H. S., man, aged 32, whose case was diagnosed as chronic gonorrhea, multiple strictures, retention of urine, uremia, gluteal abscesses (colon), and colon bacillus septicemia, came under observation Oct. 25, 1915, at which time the pulse was 120, temperature 101 F. and respirations 40 per minute. He was cyanotic and irrational and had retention of urine. The retention was relieved, but the patient continued to grow worse during the day, and 500 c.c. of blood were withdrawn by venesection. The following day (October 26) the patient's condition was apparently the same, although the blood urea concentration was higher. October 27 there was a definite improvement in the general condition, and the blood urea had fallen to 2.21 gm. per liter. From this time on the blood urea continued to fall. The urea excretion was at no time low, being at the rate of 11 gm. per twenty-four hours, when the patient came under observation. It rose to 80 gm., October 29, and then gradually returned to normal. The blood urea concentration diminished rapidly after October 26, and the index of urea excretion rose to normal. There was a much greater improvement in the general condition of the patient during the time the index of urea excretion increased from 0.5 to 26 than in the time it changed from 26 to 166. The amount of urine voided was at all times large, varying from 1,650 to 4,600 c.c. in twenty-four hours.

UREA INDEX AND PHENOLSULPHONEPHTHALEIN

Although the question as to the agreement of the phenolsulphonephthalein test and the index of urea excretion does not come within the scope of this paper, it is interesting to note that in general the two tests give parallel results. There are striking instances, however, in which the tests do not agree. A case illustrating this is seen in Chart 3. Clinically this is a case of chronic diffuse nephritis with hypertension. The presence of marked impairment of renal function was demonstrated by the presence of a high blood urea concentration and a low index of urea excretion, and the fact that improvement under prolonged hospital treatment was slight and transitory. The phenolsulphonephthalein excretion for two hours was 55 per cent. While 55 per cent. may be considered a little low, it does not indicate the degree of renal impairment that actually existed.

CONCLUSIONS

1. The index of urea excretion gives much more information as to the degree of renal impairment and the prognosis, than does the blood urea determination alone.

2. All cases of chronic nephritis with hypertension here studied have impairment of renal function sufficient to alter definitely the relation that normally exists between the urea concentration of the blood and the rate of urea excretion, that is, have a low index of urea excretion.

3. The majority of these cases of chronic nephritis with hypertension have a blood urea concentration within normal limits (from 0.2 to 0.5 gm. per liter).

4. Chronic nephritis with normal blood pressure may or may not have sufficient renal impairment to alter the relation which normally exists between the blood urea concentration and the urea excretion, that is, it may have a normal or a low index of urea excretion.

5. In general the phenolsulphonephthalein test parallels the index of urea excretion; but there are marked exceptions to this rule in which the phenolsulphonephthalein test apparently gives an erroneous idea of the degree of renal impairment.

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OBSERVATIONS ON IMMUNITY OF MONKEYS TO EXPERIMENTAL POLIOMYELITIS *

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It is a generally accepted fact that a monkey, after recovery from an attack of experimental poliomyelitis, is immune to subsequent injection with virulent virus. It is a question whether an inoculation which does not cause paralysis confers immunity. Römer believes that immunity follows unsuccessful intracerebral injection in some cases. But there are in the literature many instances in which experimental poliomyelitis has been produced in monkeys which had shown no evidence of infection from a previous inoculation.

We wish to record an experiment which appears to indicate that immunity was conferred on three monkeys by inoculations which were not followed by obvious evidence of infection. One of the apparently immune animals had previously received an intracerebral injection of a culture of pleomorphic streptococci, the second had received emulsion of central nervous system of animals paralyzed by cultures of streptococci, and the third had received virus in the usual way.

Material used for test inoculation.—A virus which had been passed successively through four monkeys was employed. A 5 per cent. emulsion in physiologic sodium chlorid solution of the brain and cord of the fourth animal (Monkey 26) was made immediately after necropsy, November 3. This was ground thoroughly with sterile quartz sand, and shaken for twenty minutes. Eight rhesus monkeys were injected in the left frontal lobe with this emulsion. Two of these were controls; five had received previous inoculations with virus, filtrate of virus, or culture; and the eighth had received a mixture of the test virus and blood serum from monkeys suspected of being immune. Seven of the monkeys which were of approximately the same weight were given 1 c.c. of the test virus; and the eighth, which was a large, old animal, was given 3 c.c.

The accompanying table records briefly the results of this experiment. For details of the source of material used in the previous injections, reference should be made to the protocols.

* From the Mayo Foundation.

Chart 3.—Chronic diffuse nephritis: solid line, milligrams of urea per hundred c.c. of blood; broken line, grams of urea excreted per twenty-four hours; dotted line, index of urea excretion; P, percentage of phenolsulphonephthalein excreted in two hours.

PROTOCOLS

EXPERIMENT 1.—Control.—Monkey 33, *Macacus rhesus*, 2.6 kg.
Nov. 3, 1916: Etherized; 1 c.c. of Virus 751^a injected into left frontal lobe.
November 10 (seventh day): Tremor of arms and legs, rapidly followed by flaccid paralysis of left arm and marked weakness of muscles of the right arm, back and legs.
November 11: Prostrate. Killed with ether. Cyst size of pea, filled with clear fluid, was found at point of inoculation. Microscopic section of brain and cord showed marked typical lesions of experimental poliomyelitis.
EXPERIMENT 2.—Control.—Monkey 34, *M. rhesus*, 7.3 kg.
November 3: Three c.c. of Virus 751^a injected into the left frontal lobe. Immediately after injection there was spastic weakness of the right arm.
November 7: Several convulsions. Right arm remained almost useless, and there was slight weakness of right face and leg. Acted sick and ate little.
November 10: Better; took food well and was active; the right arm still weak.
November 13 (tenth day): Irritable. Coarse tremor of left arm.
November 15: General tremor. Legs weak; could scarcely walk. Handling legs appeared to cause pain. Knee kicks exaggerated.
November 16: Legs flaccid; reflexes abolished. Left arm tremulous and weak; back muscles weak. Difficulty in swallowing. Killed with ether. A cyst about the size of an almond filled with clear, deep yellow fluid (old blood) was found at point of injection. Microscopic sections of brain and cord showed typical lesions of experimental poliomyelitis.
EXPERIMENT 3.—Attempt to destroy activity of virus by mixture with serum of monkeys thought to be immune.—Monkey 37, *M. rhesus*, 2.8 kg.
November 3: Virus-serum mixture made as follows: Blood was removed from the internal saphenous vein of Monkeys 19 and 21 (which see) previous to their inoculation with the test virus. The serums were mixed so that 1 c.c. contained approximately three parts from Monkey 19 and seven parts from Monkey 21. One c.c. of the serum mixture was added to 1 c.c. of the test virus. The mixture was filtered through paper, kept at a temperature of 35 C. for two and one-half hours, and then in the ice box for fifteen hours.
November 4: Etherized. Two c.c. of virus-serum mixture (containing 1 c.c. of Virus 751^a) injected into left frontal lobe.
November 19 (fifteenth day): Very excitable. Head inclined to the right; constant coarse tremor of right neck muscles.
November 20: Tremor has extended to muscles of right arm. Knee jerks brisk.
November 21: Flaccid paralysis of legs, back and right arm. Left arm weak and tremulous. Killed with ether. Small cyst containing clear fluid at the point of inoculation. Microscopic sections showed characteristic lesions of experimental poliomyelitis.
EXPERIMENT 4.—A monkey previously injected intravenously with culture from pus about the teeth of a monkey which did not have pathologic lesions of poliomyelitis, was not immune to test virus.—Monkey 21, *M. rhesus*, 2.5 kg.
Previous inoculation, Sept. 16, 1916.—Injected intravenously with 4 c.c. of a suspension in physiologic sodium chlorid solution of the centrifugal growth from 60 c.c. of ascites dextrose broth culture of pus

around the teeth of Monkey 18, Case 756. This organism appeared in smears from broth as a somewhat elongated diplococcus, occasionally in short chains; and on blood agar plate as small dry green-producing colonies. (Monkey 18 was a domesticated monkey with marked pyorrhea alveolaris; he became spontaneously paralyzed in the animal room. When muscle power began to come back he was killed with ether. Microscopic sections did not show lesions of poliomyelitis.)

September 17: Sick and irritable.
September 21: Appeared well. Etherized. Injected into frontal lobe 1.3 c.c. of physiologic sodium chlorid solution containing the growth from 20 c.c. of ascites dextrose broth culture 756.3 (Monkey 18, teeth). This was a second subculture of the culture injected September 16.

November 2: Had remained well. Blood for serum removed from saphenous vein (compare Monkey 37).

November 3: Etherized. One c.c. of Virus 751^a injected into left frontal lobe.

November 19 (sixteenth day): Irritable and tremulous, with weakness of legs.

November 20: Flaccid paralysis of both legs. Wrist drop on right.
November 26: Right arm and back muscles gone. Left arm weak and ataxic, but could be used to take food. Good appetite.

December 5: Improving; able to sit up. Arms were stronger but markedly ataxic. Legs could be moved a little.

December 15: Got about quite well. Legs paretic and began to show contractures.

EXPERIMENT 5.—A monkey, infected intracerebrally with filtrate of brain and cord of a monkey which did not have pathologic lesions of poliomyelitis, was not immune to test virus.—Monkey 24, *M. rhesus*, 2.3 kg.
Previous inoculation, October 5.—Etherized. One and five-tenths c.c. of Berkefeld N filtrate of Virus 737^a (glycerinated brain and cord of Monkey 16) injected into left frontal lobe. (Monkey 16 was inoculated with a filtrate of mixed human and monkey virus and developed muscular weakness; but microscopic sections did not give the picture of experimental poliomyelitis.)

November 3: Had remained well. Etherized. One c.c. of Virus 751^a injected into left frontal lobe.
November 10 (seventh day): Irritable, with rapid tremor of neck and shoulder muscles. Internal squint, apparently due to weakness of right sixth nerve. General muscular weakness.
November 13: Markedly ataxic. Left arm awkward.

November 17: Less tremor. Both arms weak, especially the right, which showed complete wrist drop. Right leg tired quickly. No knee jerk on right. Strabismus less marked. Photophobia.

November 26: Improving. Shaky and weak; took food well.

December 15: Very active; showed only some residual weakness of right arm; slight internal strabismus and photophobia.
EXPERIMENT 6.—Example of apparent immunity conferred by inoculation with filtrate and virus seven weeks previously, without evidence of infection.—Monkey 17, *M. rhesus*, 2.5 kg.

Previous inoculation, September 13.—Etherized. Injected into frontal lobe 1.5 c.c. of Virus 737 (compare Monkey 24) which had been passed through a dense porcelain filter.
September 19: Had remained well. Etherized. Seventy-five hundredths c.c. of fresh human Virus 729 injected into frontal lobe.

November 3: Had remained well. Etherized. One c.c. of Virus 751^a injected into left frontal lobe.

RESULTS OF TEST INJECTIONS OF A VIRULENT VIRUS

	1 Monkey 33 <i>M. rhesus</i> 2.6 kg. (Control)	2 Monkey 34 <i>M. rhesus</i> 7.3 kg. (Control)	3 Monkey 37 <i>M. rhesus</i> 2.8 kg.	4 Monkey 21 <i>M. rhesus</i> 2.3 kg.	5 Monkey 24 <i>M. rhesus</i> 2.3 kg.	6 Monkey 17 <i>M. rhesus</i> 2.5 kg.	7 Monkey 14 <i>M. rhesus</i> 2.1 kg.	8 Monkey 19 <i>M. rhesus</i> 2.8 kg.
Previous injection				Sept. 16 and 21, growth from 60 c.c. and 20 c.c. Broth Cult. 756 (Monkey 18, teeth) intravenously (not polio.)	Oct. 5, 1.5 c.c. Berk. N filt. Virus 737 ^a (Monkey 16); intracerebrally (not poliomyelitis)	Sept. 13, 1.5 c.c. porcelain filt. Virus 737 intrac.; Sept. 19, 0.75 c.c. Virus 729 intrac.	Sept. 11 and 20, intrac. injec. filt. and Virus 714 ^a (Monkeys 10 and 12, paralyzed with cultures)	Sept. 16, 1.5 c.c. Cultures 707.2 intracerebrally
Result of previous injection				Sept. 17, sick; well thereafter	Remained well	Remained well	Sept. 18, Rt. arm awkward; well thereafter	Sept. 16-18, sick; well thereafter
Virus 751 ^a (Monkey 26)	Nov. 3, 1 c.c. intracerebrally	Nov. 3, 3 c.c. intracerebrally	Nov. 4, 1 c.c. Virus + 1 c.c. serum, Monkeys 19 and 21 (incubated 2½ hrs.) intracerebrally	Nov. 3, 1 c.c. intracerebrally	Nov. 3, 1 c.c. intracerebrally	Nov. 3, 1 c.c. intracerebrally	Nov. 3, 1 c.c. intracerebrally	Nov. 3, 1 c.c. intracerebrally
Result	Paralysis 7th day; killed with ether 8th day; typical lesions	Tremor 10th day; paralysis 13th day; killed with ether 14th day; typical lesions	Excitement and tremor 15th day; paralysis 17th day; killed with ether 17th day; typical lesions	Tremor 16th day; paralysis 17th day; prostrate 23d day; improved 32d day; weak legs with contractures 45th day.	Ataxia, squint and paresis 7th day; paralysis 14th day; improved 23rd day; weak arm and squint 45th day	No symptoms; well on 45th day	No symptoms; well on 45th day	No symptoms; well on 45th day

December 15: Had continued to be perfectly normal.

EXPERIMENT 7.—*Example of apparent immunity conferred by inoculation with virus from two monkeys which were paralyzed with virus and culture from a paralyzed rabbit.* Monkey 14, *M. rhesus*, 2.1 kg.

Previous inoculation, September 11.—Etherized. One and five-tenths c.c. of a Berkefeld filtrate of fresh emulsion of brain of Monkey 19 (see below) injected into frontal lobe.

September 18: Right arm used rather awkwardly. No other symptoms.

September 20: Well; no weakness of right arm detected. Etherized. One c.c. of emulsion of glycerinated brain and cord of Monkeys 10 and 12 injected into frontal lobe. (Monkey 10 received an intracerebral injection of an emulsion of brain of Rabbit 1017; Monkey 12¹ was twice injected intravenously with a pure culture of streptococci grown from the brain of Rabbit 1017. This was the third of a series of rabbits in which a strain of streptococcus recovered from a human poliomyelitis brain caused flaccid paralysis. Both monkeys came down with flaccid paralysis, and microscopic sections showed marked cord lesions, without, however, the perivascular infiltration which is considered typical of experimental poliomyelitis in monkeys.)

November 3: Had remained well. Etherized. One c.c. of Virus 751⁵ injected into left frontal lobe.

November 17: No symptoms.

December 15: Had remained well.

EXPERIMENT 8.—*Example of apparent immunity conferred by intracerebral injection of a culture of streptococci isolated from a human cord.*—Monkey 19, *M. rhesus*, 2.8 kg.

Previous inoculation, September 16.—Etherized. One and five-tenths c.c. of suspension of Culture 707.2 injected into frontal lobe. (This strain came from a single colony of pleomorphic streptococci 2 cm. from the top of a four-day ascites-dextrose agar shake culture of an emulsion of fresh human poliomyelitis spinal cord. This colony was subcultured in tubes and bottles of ascites fluid plus sterile rabbit kidney, and ascites broth plus sterile kidney. September 16, these subcultures had been growing twenty-three days, and smears showed an extremely pleomorphic organism; lanceolate diplococci, round cocci in short chains, flat-sided meningococcus-like diplococci, and very small globoid chains. Chains could be found in which each of these types were present. On aerobic blood agar plate these cultures grew pure as fine dry green-producing colonies.)

September 17: Sick since injection; quiet, would not eat. No muscular weakness.

September 18: Better; began to eat. Arms and legs strong, reflexes normal.

October 2: Had remained well.

November 2: Had remained well. Blood removed from saphenous vein.

November 3: Etherized. One c.c. of Virus 751⁵ injected into left frontal lobe.

December 15: Daily observations had shown no abnormality.

COMMENT

Three unused and five used monkeys were injected with a monkey virus. The test virus had been carried through monkeys to a stage of virulence at which it should, according to the experience of investigators, cause experimental poliomyelitis in all nonimmune monkeys injected. The two control monkeys became severely paralyzed and were killed. The third (Monkey 37) also became a good control, as the experiment proved that the animal from which 70 per cent. of the serum was obtained (Monkey 21) was not an immune monkey.

Monkeys 21 and 24, which came down with typical poliomyelitis symptoms and recovered, are of considerable interest in that they show that inoculation with cultures or filtrate of virus from nonpoliomyelitis sources, as determined by pathologic findings, does not confer immunity to a virulent virus.

There remain the three monkeys which showed no symptoms following the test injection and were normal forty-five days after. The question whether or not these animals showed any symptoms of infection after their previous inoculation is difficult to determine. Monkey 14 had a definitely clumsy right arm for about twenty-four hours at a period seven days after his first injection; but no weakness could be made out. His awkwardness rapidly disappeared, and he showed none of the usual symptoms of irritability and tremor. No symptoms were observed in the other two monkeys.

The important point of the experiment is that two of the three monkeys which were not affected by the test virus had previously been injected with material obtained from cultures of human poliomyelitis nervous tissue. Monkey 14 received filtrate and emulsion of brain and cord of monkeys which had been paralyzed with rabbit virus and culture; the successive passages of this strain through three rabbits in the form of large lanceolate diplococci grown aerobically would seem to exclude any possibility that the small anaerobic organism described by Flexner and Noguchi could have been carried over. Similarly, the culture used in Monkey 19 came from a single colony near the top of an agar shake culture. Flexner and Noguchi² state that they have never obtained from poliomyelitic material in solid medium an initial growth of the small organism, aside from contaminations.

We wish to record these observations as suggestive of the importance of immunologic studies with the pleomorphic streptococcus which has been isolated from the central nervous system in cases of human and experimental poliomyelitis.

END-RESULTS OF THE TREATMENT OF TUBERCULOSIS OF THE SPINE, HIP, KNEE AND ANKLE JOINTS

FROM THE RECORDS OF THE NEW YORK ORTHOPEDIC
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During the past twenty years treatment of joint tuberculosis at the New York Orthopedic Dispensary and Hospital has been for the most part conservative, the main object being to procure as near as possible immobilization of the diseased joints.

Weight bearing has been considered advantageous when it did not interfere with fixation, as in the knee and ankle joints, but of considerable disadvantage when it did interfere with fixation, as in the hip and spine.

Ankle joint disease has been treated by fixation with a stiff ankle brace having a molded foot piece which fits inside the shoe, plaster having been used as temporary dressing only. The use of crutches has been necessary at times when the disease has been too acute to permit of weight-bearing.

In the treatment of knee joint disease a stiff leg support has been used; this is fastened to the shoe and extends to the groin, with a leather backing extending from the thigh band to the calf band, thus forming a trough in which the leg is firmly held by a muslin bandage, extending from the middle of the calf to the top of the brace. The bandage is changed daily, thus assuring constant fixation, and ready accessibility to inspection by the surgeon. The only exception to this

2. Flexner, S., and Noguchi, H.: Experiments on the Cultivation of the Micro-Organism Causing Epidemic Poliomyelitis, *Jour. Exper. Med.*, 1913, 18, 463.

* Read before the Section on Orthopedic Surgery at the Sixty-Seventh Annual Session of the American Medical Association, Detroit, June, 1916.

1. Rosenow, E. C.; Towne, E. B., and Wheeler, G. W.: The Etiology of Epidemic Poliomyelitis, Preliminary Note, *THE JOURNAL A. M. A.*, Oct. 21, 1916, p. 1202.