient to maintain the blood sugar, and it falls progressively to a hypoglycemic level in 5 hours.

6. When diabetic liverless dogs are injected intravenously with glucose at the rate of 0.25 gram per kilo per hour after the blood sugar has declined to a non-diabetic level there is a slowly progressive rise of the blood sugar level. It is estimated that the blood sugar would be maintained at an approximately normal level by the injection of 3/16 gram of glucose per kilo per hour.

7. On the basis of these experiments and those quoted from the literature the hypothesis is propounded that in the diabetic state the glucose requirement of resting skeletal muscle is the same as in the non-diabetic state; but that in the diabetic state contracting muscle is unable to utilize the glucose molecule for purposes of obtaining the extra energy. Apparently it is a function of insulin to elaborate the glucose molecule so that it is available for this purpose.

The Manner of Removal of Protein from Normal Joints. By CHARLES L. SHORT and GRANVILLE A. BENNETT (by invitation) and WALTER BAUER, Boston, Mass.

Information concerning the manner in which proteins are removed from joints as well as the rate of removal is necessary for a better understanding of the physiology of normal joints, and the factors involved in the production and maintenance of joint effusions.

These experiments were performed on the knee joints of normal dogs. Various dilutions of egg albumin were injected into the knee joints and the time of its appearance in the blood stream was determined by precipitation tests done at frequent intervals, using the serum of rabbits immunized against egg albumin. It was definitely shown that protein is removed much more rapidly from passively exercised joints than from joints at rest. In the case of the exercised joints, the protein could be detected in the serum as early as thirty minutes after the intra-articular injection. That there was but little tendency for the egg albumin to accumulate in the serum was evidenced by the fact that the amount contained in the serum did not increase markedly. This finding was confirmed by following the egg albumin content of the serum in dogs receiving intravenously small injections of egg albumin at frequent intervals.

In certain experiments the lymphatic vessels were tied off at their entrances into the larger vessels of the neck. In such instances no egg albumin appeared in the blood stream three hours after the intra-articular injection of egg albumin, thereby demonstrating conclusively that protein is removed from joints only by way of the lymphatics.

Similar experiments have been done in which horse serum and the albumin and globulin fractions of horse serum were injected into active and inactive joints instead of egg albumin.

These experiments aid one in concluding that in cases of long standing joint effusions, the removal of proteins is definitely interfered with. In such cases

one can state that there is definite interference with lymphatic drainage. This information suggests that a test might be devised which would enable one to state more definitely what therapeutic procedures are indicated in the treatment of a given case with a joint effusion.

The Treatment of Cardiovascular Syphilis. By J. E. MOORE and (by invitation) J. H. DANGLADE and J. E. REISINGER, Baltimore, Md.

This is a preliminary report of the outcome in 165 patients (112 with aortic regurgitation and 53 with aneurysm of the aorta) who received the same type of general medical care, but varying amounts of anti-syphilitic treatment. The scheme of treatment emphasized is based on the avoidance of therapeutic shock (the Herxheimer reaction), of the therapeutic paradox, and of drug, particularly arsenical, reactions. It is shown that by adequate treatment, as compared with little or none, symptoms may be alleviated; the mortality rate is reduced (during an observation period of 5–10 years) from 92 to 25 per cent; and the average duration of life after the onset of symptoms is increased from an approximate 24 months to 75 months or longer.

General Edema of Indeterminate Origin. By NORMAN M. KEITH, Rochester, Minn.

Five cases of general edema, indeterminate in origin, were seen between June, 1924, and July, 1925. The ages of the patients varied from nine to sixty-nine years. Edema had been present in one case for two years, and in the other four cases from two to four months. One patient gave a history of syphilis; one, a history of arrested chronic pulmonary tuberculosis, and three patients of previous good health. There was no distinct cardiovascular abnormalties nor any anemia. Daily urinalysis sometimes disclosed nothing abnormal, whereas, at other times, casts and traces of albumin were present. In two cases, the values for serum protein and blood cholesterol only were determined; in one case these values were normal; in the other, the value for serum protein was reduced to 4.6 mgm. in each 100 cc. and that for blood cholesterol was increased to 325 mgm. in each 100 cc. Treatment consisted of a diet low in salt and water, and administration of certain diuretics. In four cases the results were very satisfactory; in the fifth case, a large amount of fluid was eliminated through punctures in the skin of the legs. The ultimate prognosis in all cases was good. One patient, however, died five and a half years later with apparent cardiac failure and symptoms suggesting coronary occlusion. The most likely causative factors of the edema would seem to be some general toxic or nutritional disturbance.

Non-specific Versus Specific Serum Treatment in Lobar Pneumonia. By M. FINLAND and W. D. SUTLIFF (by invitation) and R. N. NYE, Boston, Mass.

A direct comparison between the response to the therapeutic administration of horse serum globulin solutions containing no specific antibodies and horse serum globulin solutions containing a high concentration of specific antibodies might be expected to provide an adequate control for the evaluation of the effect of specific serum and incidentally to throw some light on the nature and extent of the therapeutic response to non-specific therapy.

A concentrated solution of horse serum globulins was prepared from anti-meningococcic serum. Some patients were treated non-specifically with this serum and 20 to 60 hours later, were given equivalent amounts of antipneumococcic serum. Others received only non-specific therapy. The latter cases were compared with cases given specific therapy alone.

It was observed that non-specific therapy of the sort described had a temporary antipyretic effect, produced a temporary sense of well being in the patient, occasionally resulted in a temporary sterilization of the blood stream, but had no perceptible influence in preventing extension of the lesion. Specific serum therapy had a permanent antipyretic effect, produced a permanent amelioration of subjective complaints, regularly sterilized the blood stream and prevented extension of the pneumonic process.

It is concluded that the curative effects of Type I antipneumococcic serum in the treatment of Type I lobar pneumonia are due to its content of specific antibodies rather than to its action as a foreign protein.

Immune Reactions in Diabetic Patients. By HOBART A. REIMANN and (by invitation) JOHANNES K. MOEN, Minneapolis, Minn.

Several theories account for the increased susceptibility of diabetic patients to infection, (*a*) increased sugar in the tissue favors the growth of invading organisms, (*b*) diminished bactericidal capacity of the blood, (*c*) reduction of the opsonic index, (*d*) lack of tissue resistance.

Because of the correlation found between the suppressed formation of agglutinins and the tendency to secondary infections in leukemia and kala-azar, similar experiments were performed in diabetic patients. Four severe, 8 moderately severe and 4 controlled diabetic patients together with 10 normal controls were vaccinated in the usual manner with typhoid, paratyphoid A and B vaccine. Blood agglutination tests were made 10 days after the first injection and thereafter at 10 day intervals for 2 months.

The agglutinins appeared as usual in the normal individuals in high titer, occasionally as high as 20,000. The agglutinin titer was lower in most of the diabetics. The response was subnormal in the controlled diabetics, and distinctly low in the moderate cases. In 2 patients vaccinated during acidosis and glycosuria scarcely any agglutinins appeared.

Conclusion. The ability of diabetic patients to produce agglutinins following antityphoid vaccination is diminished. This probably indicates another factor to account for the increased susceptibility of diabetic patients to infection.

Study of Acute Respiratory Disease in Spitzbergen. By W. G. SMILLIE and (by invitation) J. H. PAUL and H. L. FREESE, Boston, Mass.

As a contrast to our year's study of "colds" in the Virgin Islands, West Indies, we selected Spitzbergen. This is a small isolated community, subjected to rigorous climatic conditions. The study began September 1, 1930. The ice closed down in October and no ships came in until June, so that isolation was complete. Almost no respiratory disease occurred in the population (500) during the winter. A severe epidemic struck with the arrival of the first ship in June. Bacteriological studies of nasopharyngeal flora of the people were made *throughout the year,* as well as observations of environmental conditions, including temperature, precipitation, relative humidity, sunlight, wind velocity and air ionization. Our results show that the "colds" in Spitzbergen were contagious, spread by direct contact, with an incubation period of about 36 hours. Environmental factors played no part in the incidence. None of the familiar organisms of the nasopharyngeal flora could be incriminated as etiological agents.

The Anginal Syndrome Induced by Gradual General Anoxemia. By MARCUS A. ROTHSCHILD and (by invitation) MILTON KISSIN, New York, N. Y.

With individuals subject to attacks of chest pain, in whom there is no evidence by physical or electrocardiographic examination of myocardial (coronary)

disease, it is often difficult to be certain of the origin of the pain. We wished to distinguish in these cases between those with pain due to impaired coronary circulation, and those in whom the pain arose otherwise. It occurred to us that if one were to produce a general anoxemia, and therefore a local cardiac anoxemia, there might appear differentiating responses in these two groups.

By means of rebreathing, we were able to produce a state of general anoxemia in human subjects. The carbon dioxide was absorbed. It usually took about ten minutes for the oxygen to become so low that the patient became uncomfortable.

Twenty-six patients were subjected to the test. Fourteen patients were used as controls. The controls consisted of four patients with normal hearts. The remaining ten cases were patients with chronic valvular disease, paroxysmal auricular fibrillation, rheumatic fever, spondylitis, gallbladder disease, and cardiospasm. None of these patients developed pain. Twelve were patients with clear-cut histories of attacks of precordial pain brought on by exertion, excitement, eating, or exposure to cold. Nine developed pain during the rebreathing test. Seven of these had no physical or electrocardiographic signs of myocardial disease. The pain appeared when the oxygen fell to about 9 to 10 per cent. This ordinarily took about 8 to 10 minutes. Subjects were advised to raise their hands when they felt uncomfortable, and the experiment was stopped.

It is furthermore interesting to observe that two other patients with clinical angina and intraventricular block developed pain and additional electrocardiographic changes during the anoxemia. The changes found were depression of the R–T segments in Leads II and III, and in another instance in Leads I and III. Unfortunately before further tests could be made, the second patient died, but the patient with changes in II and III was observed further. We were unable to reproduce the electrocardiographic changes with (1) oxygen and carbon dioxide inhalations, (2) intravenous atropin, (3) adrenalin, (4) pitressin, and (5) amyl nitrate.

There were three patients with clinical coronary artery disease, one with definite electrocardiographic changes, and two with no electrocardiogaphic changes, that responded negatively to the test.

We feel, therefore, that it is possible to reproduce the pain of angina pectoris in susceptible subjects by inducing general anoxemia. We assume in the explanation that the coronary circulation, normally adequate, becomes inadequate during anoxemia. We are not prepared to state that anoxemia per se is responsible for the pain that appears during the experiment. It is possible that the explanation of angina as being due to a cardiac ischemia combined with a piling up of Lewis's P-factor explains the pain that appears during rebreathing. We feel that our work, although not conclusive, tends however to support the anoxemic theory of angina pectoris. This test promises to be of some value in differentiating the causation of chest pain.

The Cause of Dyspnea on Mild Exertion in Persons with Cardiac Disease. By T. R. HARRISON and (by invitation) W. G. HARRISON, JR., and J. A. CALHOUN, Nashville, Tenn.

Observations have been made regarding the increase in ventilation produced by mild exercise in persons with cardiac disease. Previous studies have shown that such exertion is not associated with changes in the composition of either the arterial blood or the blood returning from the brain. Hence the increase in ventilation is not due to changes in cerebral blood flow.

It has been found that muscular movement causes a reflex increase in respiration. The evidence is as follows:

1. Moving the hands causes increased ventilation even though the circulation to and from the arm is occluded by an inflated blood pressure cuff around the arms.

2. Passive movements of a dog's leg cause increase in ventilation. If the spinal cord is cut in the mid-dorsal region moving the hind leg does not, but moving the fore leg does cause increase in ventilation.

3. If the hind leg of a dog be amputated except for the sciatic nerve and femoral vessels, movements of the leg cause increase in ventilation whether or not the vessels are obstructed. Cutting the nerve abolishes the effect.

Patients with cardiac disease have a greater ventilation for a given exercise than do normal subjects. They likewise have a greater and more sustained rise in venous pressure. Experiments on dogs indicate that the latter phenomenon may be a cause of the former because (*a*) rapid intravenous injection of fluid causes increase in ventilation when the vagus nerves are intact but not when they are cut; (*b*) increasing the venous pressure by inflating a balloon in the right auricle also increases, and deflation of the balloon decreases the ventilation. No such effects are obtained by the same procedures after bilateral vagotomy.

It is concluded that the dyspnea produced by mild exertion in persons with cardiac disease is due to reflex respiratory stimulation from the moving muscles and from the heart.

Intra-Capillary Anastomoses. By IRVING WRIGHT (introduced by H. O. Rosenthal), New York, N. Y.

We have observed in numerous patients small anastomosing vessels which connect different segments of an individual capillary loop. Some of these connect the arterial limb with the venous limb, others two portions of the venous limb; other patterns also have been seen. These vessels are smaller in diameter than the capillaries with which they are associated.

Two major considerations will be discussed:

1. The blood may cease to flow through these anastomoses while it still continues to flow through the capillary, passing the openings of the anastomoses. If this is due to an independent contraction of these minute anastomoses it would be valuable evidence in favor of the presence of an independent neuromuscular mechanism, probably the Rouget cells. Our observations lead us to believe that such is the case.

2. We have considered the development of these vessels. More than one anastomosis is rarely seen in the nail fold capillaries of a single patient, and it is impossible to see them in the capillaries elsewhere in the body. We have been able to see them more frequently since we have adapted the ultra-pak to capillary study.

These are probably residual vessels from the archiform capillaries of early infancy. We have confined these studies to mature adults in order to avoid confusion with the normal network seen in early infancy and sometimes present in childhood, especially in cretins.

Whether human capillaries bud out and produce such anastomoses we cannot say at present but studies are being made of this possibility.

Finally, these are not the arteriolar-venule anastomoses described by Heimberger, Lewis and others.

The Clinical Value of Electrocardiograms Taken in an Anteroposterior Plane at Right Angles to the Frontal Plane of the Classical Electrocardiogram. By EDWARD F. BLAND, SYLVESTER MCGINN and HOWARD B. SPRAGUE (by invitation) and PAUL D. WHITE, Boston, Mass.

On the Relationship between Cardiac Size and Basal Cardiac Work in Common Clinical Conditions. By ISAAC STARR, JR., and (by invitation) LEON H. COLLINS, JR., and FRANCIS C. WOOD, Philadelphia, Pa.

Estimations of cardiac output (method of Starr and Gamble presented before this society in 1928) and of blood pressure permit calculations of cardiac work by Starling's formula. Duplicate determinations were made in the postabsorptive state on fifty cases, viz. normals, threatened congestive failure, angina pectoris, hypertension, anemia, thyrotoxicosis and functional heart disease.

The relationship between cardiac size and work per beat has clinical significance dividing the cases threatened with congestive failure from the other cases. The latter arrange themselves along a straight line, the great majority deviating from it less than could be accounted for by the large errors inherent in the estimations; the former are far distant. Therefore in normal conditions the work of the heart is a function of its size, an extension of Starling's "Law of the Heart" to clinical conditions. In failure large hearts do but little work.

The relationship between heart size and heart work per beat was especially striking in 17 cases of hypertension. Those with hearts of normal size, by reducing cardiac output, maintained their hypertension without greater expenditure of cardiac work than normal persons. The cases with large hearts were performing increased work. Considering increased cardiac work as cause of hypertrophy in the latter group, its absence will explain the absence of hypertrophy in the former.

Comparison of the Way in Which Normal and Diseased Kidneys Excrete Waste Products. By F. H. LASHMET (by invitation) and L. H. NEWBURGH, Ann Arbor, Mich.

Under conditions which markedly restrict the fluid, but not the solid intake of the body, normal kidneys are able to excrete concentrated urine of high specific gravity. Under identical conditions, diseased kidneys excrete dilute urine of low specific gravity. This difference was at first supposed to be due to the inability of diseased kidneys to excrete the normal amount of waste products per unit of time.

If, however, the total amount of waste products and the volume of urine excreted per unit of time are determined, diseased kidneys eliminate solids at a high rate, provided sufficient water is available to permit the required dilution. The increased volume of urine is obtained at the expense of body water. The extent of the increase in urine volume is inversely proportional to the maximum specific gravity which the diseased kidneys can attain under the specified conditions.

The presence of edema changes somewhat the above findings. During the period of water restriction, patients with edema excrete urine of the expected low specific gravity, but of small volume and low total solids. If they are then allowed to drink water freely, they will excrete not only the normal amount of waste products in an increased volume, but also those retained from the period during which water was restricted.

These findings reveal the importance of adequate fluid intake in all cases of nephritis, including even those with edema. If there is to be no retention of

waste products, a large volume of urine must be assured by an adequate water intake.

The Heart Rate in "Frizzle" Fowls: its Bearing on the Human "Goiter" Heart. By ERNST P. BOAS, New York, and (by invitation) WALTER LANDAUER, Storrs, Conn.

It is still unknown in how far the increased metabolism, as such, or in how far altered thyroid secretion causes the cardiac disturbances of Graves' disease. The Frizzle fowl is a variety of chicken with peculiar upward-turning feathers and a very scanty plumage. The lack of feathers causes an excess loss of body heat, and a compensatory increase in basal metabolism. These chickens may live for a number of years and so offer a unique opportunity of studying the effect of a permanently high metabolism on the heart.

We have studied the heart rate of 22 Frizzle fowls and of 27 normal chickens of the same approximate age and weight. In some chickens the heart rate was counted for periods of several hours by means of the cardiotachometer. The usual electrodes applied to the skin of the breast were employed. Electrocardiograms were taken with needle electrodes. All readings were obtained while the chicken lay quietly on its back without struggling.

The heart rate of normal chickens weighing about 1.5 kilograms and about one year old ranges from 180 to 330 a minute. This is lower than rates reported in the literature which range around 350, and which are undoubtedly too high because the conditions of the experiments were far from basal. The heart rate of Frizzle chickens of the same weight and age ranges from 260 to 440. The average minimum rate per minute of the normal chickens was 263, of the Frizzle fowl 334.

It seems that in the Frizzle chicken the increased basal metabolism alone conditions a permanently increased heart rate. In human subjects with Graves' disease there must be a similar effect. The cardiac hypertrophy which has been observed in the Frizzle chicken is apparently related to this increased work of the heart. A similar mechanism may account, in part at least, for the cardiac enlargement that occurs in Graves' disease.

Cataphoretic Potential of Streptococci as Isolated in Studies on Arthritis. By EDWARD C. ROSENOW, Rochester, Minn.

The paper consists of a report on the cataphoretic potential of streptococci when isolated, and after long cultivation, obtained from various atria of infection, from the stool and from the blood in various forms of arthritis and allied conditions, and the effect of the patient's serum in lowering the cataphoretic potential of the streptococcus.

Renal Function During the Dissipation of Cardiac Edema. By GEORGE HERRMANN and (by invitation) E. H. SCHWAB and W. W. BONDURANT, Galveston, Texas.

Studies of the creatinine, urea, sodium chloride and the CO_2 in the blood and the urine during the mobilization and excretion of fluid under the influence of xanthine and mercurial diuretics and digitalization has yielded some interesting data on the mechanism of the action of the latter procedures. Applying Rehberg's formulae it is apparent that the diuresis from xanthine and digitalis bodies in so far as the kidney is concerned in patients with congestive heart failure is accompanied by great increase in filtration with but little decrease in reabsorption while with the mercurials the diuresis was accomplished primarily by a de-

crease in the reabsorption phenomenon. The blood CO_2 dropped as the base was lost through the kidney. The sodium chloride maintained about a normal level in the blood while the urinary output increased tremendously. The blood urea level rose conspicuously and dropped promptly back to just above the normal while the urinary excretion increased considerably during the height of the diuresis and dropped off sharply to below the resting level in ten hours.

Observations on Heart Sounds with Particular Reference to Gallop Rhythm and Sounds of Auricular Origin. By A. G. MACLEOD (by invitation) and FRANK N. WILSON, Ann Arbor, Mich.

Simultaneous phonocardiograms and electrocardiograms were taken in a series of patients with normal and pathologic hearts. A study of these records permits the following tentative conclusions.

1. In certain cases of heart block the R–T interval may be nearly twice as long as the interval between the first and second sounds.

2. Auricular systole may produce sounds as loud as, or louder than, the first or second heart sound. It often produces a double sound, the second element of which follows the P wave by a considerable interval. There are several factors which determine the intensity of the auricular sounds. Audible auricular sounds may occur in midsystole.

3. In bundle branch block associated with gallop rhythm the extra sound is presystolic and is not caused by asynchronous contraction of the ventricles.

4. In gallop rhythm the extra sound may be protodiastolic, presystolic or systolic. Presystolic gallop rhythm is by far the most common variety. In this type the extra sound seems to be of auricular origin. One interesting case was observed in which both presystolic and protodiastolic gallop rhythm were present at the same time. At ordinary rates one very loud mid-diastolic sound was heard; at slower rates this was separated into its two components.

The Electrocardiogram in Coronary Thrombosis. By PAUL S. BARKER and (by invitation) L. L. KLOSTERMYER and A. G. MACLEOD, Ann Arbor, Mich.

The electrocardiogram is useful in the diagnosis of coronary thrombosis, particularly when a series of curves is possible.

An important feature of the abnormal T-deflections is their progressive change in form. This is accompanied by QRS changes which have not been fully described. The curves fall into two groups.

The first group shows small complexes in lead I with a conspicuous and broad Q-deflection. In leads II and III the first deflection of QRS is upward, followed by an S-wave often of large amplitude. These QRS changes are associated with a sharply inverted T-wave in lead I in the late stages of coronary thrombosis, and with an upright T partially fused with QRS in the early stages.

The second group shows prominent Q-waves in leads II and III and T-wave changes of the opposite type. Corresponding to these changes there are characteristic changes in precordial leads which are of value in understanding how these phenomena are produced.

Changes in heart rhythm, particularly the occurrence of partial or complete block, paroxysmal ventricular tachycardia, and the sudden development of intraventricular block, or of very small complexes are also common in coronary thrombosis and are of diagnostic value.

Toxic Goitre and its Relation to Protein Digestion (Pancreatic). By JOHN STAIGE DAVIS, JR. and JOHN A. KILLIAN (introduced by Carl Binger), New York, N. Y.

The concentration of tyrosine and tyramine has been estimated in the blood and urine of a series of patients suffering from various types of toxic goitre. These results have been compared with those of a group of patients exhibiting nontoxic thyroid disease, and of normal subjects. When studied in relation to the basal metabolic rate, pulse rate and weight, the tyrosine and tyramine concentrations appear to have a definite relationship to the severity of the clinical manifestations.

Observations derived from animal experiments are presented which show that changes in the histopathology of the thyroid gland occur following ligation of the pancreatic ducts. These changes strongly resemble colloid goitre in man and are believed to be due to the lack of tyrosine production.

The general theoretical conclusion is reached that the absorption of the split products of protein digestion in the small intestine is related to the phenomena of thyroid disease: more specifically, that an excess in the concentrations of tyramine and tyrosine in the blood may be responsible for the manifestations of thyrotoxicosis, while the absence of these substances may result in colloid degeneration of the gland.

The Redistribution of Vital Capacity After Paralysis of the Hemidiaphragm. By JOSEPH W. GALE (by invitation) and WILLIAM S. MIDDLETON, Madison, Wis.

For a period of time after phrenic block or evulsion the vital capacity is perceptibly reduced as a rule. In certain instances after some time has elapsed the vital capacity returns to the preoperative level and may even exceed the same. Two circumstances explain this change, namely redistribution of the aerating space and decrease in the toxemia of the underlying process. The first of these factors can be evaluated and by a standard technique the area of the two hemithoraces has been determined in a series of cases before and after phrenic paralysis. The several possibilities as revealed by this method are discussed.

The Respiratory Metabolism of Acid-Fast Bacteria as Influenced by Foodstuffs, Narcotics and Methylene Blue. By R. O. LOEBEL, E. SHORR and H. B. RICHARDSON, New York, N. Y.

Utilization of foodstuffs by bacteria of the acid-fast group was described in an earlier paper and the relation of the findings to the survival of the bacteria within the body was discussed. The substances which were associated with an increase in respiration included glucose, lactic acid, glycerol, soaps, and lecithin. Reasons were given for supposing that this increase denoted an actual consumption of the foodstuff in question rather than a non-specific stimulus of oxidation. Additional evidence has now been obtained on this point by the study of the respiratory quotient, as affected by two groups of substances. The first group consisted of foodstuffs, the second of substances which are known to affect oxidation without necessarily undergoing oxidation. The latter group included the narcotics, KCN and ethyl urethane, and in addition methylene blue.

The organism used for the study was *B. phlei,* the timothy bacillus. The bacteria, after remaining for several days on a non-nutrient medium, were transferred to fresh fluid with or without the substance to be tested. The

R. Q. without nutriment was 0.75 to 0.81, with glucose 0.96 to 1.01, with sodium lactate 0.98 to 0.99, with sodium stearate and palmitate 0.74 and 0.77. With one exception the quotients observed corresponded to the theoretical value of the substance in question. This exception was sodium oleate which yielded quotients of 0.97 and 0.91, thereby resembling the second group of substances.

Both KCN and ethyl urethane caused, in addition to the expected inhibition at high concentrations, an increase in respiration in appropriate dilutions. This occurred both in non-nutrient media and in 0.2 per cent glucose, but was not apparent in lipoids. The respiratory quotients were 0.71 to 0.86 in the absence both of food and narcotic, 0.90 to 1.07 in the presence of KCN M/500 to M/5000, and 0.97 to 1.08 in 0.3 per cent ethyl urethane. Methylene blue had an action like the dilute narcotic but less marked. Since KCN can hardly be supposed to undergo oxidation, and since all three substances have the same effect on oxidation although they have nothing in common chemically, it is to be inferred that they act by increasing the oxidation of carbohydrate or other substance of high respiratory quotient.

In summary, the evidence from the respiratory quotient indicates that the foodstuffs tested are actually oxidized, in contrast to dilute KCN, dilute ethyl urethane, and 0.05 per cent methylene blue which stimulate respiration and cause a rise in the respiratory quotient, due probably to an increase in the oxidation of carbohydrate.

The Hemoglobin and its Variations in the Blood of Normal and Anemic Persons. By WM. P. MURPHY and (by invitation) I. M. HOWARD, Boston, Mass.

Studies of the hemoglobin in the blood and in crystalline form have been made. Its minimal molecular weight and percentage composition of iron have been calculated.

These are discussed together with certain relations of the hemoglobin in the blood of normal and anemic persons, particularly as influenced by treatment.

The Hypothalamus and Blood Pressure Regulation. By LOUIS LEITER and (by invitation) ROY R. GRINKER, Chicago, Ill.

Various investigators have assumed the existence of a superior vasomotor center in the hypothalamus. The experimental and clinical evidence for this hypothesis is meager, but the apparent demonstration of other vegetative centers in the diencephalon and the possible rôle of the hypothalamus in clinical hypertension seemed to justify another direct attack upon the problem.

In a large series of cats, the hypothalamic region was stimulated with the faradic current after exposure of the base of the brain from above or through the roof of the mouth. The site of the electrode was controlled histologically. The type and degree of anesthesia and the strength of stimulus were varied. The blood pressure and respiration were recorded and muscular movements carefully observed.

The results indicated that the blood pressure might rise, fall or remain unchanged during stimulation of the hypothalamus. Almost invariably, however, increases in blood pressure were associated with convulsive movements. The two phenomena ran roughly parallel in degree, regardless of the area stimulated. After the diminution or suppression of muscular activity by curare, no rise in blood pressure occurred upon excitation of the hypothalamus unless a very strong stimulus was used; in which event, the same result could be obtained from other parts of the brain.

These experiments would seem to rule out the presence of a hypothalamic center, in the cat, for the regulation of blood pressure.

The Control and Complete Remission of Polycythemia Vera Following the Prolonged Administration of Phenylhydrazine Hydrochloride. By H. Z. GIFFIN and (by invitation) E. V. ALLEN, ROCHESTER, Minn.

A group of thirty-seven patients with polycythemia vera, who were observed or given initial treatment during the years 1925, 1926, and 1927, has been reviewed in order to obtain information concerning the remote effects of treatment. Twenty-five of the patients received an initial course of phenylhydrazine hydrochloride at home. Brief abstracts of the records of seven patients, of whom adequate data were obtained and who had had an adequate amount of the drug, are presented. The records of these seven patients illustrate the excellent control which may be obtained, after the initial course of treatment, by means of the administration of small doses of phenylhydrazine hydrochloride. The condition of three of the seven patients, after prolonged treatment, underwent complete remission, varying from five months to one and a half years.

The toxicity of phenylhydrazine hydrochloride and the development of tolerance to the drug are considered. After the initial course of treatment it seems best not to allow erythrocytosis to recur but to keep the erythrocyte count and the blood volume under control with a sufficient amount of phenylhydrazine hydrochloride each week, usually from 0.1 to 0.3 gram.

A Rapid Method for Determining Magnesium in Blood and Urine. By ARTHUR D. HIRSCHFELDER and (by invitation) EARL R. SERLES, Minneapolis, Minn.

Kolthoff (1926) showed that traces of magnesium give a pink color with two yellow acridine sulpho dyes (Titan Yellow and Clayton Yellow) and that by comparison with a standard magnesium solution this reaction can be used for colorimetric determination of magnesium. Presence of calcium intensifies the color. We have used this method for determination of magnesium in blood plasma, from which the calcium has been removed by a modified Kramer-Tisdall method. The determination is very rapid, and simple. The results check closely with those obtained by methods of Denis and Briggs; and when known amounts of magnesium are added to plasma the figures obtained check closely. By using a microcolorimeter magnesium can be determined accurately in 0.1 cc. plasma. In urine, uranium acetate must be added to remove phosphates and blood pigment as well as oxalating out the calcium after which the magnesium can be determined accurately.

Purgative doses of magnesium sulphate given to normal men, dogs or rabbits does not raise blood magnesium significantly; but in nephrectomized dogs they cause blood magnesium to rise to 18 to 20 mgm. per 100 cc. plasma, and the dogs promptly go into coma. Rabbits rendered nephrotic by $HgCl_2$ react similarly and can be aroused by intravenous $CaCl_2$. Na_2SO_4 does not produce coma in nephrotic rabbits. It, therefore, seems probable that coma simulating uremic coma can be caused by Epsom salt purgation in patients with badly diseased renal tubules.

Study of the Gastric Secretion in Hyperthyroidism Before and After Operation. By W. R. BERRYHILL and H. A. WILLIAMS (introduced by M. A. Blankenhorn), Cleveland, Ohio.

Gastric analyses following histamine were done on fifty patients with hyperthyroidism before and after operation. Before operation thirty-four had an

achlorhydria, thirteen hypoacidity and three a normal acidity. After the hyperthyroidism was relieved by operation, twenty-six patients with previous achlorhydria were carefully followed, nineteen of whom had a return of normal acidity. The thirteen cases with hypoacidity returned to normal. This work shows a high incidence of achlorhydria in hyperthyroidism, but also a proportionately large return to normal acidity following the relief of the hyperthyroidism.

The Degradation of Mycobacteria into Non-acid-fast Forms. By F. R. MILLER (introduced by Gerald S. Shibley), Cleveland, Ohio.

Six strains representing four types of mycobacteria were grown in contact with the Berkefeld filtrates from a non-acid-fast chromogenic strain of H37 human tubercle bacilli. These six strains included three strains of human tubercle bacilli, one strain of bovine tubercle bacilli, one strain of smegma bacilli and one strain of timothy grass bacilli. From this treatment of acid-fast organisms seventeen non-acid-fast growths were obtained. At first these latter were all quite similar, being made up of non-acid-fast coccoid and rod forms and showing small gray-white colonies in twenty-four to forty-eight hours on agar. Four of these non-acid-fast growths, so far, have again developed acid-fast forms and colony formations similar to the parent strains from which they originated.

The filtrates of the chromogenic H37 organisms were sterile when plated for long periods of time on various media. The growth of non-acid-fast forms also occurred when acid-fast organisms were cultured in contact with filtrates which had been autoclaved.

A further study of acid-fast organisms by microcultures of single cells in contact with both autoclaved and unautoclaved Berkefeld filtrates of chromogenic H37 organisms is resulting in similar non-acid-fast growths.

Distribution of the Blood Entering the Coronary Arteries. By A. R. MORITZ, C. L. HUDSON and E. S. ORGAIN (introduced by Elliott C. Cutler), Cleveland, Ohio.

In order to study the extent and distribution of the blood supply entering the coronary arteries experiments were made by injecting an opaque substance into the coronary arteries at a pressure of 220 mm. Hg with the heart in situ. The coronary arteries were cannulated by making a small slit in the wall of the aorta. It was found that the substance injected into the coronary arteries filled the vasa vasorum of the aorta down to the level of the diaphragm; that the pericardium obtained a considerable proportion of its blood supply from the coronary arteries and that the diaphragm obtained a fair portion of its blood supply from the coronary arteries. These vessels formed a rich anastomotic network over the organs mentioned. It is felt that this distribution of blood, particularly in the wall of the aorta and in the pericardium, is of significance, particularly in luetic aortitis and other diseases of the aorta.