The larger apparently broken-up Negri bodies (Fig. 1, *e-j*) could not be found except in cases in which the possibility of having a piece of the original brain material in the smear could not be ruled out.

Of course in each brain mass "pleomorphic chromatoid granules" arose, but so did they in the controls, and no difference could be determined between them except that they were somewhat fewer in the controls.

Noguchi says that in culture mediums similar to that employed for the cultivation of the spirochetes of relapsing fever (are we to infer from this that it was the method he found best for these spirochetes, or one of the others, or all?) "very minute granular and somewhat coarser pleomorphic chromatoid bodies arise which on subsequent transplantation reappear in the new cultures through many generations."

Here is nothing definitely new. From Pasteur down, nearly all investigators on this subject have stated at one

In regard to the specific virulence of his "cultures" Noguchi says, "By inoculating cultures containing the granular, pleomorphic or nucleated bodies, rabies has been produced in dogs, rabbits and guinea-pigs."

Here again the culture generation is not stated. Furthermore, as nothing is said about the amount of material transferred, or about the number of days before the transfer is made or about control dilutions in testing virulence, the question may be raised as to whether the positive results asserted were not due to dilution of the original material rather than to continued growth and division of a specific organism. It is hoped that later reports, by making clear these details, will help decide this question.

A CLINICAL REPORT OF SEVEN CASES OF HYDROPHOBIA

TOGETHER WITH A CASE CLINICALLY SIMILAR, WITH
RECOVERY FOLLOWING THE INJECTION

OF QUININ *

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The following seven cases of hydrophobia (Cases 1-7) are reported because of the persistent assertions of so many misinformed persons that no such disease exists, and because of the strenuous opposition which these make against any plans looking toward the elimination of the dog nuisance. Unfortunately, this opposition has the support of a few members of the medical profession and of several widely circulated newspapers. The efforts of the Health Department of St. Louis to lessen the danger of rabies by the capture of stray dogs and the temporary muzzling of owned dogs have been greatly hindered by the editorial opposition of two of the local papers. It is hoped that the brief clinical review of the seven deaths here recorded may in a measure add strength to the documentary and experimental evidence of the existence of hydrophobia, and give pause to those opponents who desire light.

I have also added to these cases the record of a patient (Case 8) whose clinical symptoms were strikingly similar to the others, and whose recovery followed the intravenous injections of quinin and urea hydrochlorid. Although in the latter case biologic proof of the existence of rabies is wanting, I am disposed to regard the diagnosis of hydrophobia as correct and attribute recovery to the drug employed.

REPORT OF SEVEN FATAL CASES

CASE 1.—W. U., aged 12, was bitten, May 18, 1911, by a rabid dog. The injury consisted of two deep punctured wounds on the forehead, one of these just over the supra-orbital notch, 1 cm. long. The wounds were cauterized within an hour with a stick of silver nitrate. Antirabic treatment (Pasteur) was begun on the following day and continued for fifteen days.

On June 18, the twelfth day after the last injection, the twenty-eighth day following the injury, the boy was nauseated and vomited several times. The following day he attended school but felt ill all day and complained of a severe headache. In the evening his physician was called and found him very restless and in great mental distress. He slept but little that night and symptoms steadily increased. Forty-eight hours after the onset he was unable to remain in bed. He ran excitedly around the house, screaming, moaning, groaning and beating his hands against the wall and furniture.

Short periods of comparative quiet alternated with others of pronounced manic restlessness. The saliva flowed freely,

* From the Municipal Laboratory of Pathology and Bacteriology, St. Louis.

Fig. 2.—From dog "street-virus" brain; *a, b, c* and *f*, types of Negri bodies seen at death of dog; *d, e, g* and *h*, apparent multiplication and segmentation of the bodies after three days at 24 C.

time or another that minute and coarse granular pleomorphic bodies are the cause of rabies, and any observer may see granular bodies answering to Noguchi's description, arising in uninoculated tissue mediums after the tissue has undergone a certain amount of degenerative change.

Noguchi continues: "On four different occasions I observed in the cultures from "passage" and "fixed" virus nucleated round or oval bodies surrounded with membranes totally different from the minute granular bodies, although arising in the cultures in which the latter occurred."

Is it certain that these bodies are not merely segmented bodies which are carried over from the original material? We cannot be sure, since no mention is made of culture generations in Noguchi's article, except in the description of the illustration, in which the only note is that two of the observations were made on "a culture (second and fourth generations, five days old)."

was tenacious and ropy, and smeared over his lips and chin. In the periods of relaxation he talked rationally and spoke of his approaching death.

On the third day his restlessness was uninterrupted, convulsions were frequent, he developed delusions and was mildly delirious until his strength gradually failed and he died seventy-two hours after the onset.

Though intensely thirsty, the patient was seized with spasmodic contracture of the pharynx at every effort to swallow. He suggested and tried various devices to drink. He would, for example, close his eyes to avoid the sight of the glass, or he would try to bring it to his mouth suddenly before a spasm would come on. But before he could complete the motion his arm would tremble violently and then stiffen, his pharyngeal muscles contract and his whole body would be held in a rigid spasmodic seizure.

During the twenty-four hours preceding his death he was given six hypodermic injections of morphin sulphate, $\frac{1}{4}$ grain each, and 80 grains of chloral hydrate by rectum. The only effect of those was to lessen the severity of the convulsive seizures, which came more and more frequently.

No Negri bodies were found in the brain, but rabbits were inoculated with the medulla and all of these died within three weeks. Negri bodies were abundant in all of these.

CASE 2.—On Aug. 3, 1911, G. B., a well-nourished, well-developed Irishman, aged 51 years, walked into the laboratory, having been sent to me by his physician who had not intimated to him the nature of his trouble. On being questioned, the patient said that for two nights he had not slept, that he was nervous and worried, that he had a severe pain radiating down his left arm, and that for the past twenty-four hours he had some peculiar trouble in his throat whenever he tried to swallow. I asked him the cause of a small and insignificant scar on his little finger and he replied that some time during the latter part of April he was bitten by a stray bulldog that had attacked his cat. In driving the dog away it had bitten him on the finger. The wound was not cauterized. On further questioning he admitted a strong aversion to water, even to the thought of drinking it. He was quite convinced, however, that there was no relation between the insignificant dog bite and his present "nervousness."

The symptom of hydrophobia was acutely developed in this case. The suggestion of a bath on admission caused him to tremble from terror and fear. Some hours later the question of a physician, "Have you passed any water to-day?" was sufficient to start a general convulsion. In spite of this and the patient's clear mental grasp, he did not once associate his condition with the dog bite, nor did he recognize his disease as hydrophobia.

On admission to the City Hospital he rapidly became more restless and hypersensitive to noise, light and drafts of air. Convulsive movements became pronounced, notwithstanding repeated injections of morphin ($5\frac{1}{2}$ grains in twenty-four hours) and enemata of chloral hydrate. Twenty-four hours after admission he was seized with a prolonged and general convulsion, after which he rapidly weakened, followed by diaphragmatic paralysis and death August 4, thirty-four hours after admission, and eighty hours after the onset.

A necropsy was held, but the only gross pathologic lesion found was a congestion of the meninges. No Negri bodies were found in the brain, but two rabbits were inoculated with an emulsion of the medulla. These died within three weeks of dumb rabies, and in the brains of both Negri bodies were numerous.

CASE 3.—Feb. 14, 1912, I was invited to be present at a coroner's necropsy on a woman who had died in convulsions. A physician, who had been called in a few hours before death, had pronounced the case one of hydrophobia. The following history was obtained.

A. W., a middle-aged woman, was bitten, Dec. 25, 1911, by a stray dog which her little daughter had found on the street and had brought into the house. After biting the woman, her husband and her daughter the dog was put out of the house and disappeared. The wound was not cauterized.

Five days before death the woman developed a marked pain and itching on her right leg. At the same time she

became very excitable, extremely restless and could neither sleep nor remain quiet. A physician who saw her at that time reported that he regarded it as a case of hysteria and prescribed a mild sedative and a local treatment for the itching of the leg. He did not suspect hydrophobia. Her condition grew worse, she became delirious, fought, screamed and was restrained with great difficulty. Another physician was called and found that she could not swallow. Her death occurred a few hours later.

At the necropsy both legs were excoriated and covered with deep scratches. There was a small scar over the left ankle, with a pronounced cicatricial induration. The meninges were congested, otherwise there were no gross pathologic changes. Rabbits injected with an emulsion of the brain developed paralysis and died three weeks later. Their brains contained many Negri bodies.

CASE 4.—H. M., a white man, aged 18, was admitted to the City Hospital, May 22, 1912, with the following history:

April 20, while urinating behind a large signboard, he was bitten on the glans penis by a stray dog. The wound was not cauterized. He at once began reading about the symptoms of hydrophobia, and when a week previous to his admission he began to be restless and nervous and to talk about having hydrophobia his family attributed his condition to worry and fear, and he was given bromids by the family physician. When he attempted to urinate he would have a seminal emission.

Immediately after his admission he was examined by two very competent neurologists. He was rational, but at frequent intervals there were convulsive movements, during which he would throw himself about the bed, seize his throat with both hands and complain that he could not breathe. After such attack he would expectorate large amounts of saliva. These seizures came on every two or three minutes, and a diagnosis of hysteria or pseudohydrophobia was made. He was given $\frac{1}{4}$ grain morphin sulphate and placed in a quiet, dark room. Four hours later he had a severe convulsion and died suddenly.

At the necropsy the only pathologic condition found was a greatly congested left lung, with large petechiae over the pleural surface. The brain was moderately congested. There was an old healed scar 3 mm. long on the glans penis. No Negri bodies could be found in smears of the cortex, the cornu ammonis or the cerebellum, and none could later be demonstrated in sections. Three rabbits were inoculated subdurally with the brain, and all developed paralysis during the third week. In all the rabbits Negri bodies were abundant in smears of the cornu ammonis.

CASE 5.—June 14, 1913, H. C. H., a man, aged 80, walked into the laboratory and stated that he had come to have an examination made to determine whether or not he was developing hydrophobia. He said that three weeks before he had been bitten on the right wrist by a stray dog. The wound was slight—a single tooth-wound—healed promptly without cauterization and he had given the incident no further thought.

June 11 he did not feel so well as usual and there was or seemed to be a peculiar odor about water which made drinking very difficult. This dislike for water soon extended to milk, beer and all liquids, and later to solid food. He slept but little the night of the 11th and 12th and not at all on the night of the 13th. Partly because of his extreme thirst and partly from something which he could not explain, he became very nervous and irritable. "Choking-spells" developed on the 13th, especially when he lay down, so that he could rest only when sitting in a chair.

As he talked of his condition, his voice and manner indicated a slight excitement. When he lay down on the examining-table he had a spasmodic contraction of the throat muscles that momentarily suffocated him. The pulse was normal, of good quality and there was no apparent fever.

A glass of water placed before the patient produced a most striking excitement. He could look at it from a distance calmly, but could not, try as he might, bring himself to approach nearer. When, unexpectedly, the water was suddenly placed before him he recoiled in a paroxysm of fear, clutched

his throat, and for a few moments breathed spasmodically and with great difficulty. He tried to drink milk, but, as he seized the glass in his hand, he turned his face away and his arm trembled so violently that the contents were shaken to the floor. He had not the control of his muscles to bring the glass to his mouth.

He was advised to enter the hospital, which he did four hours later. On admission he was found to have a temperature of 103.4 and a pulse of 128. He was very irritable and excited and restless. Morphine hypodermically and chloral hydrate by rectum quieted him for short periods. Respiration was difficult at times. He died twelve hours after admission.

At the necropsy no gross lesions were found. There was a moderate congestion of the meninges. Negri bodies were numerous in the cornu ammonis, and two rabbits inoculated with parts of the brain developed paresis during the third week. In the brains of these rabbits Negri bodies were also found in numbers.

CASE 6.—E. A., a white girl aged 13, was bitten, May 20, 1913, by a neighbor's dog which became so irritable and dangerous that on the following day it was shot by a policeman. Neither the owner nor any one else thought the dog had rabies and no report was made to the laboratory. The injury consisted of one punctured wound on the instep of the right foot, the dog's tooth passing through a shoe and stocking. The wound was not cauterized, healed readily, and no further thought was given to the accident.

July 4, forty-five days after the bite, she attended a picnic but came home in the afternoon complaining of a headache and a pain in her throat on swallowing. She was assured by her family physician that there was no connection between this and the bite. She could not sleep that night and on the following day developed a marked fear of water, was very restless and irritable, and was brought to the hospital twenty-four hours after the onset. She was then extremely restless and nervous, with marked hyperesthesia. She could not swallow. Morphine and chloral were administered. Six hours after admission she was seized with general convulsions and died from exhaustion one hour later.

The necropsy showed no gross changes other than congestion of the meninges. Four rabbits were inoculated with the brain. One developed paresis in the hind quarters on the eighteenth day, another became similarly paralyzed on the thirty-fifth day and died on the forty-first. No Negri bodies were found in the patient's brain. In the second, third and fourth rabbits Negri bodies were numerous and relatively large.

CASE 7.—L. S. P., a farmer aged 52, was attacked by his own dog, July 1, 1913, thrown to the ground, and badly bitten on the hand and wrist. The hand was severely mangled and there were punctured wounds on the wrist. The wounds were dressed with an antiseptic, but not cauterized. Five days later, July 6, antirabic treatment was begun, the examination of the dog's head having revealed the presence of Negri bodies.

July 21, twenty days after the injury and fifteen days after the first injection, the patient's hand and arm became very painful. The pain, which was so severe that he could not sleep, continued for forty-eight hours, and on the 23d extended over his shoulder, back and arms. On the 24th he was very nervous, restless and suffering intensely. On the 25th he had difficulty in swallowing, and he was mildly delirious at times. Paralysis had developed in the arm, and he was extremely hypersensitive to touch. He talked constantly and was extremely restless, though no convulsions were noted. He was from the first given large doses of morphine hypodermically.

On the 27th he became more quiet, paralysis and exhaustion grew more pronounced and he died six days after the onset of the first symptoms. No post-mortem was made.

Of these seven cases, necropsies were held in six. Prolonged and careful search of the brain in Cases 1, 2, 3, 4 and 6 failed to reveal a single Negri body, though many smears and sections were made of the cortex, basal ganglia, cornu ammonis, medulla oblongata and cerebellum. In Case 5 Negri bodies were large and abundant.

Brain substance from each case was injected into two or more rabbits and all of these without exception developed a paralysis typical of the disease and died. In the brain of every animal Negri bodies were abundant and easily recognized. The shortest period of incubation in the rabbits was twelve days, the longest thirty-five days.

REPORT OF CASE TREATED WITH QUININ

CASE 8.—*History.*—C. B., a white man, aged 73, an itinerant umbrella mender, walked into the laboratory Aug. 29, 1913, and asked for advice about an old dog-bite which had given him a great deal of pain during the past four or five days. He said that five or six weeks before he had been bitten on the right leg by a dog, but, as his occupation made him a frequent object of attacks by dogs, and as he had had "several hundred" during his lifetime, he gave no special attention to this one. The wound healed promptly without medical attention and he had entirely forgotten the incident.

Four or five days before he had felt a tingling and prickling in the right thigh. Then the scar became more and more painful, and the burning and shooting pains were so great that he had not been able to sleep for two nights. He had eaten nothing for two days, and had not been able to swallow without becoming choked. A glass of water was handed to him, but only after a great effort could he swallow one small sip. An intense and suffocating pharyngeal contraction occurred at subsequent attempts.

He was visibly nervous and anxious, and though no mention was made either by him or by me that his symptoms were in any manner connected with the bite, he later confessed that he was so sure he had hydrophobia that he had not dared ask the question lest I should confirm his suspicions.

He was urged to enter the City Hospital at once for treatment, but refused to do this until he could go back to his home. Four hours later he returned, having meanwhile drunk in saloons as much straight whisky as he could force down his throat. The fact that most of these "bracers" never got farther than his mouth, but were immediately expelled, was to my mind valuable proof of the genuineness of his difficulty in swallowing. On admission to the hospital he was somewhat exhilarated by an acute alcoholism, but the difficulty in swallowing had increased perceptibly.

The physical examination revealed several red and painful scars on the outer surface of the left thigh. The cicatricial thickening and induration around these scars was pronounced and somewhat in excess of that usually observed in ordinary wounds of equal severity. Otherwise, the examination disclosed no physical abnormality. Temperature, 99.2 F., pulse 102, respiration 24. Reflexes normal.

These symptoms warranted, in our opinion, a diagnosis of hydrophobia, and in consultation with Dr. Ralph Kinsella, resident physician of the City Hospital, it was agreed that he should be given injections of quinin as suggested by Moon.¹ Quinin and urea hydrochlorid was chosen because of its solubility.

Treatment and Result.—At 5 p. m., August 29, 15 grains of quinin and urea hydrochlorid, dissolved in 3 c.c. of salt solution, were administered intravenously. This dose was repeated at 7 p. m., 9 p. m., 11:30 p. m., and on the next day at 9:45 a. m. and 11:30 p. m., making a total of 90 grains within twenty hours. Following the second injection at 7 p. m. the patient said all pain in the thigh and over the area of the bite had disappeared. At 7:30, August 29, he drank without difficulty 6 ounces of milk and an equal amount at 11:30 p. m. At 7 a. m., August 30, he drank 6 ounces of milk, 6 ounces of coffee, and ate two crackers and a slice of bread.

He had, however, spent a very restless night, and on account of a fine tremor and a nervousness which suggested delirium tremens, he was given at 9:30 a. m. 4 drams of paraldehyde, and an equal amount at 1:30 p. m. He slept at intervals throughout the day and the following night. He had no return of the pains or the difficulty in swallowing and was discharged September 2, four days after his admission.

1. Moon: The Effect of Quinin on Rabbits in Dogs, Jour. Infect. Dis., 1913, xiii, 165.

Nine hours after the fourth injection of quinin and urea, a spinal puncture was made and 25 c.c. of clear cerebrospinal fluid were withdrawn; 0.5 c.c. was injected subdurally into two rabbits and one guinea-pig and 1 c.c. was injected into the region of the cervical plexus of three guinea-pigs. After thirty-five days none of these animals has shown any symptoms of rabies.

CONCLUSION

This experiment, and the fact that the patient recovered, creates a question as to the correctness of the diagnosis, which, as has been seen, rests solely on the clinical history. The failure of the inoculated animals to develop rabies is in no sense proof that the disease was not rabies. Marie records that Lesieur and Wissokowitch have inoculated animals with the spinal fluid obtained from six cases of hydrophobia with negative results. Cell-free spinal fluid is rarely infectious in rabies.

The fact that the patient had been bitten many times before by dogs and had come to regard these as incidents to his trade, that he had not considered the last one of sufficient importance to seek medical attention, and that it had altogether escaped his attention until the pain began, is an important factor in excluding hysterical fear of the disease.

The general appearance of the patient, the onset with pain localized in the region of the bite, followed by restlessness, a profound anxiety, insomnia and finally his utter inability to swallow water and his dread of attempting it, seem sufficient to warrant the diagnosis of hydrophobia.

If it was a case of this disease, did quinin cure? Although only further use can determine the value of this drug in hydrophobia, the experiments of Moon, though few, seem to support this conclusion.

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HOLDING FRACTURES WITH ABSORBABLE MATERIAL—IVORY PLATES AND SCREWS

A NEW METHOD *

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Since 1908, while working in the research laboratories of the University of Pennsylvania, at the problem of lengthening shortened bones of the leg, I have been trying to devise some method of holding fractures by inserting into the fractured bone some retention apparatus which would not act as a foreign body, and which would be absorbable by the surrounding structures, eliminating the necessity of subsequent removal, which is so often necessary when steel is used. In our experiments¹ we found that ivory was very acceptable to human bones, did not cause softening of the surrounding bone, was gradually absorbed and did not become loose, since the bone grows in as the ivory is absorbed. The ivory also has the property of being strong enough to stand any strain the muscles attached to the broken fragments may put on it.² It was a simple matter, therefore, to devise ivory screws of proper size to hold the oblique fractures,

but screws alone could not be used in holding transverse fractures. It was necessary to devise some other method for holding these.

Let us first take up the action of the tissues on ivory, then the method of holding oblique fractures, and last the method here reported for the first time of plating transverse fractures with ivory. In our experiments, it was found that ivory, being an animal matter and capable of absorbing some moisture, could be inserted into the bone with very little force, and after remaining for twenty-four hours it absorbed enough

moisture to make a plate or screw which, when first inserted, was only moderately close to the surrounding bone, fit into the place made for it so tightly that it could not be moved without a great deal of force. This led us to believe that this advantage alone would be enough to warrant trying it in place of steel plates, since steel plates and screws when in close contact

with bone cause softening of the bone immediately in contact with the steel, and eventually loosen up, causing irritation of the surrounding structures and allowing angulation of the bone at the seat of fracture, if the muscles tend to a displacement. Ivory does not offer this advantage alone. When in close contact with living healthy bone, ivory is gradually absorbed (Fig. 1). The process of absorption is somewhat of a mystery at present, since we were unable to find osteoclasts except in a few places. The fact remains, however, that plates in the human bone were greatly eroded in six weeks (Fig. 2), and the screws removed from a dog's tibia showed great erosion in three to four weeks, with absolutely no loosening of the hold of the ivory on the bone or vice versa.

The method of applying the screws is as follows: In an oblique fracture the fragments are pulled down into place and clamped with a Lohman clamp. A hole is then drilled through the two fragments, the diameter of this hole being the diameter of the screw to be used, taken at the base of the thread (Fig. 3 D). A tap (Fig. 3 C), such as mechanics use for cutting a thread on the inside of a nut, is then put through this hole and threads cut on

Fig. 2.—Ivory plate and pegs removed from patient after six weeks. Fracture became infected on account of necrosis of skin from trauma although three weeks elapsed between date of injury and first operation. Note erosion of pegs and plate at each end. The ivory stimulates new bone formation when inserted in medullary cavity. Note large amount of erosion at ends which were farthest from fracture. Plate was in close contact with bone and still holding fragments firmly when removed.

Fig. 3. — A, Ivory screw with removable brass head; B, carving chisel used for loosening fragments. Thin blade, double bevel, makes it much easier to handle than ordinary bone chisel; C, tap used for cutting threads on inside of hole in bone; D, V-point drill cuts through bone and ivory much faster than other types.

* Because of lack of space, this article is abbreviated in THE JOURNAL. The complete article appears in the Transactions of the Section and in the author's reprints. A copy of the latter will be sent by the author on receipt of a stamped addressed envelope.

* Read in the Section on Orthopedic Surgery of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

1. Lengthening Shortened Bones of the Legs by Operation, Univ. Penn. Med. Bull., May, 1908.

2. Lengthening Shortened Bones of the Leg by Operation, Surg., Gynec. and Obst., July, 1913.