cles plus nephritis serum has nearly as great a streptococidal power as the defibrinated blood from the patients without nephritis. The corpuscles were washed twice in a large amount of NaCl solution which is usually sufficient to prevent phagocytosis in a suspension of corpuscles in NaCl solution. It is not likely, therefore, that the washing had not been carried far enough. But the results of these experiments seem to indicate rather that the leucocytes as well as the serum from these nephritis patients have undergone some change which renders them less efficient in the destruction of bacteria. In fact, it would seem that the leucocytes have suffered more than the serum. Whether or not these facts may serve to throw light on the cause of some of the terminal infections can not be determined at this time.

It is an interesting question whether the opsonin is increased or not during the acute infections. Normal leucocytes in normal serum take up large numbers of cocci; hence, it is difficult to determine if leucocytes in erysipelas serum, for instance, take up more cocci than those in normal serum. This question had, therefore, to be approached in a different way.

EXPERIMENT 4.—Two sets of tubes were made and 0.2 c.c. of washed corpuscles introduced into each. To one set of tubes were added falling quantities of normal serum and to the other set falling quantities of erysipelas serum. The contents of each tube were made up to 0.4 c.c. with NaCl solution, and to each tube was added 0.4 c.c. of a suspension of streptococci. The tubes were incubated for one hour at 36 C., smears were made and the average number of cocci in each leucocyte determined by counting those in 30 leucocytes. The results are shown in Table 7.

TABLE 7.

Normal serum.	Phagocytosis.	Erysipelas serum.	Phagocytosis.
0.2 c.c.....	13.5	0.2 c.c.....	11.5
0.1 c.c.....	9.4	0.1 c.c.....	11.2
0.05 c.c.....	6.7	0.05 c.c.....	8.2
0.025 c.c.....	4.7	0.025 c.c.....	6.9
0.012 c.c.....	2.2	0.012 c.c.....	4.3

This experiment indicates that there is a slight increase of opsonin in the erysipelas serum as compared with normal serum. A similar increase of opsonin has been noted by Wright and Douglas⁹ after treating with their staphylococcus vaccine a person afflicted with furunculosis. A diminution of opsonin in persons subject to attacks of furunculosis, sycosis, etc., has also been observed by these investigators.

CONCLUSIONS.

1. Human serum does not acquire streptococidal properties during the course of a streptococcus infection.
2. The blister fluid from erysipelas patients has no streptococidal powers.
3. Defibrinated human blood has a streptococidal power which, with few exceptions, is roughly proportional to the leucocytosis.
4. The destruction of cocci in the defibrinated blood is brought about by the leucocytes, but before this can be accomplished the cocci must be acted on by the opsonin of the serum. There is no phagocytosis and hence no destruction of unsensitized cocci by washed leucocytes.
5. The opsonin is increased during the course of an attack of erysipelas.
6. In an attack of acute nephritis the opsonin is diminished, but the leucocytes also undergo a change which renders them less effective in the destruction of streptococci. This fact may serve to throw light on the cause of many terminal infections.¹⁰

9. Proc. Royal Soc., Sept., 1904.

10. I wish to thank Professor Hektoen for many suggestions, and the internes of Cook County Hospital for courtesies.

DISCUSSION.

DR. M. J. ROSENAU, Washington, D. C., said that the results which Dr. Ruediger has obtained from his work on streptococcus infections have more than theoretical significance, for it is plain that this line of thought must eventually give practical results in the prevention and cure of the virulent infections caused by the various strains of streptococci. He said that Dr. Ruediger's paper clearly shows that the destruction of streptococci in the body is not the result of the serum or inflammatory fluids alone, but bears a direct relation to the number of leucocytes. This work gives a deeper insight into the process of phagocytosis and the part played by the leucocytes, especially in their relation to streptococci. Dr. Rosenau said that as a further confirmation of the opsonins described by Wright, it is a distinct advance in our knowledge of immunity.

PAROXYSMAL TACHYCARDIA: ITS RELATION TO EXOPHTHALMIC GOITER.

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It is my wish to emphasize the relationship apparently existing between certain cases of paroxysmal tachycardia and exophthalmic goiter, and to suggest that a more thorough examination of such cases may serve to trace the connection in a considerable proportion of instances. The more I see of this symptomatic disturbance, the less inclined am I to regard it as a definite entity or deserving of special caption in the category of disease. A superficial survey of the literature shows some 160 references to the subject, and as yet there has been no opportunity to observe what proportion of the cases are regarded by their reporters to have been due to exophthalmic goiter, though it is apparent that the percentage is small. It is hoped that a thorough resumé of the subject may be embodied in a future note. The present communication is actuated by two recent cases in my practice, of which full histories and notes to date follow:

CASE 1.—*History*.—Mrs. C., aged 38, married 16 years; has two children, the younger of whom is 8 years old. No miscarriages. Puberty at 12. Menstrual periods have always been accompanied by pain, which was relieved when the flow became established. Ordinary diseases of childhood, but no specific or rheumatic history.

Present Sickness.—The patient complains of constant pain in the legs, mostly at the knees, especially the right knee. This pain extends upward at times, and again downward, is dull in character but liable to acute phases, at which times there is apt to be locking of the right knee joint. There is a limp in walking which has been noticeable for twenty years. She also complains of hemorrhoids. The chief symptom and the one for which she seeks relief is periodic palpitation of the heart with hurried breathing, and some pain in the chest at such times. The attacks come on without warning, but usually follow fatigue or excitement. There is no regularity in occurrence, nor association with the menstrual period. Of late she has had one each month, lasting from two to ten hours. The duration of the complaint covers a year's time.

In the family history there is nothing to note beyond rheumatism in the father and "an asthmatic complaint" in the mother.

Examination.—Patient is above average height, well nourished, weight 125 (below her normal); the skin is soft, smooth and elastic, and the exposed portions are somewhat bronzed; the palms are moist, the fingers broad but not clubbed. Pulse 114, soft, low tension, fairly full. There is apparent and palpable enlargement of the thyroid body of which she was unaware. Circumference of neck over greatest prominence, 13½ inches. Lungs negative; expansion is free and symmetrical; epigastric angle acute. Apex beat is in the sixth space inside the mammary line. Dullness one finger breadth to right of sternum. Heart sounds are distinct and clear. A rough sys-

toxic murmur is present over the base and is not transmitted. Epigastric pulsations are apparent and the systolic murmur is heard here, but not elsewhere in the vessels.

Liver, stomach and splenic outlines are normal in size and position and the abdomen generally is negative.

The grasp is firm, stronger in the right hand. Supinator jerks diminished on both sides. There is tremor, fine, about seven to the second, most noticeable in the extended fingers, but palpable in the thighs on shifting the body weight from one leg to another. The knee joints are normal and symmetrical to inspection and palpation. Knee jerks are exaggerated. Normal flexor response on both sides. There are no disturbances in tactile or thermal senses.

The back shows the remains of an old kyphoscoliosis. She wore a brace for this condition for four years, but for the past two years has had no trouble.

The mucous membranes show no bronzing. The pupils appear large, but are equal and react to light and accommodation. There is no Stellwag or von Graefe sign or exophthalmos.

Pelvic examination shows the uterus in good position and freely movable, a tenacious discharge coming from a large and eroded os. The fundus has a depth of $3\frac{3}{4}$ inches and the interior is somewhat granular. Rectal examination shows some hemorrhoidal tissue, but not exuberant, and a few anal tags.

Lavage shows a normal gastric secretion. Blood: erythrocytes, 3,400,000; hemoglobin, 70; leucocytes, 8,700. Urine, total, 24 hours, 1,060 c.c.; acid; sp. gr., 1.016; urea, 1.7; no albumin or sugar, amorphous urates, mucus and vaginal epithelia.

Diagnosis and Treatment.—A diagnosis of exophthalmic goiter was made and the patient put on the following treatment: Graduated tub baths, 85 to 105 degrees, three times weekly, alternating with salt glows and alcohol rubs, with gentle massage to promote a healthy skin function; nutritive, full, easily assimilable diet, daily exercise out of doors; the application of the direct current, 20 milliamperes, the anode over the thyroid and the cathode on the cervical spine, for ten minutes three times a week; liquor potassii arsenitis, 2 mm. t. i. d. Treatment was begun April 25, 1904. The pulse ranged daily from 100 to 115.

First Attack.—On May 8 at 8:30 a. m. a paroxysm began and continued until 4:30 p. m. The patient took the position of greatest comfort for her, dorsal with a very low pillow, and lay quietly throughout the attack. The skin was flushed, moist, the expression good, the pupils dilated and sluggish to light and accommodation. The pulse was soft and weak and many waves failed to reach the wrist. The cardiac impulse covered an area the size of the palm and was observed to be forcible and sharp. The sensation conveyed to the hand was of a machine tapping from below. At a distance of a foot from the chest the quick systolic thumping of the heart could be distinctly heard. With the stethoscope the first sounds were loud and ringing, the second almost in abeyance everywhere. With the hand or the stethoscope the rate of the tachycardia could easily be noted, ranging from 190 to 240 throughout the paroxysm and recorded every hour. She complained of rather severe pain, also paroxysmal, and not related to the frequency of the heart, in the heart area radiating to the back. Once or twice during the day she took nourishment.

About 4 p. m. the patient's condition was as follows: Sweating and diuresis (the latter 1,120 c.c. since 8:30 a. m.), moderate cyanosis of ears, lips and fingers, expression one of great fatigue, pupils unchanged, pain intermittent and severe, heart rate 198. Heart dullness extended two fingers to right of sternum, the veins of the neck pulsating and full. Heart sounds weak and flapping. Respirations 30 and sighing.

At 4:30 p. m. the cessation of the attack was marked by a fall in respirations to 20, a general feeling of betterment, absence of pain and diminution of sweating. The behavior of the heart was most interesting. Now and then with the weak beats came a strong one, and occasionally a strong beat would take the place of the two or three weak ones, giving a curious arrhythmia and force wave. The strong beats all sent waves to the wrist. Gradually the strong beats gained supremacy over the weak ones until the ratio became about 3 to 1, and from then on there was a widening ratio until within an hour the heart settled down to steady work at 105.

At 9:30 a. m., after having made use of such therapeutic measures as stretching vagi by posture, pressure on them, holding the breath, iced and hot drinks, heat and cold to the precordia, there were given digitalin 1/100 gr. and ergot 1 dram hypodermatically; at 11:30 morph. sulph. $\frac{1}{4}$ grain; at 2 p. m. spartein 1 grain; at 4 p. m. morph. sulph. $\frac{1}{2}$ grain and digitalin 1/50 hypodermatically. We were under the impression that the last medication was effective, but were not unmindful of the fact that the paroxysms not infrequently terminate without medication.

The following day the patient was out of bed and feeling about as well as usual. From this time until June 5 she improved generally. The tachycardia diminished from 105 to 110 to 90 to 96 and the neck measured 13 inches. She continued taking arsenic and was put on the infusion of digitalis, half an ounce t. i. d., gradually diminishing it as the tachycardia grew less pronounced.

Subsequent Attacks.—June 5, however, she had another seizure, commencing at 10:30 a. m. and ending at 3 p. m. At the outset she was given digitalin 1/50 grain, and this was repeated at 2:30 p. m. The attack was much the same as the preceding, but with less pain. The highest heart rate was 240. There was less sweating and no cyanosis. In the next two months the patient was without attacks. She then passed from immediate observation. Since then there have been seizures of moderate severity, but a recent communication, June, 1905, tells me that she is much improved. What medication, if any, she is having is not made clear, but at last accounts she was taking a combination of strophanthus, digitalis and nux vomica tinctures, 5 minims each, t. i. d.

CASE 2.—History.—Mrs. P., aged 40; has three children, youngest 16, no miscarriages, had difficult labors, with lacerations each time, which were repaired. Menstruation regular, no pain, flow slight and becoming more so; duration one day.

Present Sickness.—She was well up to four years ago, when she began having palpitation of the heart, accompanied by shortness of breath at irregular intervals, the attacks coming on suddenly and lasting from one to five hours. Later she began to have pain with the attacks, severe, in the cardiac regions and neck, radiating into the left arm. She states that her nervousness in general has increased. The longest interval between attacks has been three months, and on the other hand she has had as many as three in one month. Occasionally she is able to foretell oncoming paroxysms by increased nervousness; at other times they appear without warning. During the attacks she sits on a chair or the bedside, or lies back on the pillows between the exacerbations of pain. The pain is severe but not overwhelming, and is relieved by pressure. Between attacks she feels and looks well. The appetite is excellent, there is no constipation, and she sleeps well.

In February of 1905 she had right lobar pneumonia and made a good recovery. Her personal and family history are otherwise negative.

Examination.—Height 5 feet 2 inches; weight 130. Fairly nourished, muscles somewhat flabby, skin dry and scaly. Slight bronzing in the posterior cervical regions and a muddy color of the face. The neck measures $13\frac{3}{8}$ inches. The thyroid body is not apparent on inspection, but can be made out by palpation. The thorax shows the scar of an old abscess in the left breast. A thickened pleura and impaired resonance over the upper right lobe mark the site of the pneumonia area.

The heart is enlarged to the left, the apex lies in the sixth space just inside the anterior axillary line; the sounds are clear; the pulmonary second sound is accentuated. The right heart is not demonstrable. Pulse 105, respiration 20, temperature normal. The abdomen is negative. The pelvic examination shows the repairs, and a slightly enlarged but otherwise normal uterus.

There is no exophthalmos apparent, but occasionally there is observed von Graefe's sign. The pupils are slightly dilated and sluggish to light, but react briskly to accommodation. Muscular power is fair.

There is tremor, fine (6 to 8), particularly noticeable in the extremities, but present in all muscles that are called forcibly into play. The deep reflexes are exaggerated. The sensory apparatus is keen. There are no hysterical stigmata.

Urine, 1,420 c.c., acid, sp. gr. 1019; urea, 2.1, no albumin or sugar.

First Attack.—Blood: Reds, 3,125,000; hemoglobin, 62 per cent.; whites, 6,400. On the night of May 17, 1905, she had a paroxysm, commencing at midnight. She was seated in a chair, her posture of greatest comfort. The heart rate was 220, respirations 30, the pain was endurable and not constant, her face was flushed, the skin moist, and the kidneys were active. Before I saw her she had already taken strychnin, 1/50 gr., and digitalis, 1/100 gr.

This seizure occurred before I had examined the patient, and when I reached her side her husband told me his physician had said she had angina pectoris. Without waiting to examine her with any degree of care, I gave her hypodermically, at 12:30 a. m., nitroglycerin, 1/100 gr. Between that time and 1 o'clock, when the paroxysm ceased, I was able to observe her more closely and to recognize the nature of the disturbance. I am by no means convinced that the injection availed whatever, yet I am certain that it did the patient no harm. It was the slightest paroxysm she had ever had. The character of the heart's action, its behavior during the continuance and decline of the seizure and the general features of the circulatory disturbance were so similar to the case previously outlined as to require no further description.

Subsequent Attacks.—The following day she was apparently as well as ever. The patient went to her home, at some distance from the city, and did not return until June 15. The multiplicity of her household duties and the fatigue of travel made her very nervous and she was able to foresee another paroxysm, which eventually appeared at 7 p. m. on June 19 and continued for three hours. Before I reached her she had taken, as usual, the strychnin and digitalin. I promptly gave her nitroglycerin, 1/100 gr., with no damage and no relief. She was then given morphin sulphate, 1/4 gr., and digitalin, 1/100 gr., at half-hour intervals for three doses, when the pupils indicated their discontinuance; with this medication were employed all the customary physiologic remedies. There was no cyanosis or dilatation during the attack and the course was generally characteristic. The morphia controlled the pain, but rendered the patient very restless and caused considerable nausea and vomiting after the subsidence of the paroxysm. A few days later the patient was put on the tinctures of digitalis, strophanthus and nuxvomica, of each 5 minims t. i. d., and a pill of arseniate of iron, 1/12 gr., after meals, and was treated three times weekly with the direct current of 10 milliamperes for 15 minutes, the anode to the thyroid body and vagi and the cathode to the cervical spine. This treatment was given daily after the first fortnight.

July 5 the neck measured 12½ inches, with no change in body weight.

July 7 there occurred a curious variation of conditions. Following a regimen of the cardiac tonics above mentioned and a rather prolonged seance of electrization, the patient had a headache, neuralgic in type, gradually increasing in severity, worst at the occiput. The pupils became moderately contracted and sluggish both to light and accommodation. The pulse was full, hard, of high tension, 60 beats to the minute. The attack persisted for 24 hours. On July 9 the pulse rate had returned to 100 and was soft and compressible.

July 16 and 17 the patient had premonitions of a seizure. There were slight momentary attacks of tachycardia, the pulse being 200, with occasional pains in the chest.

At 5 p. m., July 18, a paroxysm came on. The pain and flushing were pronounced, diuresis was marked, the catheter being called into use hourly. In this attack, in addition to the customary medication, there was given atropin, 1/50 gr., but with no effect whatever.

August 4 was the date of the next seizure. It was 2 hours in duration, with all symptoms characteristic.

August 21 occurred the last paroxysm up to the present time, October 10. It was characterized by pain, less severe than usual, and absence of extreme tachycardia. At its height the pulse rate did not exceed 120.

At the conclusion of the patient's residence under my care, September 1, her weight was 140, her general condition excellent. The neck measured 12¾ inches. The tremor was much

less evident. A recent communication from her informs me that she has continued to do well and is feeling much improved.

I was so fortunate as to have both these cases under immediate and constant observation, personally and by competent nurses. The cardiac rate was taken invariably at the heart, for often at the wrist the pulse was uncountable and occasionally unappreciable. Sources of error have been allowed for. The counting was done by the hand over the precordia, by stethoscope and by flags on the chest wall. Considerable doubt has been expressed by not a few of my colleagues as to one's ability to count 240 to the minute. The average watch ticks 5 to the second, or 300 to the minute, and is readily countable, particularly if taken by tens. Some practice is necessary in recording observations in tachycardia by any method other than instrumental. The rather exceptional advantages afforded for observation in the two cases submitted have made me confident that the records are approximately exact. Of late good results have been obtained, in some instances, by treatment with thyroidecine. I have had no personal experience with the remedy.

THE PRESENT STATUS OF THERAPEUTICS.*

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ST. LOUIS.

When I was a student at Jefferson Medical College one of the members of its distinguished faculty made the assertion that he "could encircle the globe and cure more diseases with four remedies than could be cured with all the balance of the materia medica." The four remedies named were quinin, opium, mercury and iodid of potassium. None will deny the therapeutic power of these drugs nor the vast scope of their usefulness. Indeed, the more we consider the statement the more we question whether it does not hold good to-day, notwithstanding that it was made more than twenty-five years ago.

We are forced to ask ourselves whether therapeutics has been standing still while pathology, bacteriology, chemistry, diagnosis and surgery have rushed into such prominence as to challenge the admiration of all who keep pace with the progress of the sciences, and while preventive medicine and sanitation, which stand alone in achievement for the welfare of men in every walk of civilization, have made habitable the squalid tenements of the dependent poor, protecting the middle and moneyed classes against the results of their own follies in social life, making possible the great commercial undertakings of nations, and encompassing the most remarkable saving of life from disease in the latest and most destructive war of modern times?

It is not my purpose to discuss the therapeutic action of individual remedies nor to rehearse what has been written concerning the numberless new remedies which are constantly forced on our notice through the energy of the army of manufacturers, all of whom claim special therapeutic advantages for their products, and whose assertions, if true, would leave nothing to be desired in remedial agents. This multitude of new remedies comes to us like the leaves of the forest—they hold the attention for a season, then fade, die and pass away. Many of them prove totally worthless, but they disappear only to be replaced by others of a similar kind, going to a similar fate.

The effect on the status of therapeutics is to make con-

*Read before the Missouri State Medical Association at Excelsior Springs, May, 1905.