Replacement of a displaced epiphysis after aseptic exposure is followed in most cases by union and normal growth of the epiphysis.

TECHNIC OF THE OPERATION.

The operative treatment differs from that used in the treatment of fractures in the adult. The introduction of sutures, and especially of metal and ivory screws, nails and pegs, is often followed by permanent atrophy of the epiphysis and subsequent failure of development of the involved limb. It is advisable in these cases, after exposure of the epiphysis under rigid aseptic precautions, to suture the torn periosteum, and if the capsule of the joint is ruptured, it should also be repaired. After approximation of the epiphysis and suture of the torn periosteum and capsule, the part should be held by an assistant until the operation is completed and the parts immobilized by a plaster-of-paris dressing.

Fractures associated with dislocations have always been followed by considerable deformity and impairment of the joint functions, when treated by non-operative methods. It seems rational that in cases in which the dislocation can not be reduced and the fracture treated at the same time, that recourse should be made to operative intervention. Under aseptic precautions the joint should be exposed, the capsule opened, the head of the bone replaced and the tear in the capsule repaired. If the associated fracture is one that is difficult to treat by non-operative methods, as a fracture of the surgical neck of the humerus combined with a dislocation of the head of the same bone, the fracture should also be exposed and the fractured ends sutured together with chromicized catgut. The part should then be immobilized in a plaster-of-paris dressing. Massage and passive motion may be instituted earlier under this method of treatment, and the chances of securing a movable joint, and absence of deformity will be greater when the condition is treated by operative measures.

V. THE OPERATIVE TREATMENT OF DEFORMITIES FOLLOWING FRACTURES.

The deformities following fractures may consist in (1) shortening; (2) shortening combined with alterations of rotation of the distal fragment; (3) angularity at the seat of fracture; and (4) limitation of motion, due to changes in the normal relations of the joint surfaces. Deformities most frequently occur in fractures of the clavicle; in fractures of the lower end of the humerus; in Colles' fractures; in fractures of the lower end of the femur; in spiral fractures of the tibia; and in Pott's fractures. In the correction of deformities following fractures, depend to a great extent the future usefulness of the patient, and in laborers it is of the greatest importance to leave his skeletal mechanics in as normal condition after the injury as they were before.

TECHNIC OF THE OPERATION.

While some deformities following fractures may be corrected to a certain extent by osteotomy (subcutaneous), or by the resection of a wedge-shaped piece of bone, the best results can only be obtained by exposing the seat of the former fracture and resecting the deformed area of bone. The operation should be performed under aseptic precautions. The site of the deformity should be exposed as detailed above. Care should be taken to separate the periosteum from the bone without tearing it. The section of bone may best be removed with a Gigli chain saw or with a chisel. The plane of section and the amount of bone to be removed will depend on the individual case. In a double bone limb it may

be necessary to remove a section from the fellow-bone, to allow of approximation of the resected surfaces, and to prevent angularity at the seat of the fracture. This, of course, produces some shortening of the limb, but it is preferable to angular deformity. An intact periosteum may, however, fill in the gap between the resected ends, thus not necessitating resection of the fellow-bone. As frequently happens, however, the periosteum is destroyed to a certain extent at the time of the injury, and has been replaced by fibrous tissue, so that in this event regeneration from the periosteum may not occur, or at best it will be greatly delayed. In patients in whom the element of time is a consideration, resection of the fellow-bone is advocated. After resection, the ends may be held approximated by means of heavy chromicized catgut. The further technic is the same as that of recent fractures.

(To be continued.)

FURTHER STUDIES ON STREPTOCOCCUS INFECTIONS.*

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CHICAGO.

About two years ago Dr. Weaver and I¹ showed that the blood serum from patients with scarlet fever has no streptococidal power during life in any stage of the disease. Through the researches of Lemoine, Slawyk, Hektoen and others we know that streptococci occasionally are found circulating in the blood of these patients and that the patients in whose blood cocci are found often make an uneventful recovery. Joehmann,² however, is of the opinion that the prognosis is very bad when streptococci are found in the blood.

What is true of scarlet fever may equally well be said of tonsillitis. Here, too, streptococci may invade the blood stream, but, in spite of this fact, the patient may make a rapid and satisfactory recovery.³

In erysipelas and in many wound and puerperal infections the tissues are invaded by virulent streptococci, but in a great majority of these cases the organisms disappear sooner or later and the patients make a complete recovery.

We know that normal human serum has no streptococidal powers. Hence, the disappearance of the cocci from the blood and tissue can not be explained by assuming that the serum loses something during the height of the disease, but regains this substance as convalescence sets in and thus destroys the cocci. It is evident, therefore, that we must look for some other agent than the serum alone to account for the disappearance of the cocci from the blood and tissues during convalescence. According to Metchnikoff, Denys and Leclef, Bordet, Marchand and others,⁴ this agent is found in the phagocytes. This view has not been universally accepted, although experiments show that it explains the facts better than any other theory that has been advanced. In a previous paper⁴ I was able to show that the

* This work, done at the Memorial Institute for Infectious Diseases, Chicago, was aided by a grant from the American Medical Association.

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Fifty-sixth Annual Session, July, 1905.

1. Trans. Chicago Path. Soc., 1903, v, p. 285. *Medicine*, 1903, ix, p. 515.

2. D. Arch. f. klin. Med., 1903, v. 78, p. 209.

3. Rosenow, Am. Jour. of Obstetrics, 1904, vol. 1, p. 766.

4. For a more complete review of the literature on phagocytosis see THE JOURNAL A. M. A., 1905, vol. xlv, p. 198.

leucocytes are the most important, if not the only, factor concerned in the destruction of streptococci in the body of infected rabbits and guinea-pigs. The view was expressed there that in man also the leucocytes play an important rôle in combating infection by these organisms, although not much work had been done on human infections.

In this paper are set forth the results of further studies of streptococcus infections in human subjects in the hope of determining just what factors are concerned in the destruction of the invading cocci, and an attempt is made to analyze more fully this phenomenon. In all instances where blood was used it was drawn from the vein at the elbow by means of a Luer syringe and defibrinated by gently whipping with a sterile wire. If the defibrinating is carefully performed not a very large proportion of the leucocytes are destroyed. In the experiments each tube contained from 0.8 to 1.0 c.c. of blood or serum which was inoculated with one loopful of streptococcus culture and two loopfuls from each tube were plated in glucose agar at intervals. The tubes were always kept in the incubator at 36 C. When highly virulent organisms were used 0.3 to 0.4 c.c. of defibrinated rabbit blood was added to each tube of melted agar to facilitate the counting of colonies, which often are very small if no blood has been added.

Table 1 shows that, although human serum in vitro is a good culture medium for streptococci, normal defibrinated blood has a slight streptococcidal power. Occasionally we may find a sample of normal blood which destroys many non-virulent streptococci, but the virulent organisms usually multiply in this blood.

TABLE 1.—THE EFFECT OF DEFIBRINATED NORMAL HUMAN BLOOD AND HUMAN SERUM ON STREPTOCOCCI.

Strepto-cocci.	Defibrinated Blood.	Immed.	2-3 hours.	Colonies in Agar Plates. 5 hours.
300	I	1100		160
300	II	3000		1060
300	IIa	680	675	1300
300	III	2600	2700	3500
300	IV	3000	1050	2600
300	V	540	360	240
300	VI	1100	500	390
298	VII	1600	600	315
298	VII	1600	600	315
298	VIII	600	80	16
B104	IIa	76	55	510
B104	III	1800	2800	Many
B104	IV	1600	3000	Many
B104	V	500	600	900
381	VI	2000	2300	Many
300	Serum IV	1400	2000	Many
298	Serum VII	1700	2500	10000

Source of streptococci: Strains, 298, 300 and 381 from heart blood of scarlet fever bodies, postmortem. B104 from an abscess in guinea pig; 298 and 300 are not virulent; 381 and B104 have been passed through rabbits and are highly virulent.

Table 2 shows that defibrinated blood from patients suffering from an acute infection has a much greater destructive effect on these organisms than has normal blood.

In these infections the leucocyte count is usually somewhat increased, and it seems that the streptococcidal power of the blood in vitro is roughly proportional to the leucocyte count. That is, the higher the leucocyte count the greater will be the streptococcidal power of the blood. This is a general rule, to which there are, however, a few exceptions, as will be pointed out later. The virulent organisms frequently multiply in these bloods unless the leucocytosis is very high. In no instance could a streptococcidal power of the serum alone be detected. It might be objected that we are not dealing here with an actual destruction of cocci, but that the decrease in the number of colonies on the plates is

due to adherence of the cocci to the leucocytes. This objection is ruled out by the fact that the twenty-four-hour plates from tubes containing blood with a high leucocytosis are very often sterile or nearly so.

TABLE 2.—THE EFFECT OF DEFIBRINATED BLOOD FROM CASES OF SCARLATINA, ERYSIPELAS, TONSILLITIS AND PNEUMONIA ON STREPTOCOCCI.

Strepto-cocci.	Defibrinated Blood.	Colonies in Agar Plates.			
		Leucocyte count.	Immed.	2 to 3 hours.	5 hours.
300	Scarlatina I	10500	1100		6
300	" II	10600	2000		140
300	" III	15000	690	270	116
300	" IV		550	18	3
300	" V		1500	300	150
300	" VI		1900	350	43
300	" VII		500	32	12
300	" VIII	13000	1380	102	9
300	" IX		1200	125	14
300	" X	13400	1250	245	120
300	" XI		1950	150	19
300	" XII	10800	1800	700	130
300	" XIII		1800	300	45
300	" XIV	12300	1500	31	2
381	" III	15000	1200	1500	3500
B104	" IV		600	462	415
B104	" V		1800	1800	5000
381	" VI		220	51	1100
381	" VII		130	41	Many
381	" VIII	13000	360	1180	Many
381	" IX	13000	2200	1950	Many
B104	" IX		330	190	1500
381	" X	13400	640	290	2500
B104	" X		400	160	165
381	" X		320	650	Many
381	" XII	10800	200	2000	Many
381	" XIII		540	900	Many
300	Erysipelas I		630	64	0
300	" II	15000	800	14	4
300	" IIa		1100	41	8
300	" III		740	120	160
300	" IV		1650	480	150
298	" V	10400	3100	420	92
B104	" I		1200	1080	960
B104	" II		96	30	13
B104	" IV		133	110	480
300	Tonsillitis I	16000	620	34	2
B104	" I		300	59	70
300	" II		1400	74	6
300	Pneumonia I		2600	0	3
300	" II		600	5	0
300	SERUM.				
300	Scarlatina VII		1500	3500	10000
300	" XIV		1200	1400	1300
300	Erysipelas II		670	760	750
300	" III		700	1800	6000
300	" V		3000	3500	5000
B104	" V		190	360	1140

It has been thought possible that the serum during the course of an infection which terminates favorably might acquire streptococcidal properties for that particular race of streptococci which is responsible for the infection, while at the same time it had no such properties for other races of these organisms. Three strains of streptococcus were, therefore, isolated from erysipelas patients and the serum of each patient tested on the corresponding organism. All of the patients made a satisfactory recovery, but at no time could streptococcidal properties be demonstrated in their serum. The defibrinated blood, on the other hand, killed many of the homologous and other organisms as long as there was a high leucocytosis.

We know that there is an intense local reaction in the localized streptococcus infections, and it has been thought by some that there may be lysis of cocci by the inflammatory serum in these areas. It is difficult to confirm or refute this theory on account of the difficulty of obtaining inflammatory serum in the same condition as it is found in the tissues. As it is not uncommon to find blebs of considerable size on the affected parts of erysipelas patients, the fluid from these blebs was taken as the nearest approximation to the inflammatory serum. This blister fluid from several cases of erysipelas was tested for streptococcidal properties, but gave negative results.

The importance of a high leucocyte count in the destruction of streptococci by blood is clearly shown by the following experiment:

EXPERIMENT 1.—Ten cubic centimeters of blood were drawn from the vein at the elbow of an erysipelas patient and carefully defibrinated. One cubic centimeter of the defibrinated blood, which contained 9,800 white corpuscles per cubic millimeter, was put into a small test tube, inoculated with one loopful of virulent streptococcus culture and two loopfuls of the inoculated blood, plated at intervals. The remaining eight cubic centimeters were centrifugated and the serum drawn off. We know that the uppermost stratum of centrifugated corpuscles contains a high percentage of leucocytes, because they are thrown down less easily than the red corpuscles. This stratum was therefore drawn off with a sterile pipette and mixed with a small quantity of serum. The resultant mixture contained 17,200 leucocytes per cubic millimeter. One cubic centimeter of this "suspension of leucocytes" was introduced into a small test tube, inoculated, and plates made as before. To complete the experiment one cubic centimeter of the clear serum was put into a small tube, which was likewise inoculated, and plates made at intervals. This experiment was also performed with normal blood and a non-virulent streptococcus. The plates were incubated for twenty-four hours, and the colonies that developed on each were counted with the results shown in Table 3.

TABLE 3.

Strepto- cocci.		Leucocyte count.	Colonies on Agar plates.		
			Im- med.	2 to 3 hours.	5 hours.
B104	Erysipelas blood.....	9800	390	168	350
B104	Suspension erysipelas leuc.	17200	260	58	21
B104	Erysipelas serum.....		200	360	1100
298	Normal blood.....	4400	1650	600	315
298	Suspension normal leuc....	6600	1600	420	62
298	Normal serum.....		1700	2500	10000

The table shows that both strains of streptococcus used multiplied in the cell-free serum; that the defibrinated blood destroyed many of the non-virulent and some of the virulent cocci, and that the "suspension of leucocytes" destroyed more cocci of either strain than the defibrinated blood. The only difference between the defibrinated blood and the suspension of the leucocytes lay in the fact that the latter contained nearly twice as many leucocytes as the former.

The fact that the streptococidal power of the blood is dependent on the number of leucocytes it contains per cubic millimeter has also been demonstrated by a second experiment.

EXPERIMENT 2.—Shortly after a patient's admission into the hospital, 3 c.c. of blood was drawn from a vein at the elbow and defibrinated. The leucocyte count at this time was 11,000. The blood was divided equally among three tubes, and each tube was inoculated with streptococcus culture and two loopfuls from each were plated at intervals. Shortly after drawing the blood, the patient was injected under the skin of the back with 10 c.c. of an antistreptococcus serum. This brought about an increase in the leucocytosis⁵ up to 15,000, five hours after the injection. Three c.c. of blood was again drawn from the vein at the elbow and its effect on streptococci tested as before. The results of the experiment are shown in Table 4.

The blood drawn after the injection of the serum, when the leucocytosis was high, has a greater streptococidal power than that drawn before the injection. It would not be safe to conclude that this difference in the streptococidal power is due entirely to the difference in the leucocyte count. Some of it may be due to an antitoxic or opsonic action of the serum or to a stimulation of the leucocytes. This supposition loses most of its

force when we consider the fact that the addition of from 1 to 5 per cent. of antistreptococcus serum to defibrinated blood in vitro does not increase its streptococidal power, as shown by Dr. Hektoen and myself.

TABLE 4.

Strepto- cocci.		Leucocyte count.	Colonies on Agar Plates.		
			Im- med.	2 to 3 hrs.	5 hrs.
300	Blood before injection.....	11000	1100	360	200
B104	Blood before injection.....		390	380	4000
381	Blood before injection.....		100	500	Many
300	Blood 5 hours after injection..	15000	1300	44	
B104	Blood 5 hours after injection..		412	246	600
381	Blood 5 hours after injection..		150	270	3000

Wright and Douglas have shown⁶ that phagocytosis takes place only after the bacteria have been sensitized, that is, have been acted on by the opsonin of the serum. There is no phagocytosis in a suspension of washed leucocytes in NaCl solution or in heated serum, regardless of the number of untreated bacteria that are added. This work has been confirmed and extended by Hektoen and Ruediger⁷ and by Bulloch and Atkin.⁸ In view of these facts there should be no reduction in the number of streptococci in a test tube containing a suspension of washed corpuscles in salt solution or in heated serum, and the following experiment shows that such is the case:

EXPERIMENT 3.—Ten c.c. of blood was drawn from a vein at the elbow of a scarlet-fever patient, defibrinated, centrifugated and the serum drawn off. The corpuscles were washed twice in a large amount of NaCl solution, and 0.5 c.c. of the centrifugated corpuscles placed into each of three small tubes containing 0.5 c.c. of normal serum, 0.5 c.c. of heated serum (58 degrees for one-half hour) and 0.5 c.c. of salt solution, respectively. The tubes were inoculated with one loopful of streptococcus culture, and two loopfuls from each were plated at intervals with the results shown in Table 5.

TABLE 5.

Strepto- cocci.		Colonies on Glucose Agar Plates.		
		Im- med.	5 hours.	24 hours.
300	Washed corpuscles + serum.....	1500	7	21
300	Washed corpuscles + heated serum...	1400	5000	Many
300	Washed corpuscles + NaCl solution...	1700	3500	Many
500	Serum.....	1200	1400	Many

The importance of opsonin in the destruction of streptococci is further shown by the fact that the defibrinated blood from two obstinate cases of post-scarlatinal nephritis had no streptococidal powers, although in one of these cases the leucocyte count was 14,000. When the blood from these patients was centrifugated and the corpuscles suspended in serum from a patient who was convalescent and had no nephritis, the resultant suspension had a small degree of streptococidal power, as shown by Table 6.

TABLE 6.

Strepto- cocci.		Colonies on Agar Plates.		
		Im- med.	2 hours.	5 hours.
298	Convalescent blood.....	800	450	14
298	Nephritis blood.....	720	1900	6000
298	Nephritis corpuscles + conv. ser..	850	500	540
298	Conv. washed corp. + neph. ser..	725	600	61

The interesting fact came to light in these experiments that the combination convalescent washed corpus-

5. I am indebted to Dr. Tunncliffe for the leucocyte counts and the injection of the serum.

6. Proceedings of Royal Soc., 1903, vol. lxxii, p. 357, and 1904, vol. lxxiii, p. 128.

7. Jour. of Infect. Diseases, 1905, vol. ii, p. 128.

8. Proceedings of Royal Soc., 1905, vol. lxxiv, p. 379.

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-