

BRIEF COMMUNICATIONS AND CASE REPORTS

HYPERTENSION EXPERIMENTALLY PRODUCED BY CONSTRICTING THE ARTERY OF A SINGLE TRANSPLANTED KIDNEY*

ADDITIONAL OBSERVATIONS

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IN A recent paper¹ dealing with the experimental production of hypertension, a series of experiments on dogs were reported which demonstrated that a transient elevation of blood pressure was produced by constricting the artery of a single transplanted kidney. Three of the eight dogs subjected to this experiment were alive when the preliminary report was published. The observations on these three dogs, continued for six additional months, show that in each a permanent hypertension developed.

SA-37-73 Transplantation, nephrectomy, hypertension

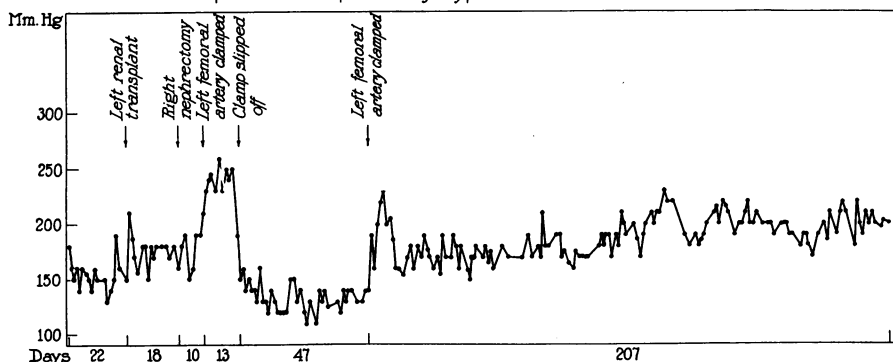


CHART 1.—*Experiment V* (Dog SA-37-73): Constriction of femoral artery; rise in blood pressure from 140 to 240 Mm. Hg.; blood pressure maintained at 240 Mm. Hg. for eight days, then sudden fall to 130 Mm. Hg. Roentgenologic examination showed that the clamp had slipped off the artery. Further constriction of the femoral artery; rise in blood pressure from 130 to 230 Mm. Hg.; return to 160 Mm. Hg. The blood pressure remained between 160 and 190 Mm. Hg. for a period of two months and then slowly began to rise to a level of nearly 200 Mm. Hg. which has been maintained for over four months. The animal is living and well, ten months after the transplantation of the kidney.

Method.—By means of a Van Leersum carotid loop, daily observations of the blood pressure were made for one month or more to determine the average normal level for each dog. The left kidney was then transplanted to the groin by the following technic: The femoral artery and vein were dissected free in the groin; the peritoneal cavity was entered through an in-

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cision extending from Poupart's ligament to the costal margin. Through this wound the kidney was freed and its vessels divided. By sufficient mobilization of the ureter the kidney could be brought down and fixed in the groin without tension. Its blood supply was reestablished as quickly as possible by an end-to-end anastomosis of the renal and femoral vessels. The abdominal wound was closed over the transplanted kidney. Following this pro-

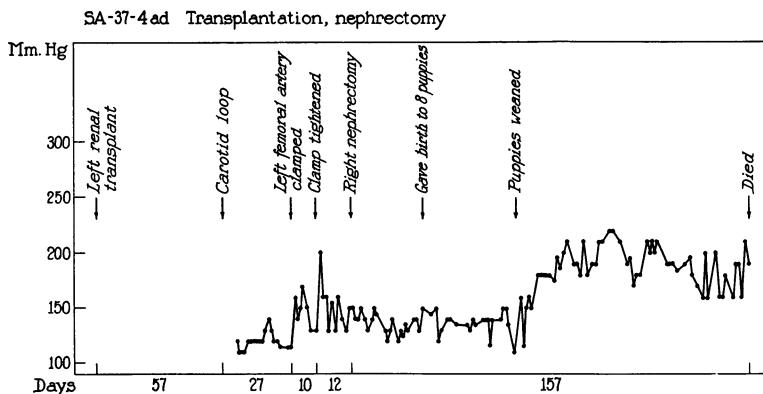


CHART 2.—*Experiment VI* (Dog SA-37-4ad): Constriction of femoral artery; rise in blood pressure from 120 to 170 Mm. Hg.; return of blood pressure to 130 Mm. Hg. Further constriction of femoral artery; rise in blood pressure from 130 to 200 Mm. Hg.; return to 130 Mm. Hg.; right nephrectomy. Animal gave birth to eight puppies. Blood pressure remained between 130 and 150 Mm. Hg. until puppies were weaned when it began steadily to rise, reaching a level of 190 to 210 Mm. Hg. which was maintained for a period of almost four months. Animal then became uremic and died during a convulsion. Autopsy revealed gross infarction of the kidney secondary to erosion of the vessel by the silver clip.

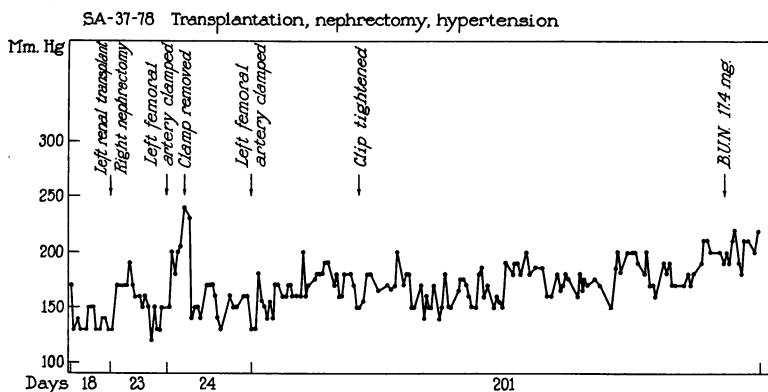


CHART 3.—*Experiment VIII* (Dog SA-37-78): Constriction of the femoral artery; rise in blood pressure from 130 to 260 Mm. Hg.; symptoms of acute intoxication necessitated the removal of the clamp; complete recovery. Further constriction of the femoral artery; rise in blood pressure from 140 to 180 Mm. Hg.; return to 150 Mm. Hg.; then a gradual rise in blood pressure to a level between 170 and 200 Mm. Hg. which is maintained. Animal living and well nine and one-half months after transplantation of the kidney.

cedure the blood pressure was recorded daily for approximately three weeks to determine the effect of the operation upon the level of blood pressure. The second kidney then was removed and blood pressures recorded for ten more days. At the expiration of this period the artery of the transplanted kidney was constricted by means of a Goldblatt clamp or other method.

Brief protocols and corresponding charts are submitted for the three dogs

which survived the experiment. A composite chart has been introduced to show the highest and lowest pressures observed in the three dogs during the various stages of the experiments.

Summary.—It will be seen from the protocols and composite chart that the hypertension produced in these dogs by constricting the artery of a single transplanted kidney appeared at first to be transient. Within two months after the application of the clamp, however, the blood pressure rose to a definitely hypertensive level and remained there as long as the observations were continued.

No.	Normal	After transpl.	1 st constriction	2 nd constriction	Later well maintained level
⑤	140	140	140 → 240* → 130	130 → 230 → 160	→ 200
6		120	120 → 170 → 130	130 → 200 → 130	→ 210 [†]
8	130	130	130 → 260 ⁺ → 140	140 → 180 → 150	→ 200

• Clamp slipped + Clamp removed

CHART 4.—Composite representation of blood pressure changes produced in the preceding three experiments.

DISCUSSION.—The experiments upon the transplanted kidney were undertaken in the hope of establishing the rôle played by the renal nerves in the development and maintenance of hypertension in experimental animals. Our observations seem to indicate that they play no important part in the initiation or maintenance of this type of hypertension. The question may be raised as to whether the nerves might have regenerated following transplantation. It is difficult to believe that complete regeneration could take place during the period of observation. The fall in blood pressure following the immediate rise after constriction of the artery of the transplanted kidney still awaits explanation.

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THE USE OF SULFANILAMIDE IN THE TREATMENT OF BRAIN ABSCESS

REPORT OF TWO CASES

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RECENT clinical and experimental reports of the efficacy of sulfanilamide in the treatment of pneumococcic and streptococcic infections led us to use

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this drug in two cases of brain abscess. Because active surgical therapy was instituted at the same time, the effects of the drug were somewhat difficult to evaluate, but the initial condition of each patient was so poor and the results of treatment so satisfactory, that the experience seemed to warrant reporting.

Case 1.—F. H., white, male, age 14. Hospital No. 8472. Admitted March 3, 1937. Discharged April 2, 1937.

History.—The patient had suffered occasional attacks of left otitis media for eight years, but had been symptom free for two years, when his present illness began, February 16, 1937, with an earache. The drum was opened promptly, a small amount of pus evacuated, and all symptoms and signs referable to the ear disappeared very rapidly. Four days later, however, fronto-occipital headaches appeared and became progressively worse. The patient became drowsy and irritable, complained of photophobia, and, after about ten days, grew stuporous. It was observed that he was somewhat awkward in using his hands—particularly the left.

On admission to the Homestead Hospital, his temperature was 100° F. (by rectum), pulse 150, respirations 14. The temperature became normal after a few hours, but the pulse remained rapid and the respirations occasionally dropped to ten and eight per minute. Lumbar puncture showed an increased cerebrospinal fluid pressure, 50 cells (largely polymorphonuclear) per cmm., and no organisms. At this time, two weeks after the otitis media, the patient was referred to us by Dr. L. P. Losa and Dr. W. E. Brown, of Homestead, Pa.

Examination.—Neurologic examination showed the following: (1) The patient was semistuporous and slept when not disturbed, but could be aroused by painful stimuli to a state in which he would obey simple commands and answer simple questions with monosyllables. He was quite irritable and preferred being left alone. (2) The right pupil was larger than the left, but both reacted normally. Both eyes tended to turn to the right, and the patient could not carry out conjugate movement to the left past the fixation point, although other extra-ocular movements were normal. The optic disks were not raised, although the retinal veins were congested. (4) The tendon reflexes in the legs were hyperactive, and a bilateral sustained ankle clonus, Oppenheim, and Babinski reflexes were present. (5) Finger to nose test on the left was performed very awkwardly. (6) The left suboccipital region was tender to percussion and firm pressure. (7) On extreme flexion of the neck, some stiffness was noted, but Kernig and Brudzinski reflexes were not present.

Operation.—First Stage: March 2, 1937. It was decided to confirm the diagnosis of left cerebellar abscess by ventricular estimation, and at the same time temporarily reduce the very high intracranial pressure. This procedure disclosed symmetrically dilated lateral ventricles, apparently placing the lesion in the posterior cranial fossa. Accordingly, through a vertical incision, the bone over the left cerebellar hemisphere was exposed, and an opening 4 cm. in diameter made. A canula introduced into the cerebellum met slight resistance at a depth of 4 cm. The dura was opened widely, the wound was lightly packed and closed loosely.

The patient improved slightly for about 24 hours, and was transferred to the Western Pennsylvania Hospital. About 36 hours after the first operation, however, he became completely unconscious and developed such marked signs of medullary compression in spite of repeated ventricular tap, that drainage of the abscess seemed imperative.

Operation.—Second Stage: March 3, 1937. The patient's wound was reopened, the edges of the exposed cerebellar cortex were sealed to the arachnoid with the electric coagulation and an effort was made to remove the small cortical fungus which had developed and a core of brain tissue down to the abscess wall. Because of the depth of the lesion and the limited size of the opening in the bone, it was not possible to expose

the capsule. Accordingly, a small tube was introduced into the abscess. It was possible to aspirate 20 cc. of pus with a syringe and about an equal amount escaped spontaneously. The wound was closed loosely with silkworm gut, and the tube sutured to the skin edge.

Sulfanilamide Therapy.—The patient was given a subcutaneous injection of 5 cc. of prontosil within an hour after the operation, a dose which was repeated in 12 hours and again in 36 hours. On the day following operation, prontosil, grains ten every six hours, was begun by mouth and continued for five days. During this time, examination of the ventricular and spinal fluid disclosed the presence of the drug in a concentration only slightly less than that in the blood.¹ Because the patient began to experience nausea and vomiting, the dosage was reduced to grains five every six hours for two days, when the medication was discontinued.

Antipneumococcus Therapy.—Culture of the pus removed from the abscess showed a pure growth of Type V pneumococcus* (Table I). Accordingly, antipneumococcus serum of this type (Lederle) was given intravenously in dosages of 20,000 units every 12 hours, until a total of 220,000 units had been administered.

TABLE I

RESULTS OF SERIAL SMEARS AND CULTURES FROM ABSCESS IN CASE I

Date	Smear	Culture
3-3-37	Abscess drained	
3-3-37	Diplococci	Pneumococci Type V (pure culture)
3-5-37	Diplococci	Pneumococci Type V (pure culture)
3-8-37	Staphylococci	Staphylococcus albus pure culture. No pneumococci present
3-11-37	Staphylococcus predominating. Pneumococcus present	Staphylococcus and pneumococcus
3-13-37	Few organisms present. Staphylococcus and pneumococcus. More phagocytosis	
3-18-37	Negative	Hemolytic <i>Staphylococcus albus</i> . No pneumococcus present
3-20-37	Negative	
3-23-37	Numerous Staphylococci	Partially hemolytic <i>Staphylococcus albus</i>
3-29-37	Negative	All cultures negative
3-29-37	Drainage tube removed	

Course.—Five days after the drainage of the abscess, Staphylococci were found in the smear from the discharge. Accordingly, the tube was irrigated daily with Dakin's solution. The tube in the abscess was gradually shortened beginning on the third post-operative day. When the discharge ceased, and culture from the depths of the tube was negative, on the twenty-sixth day, the remaining two inches of tubing were removed. The wound in the superficial tissues healed rapidly within the next few days.

From a clinical standpoint, the patient improved slowly at first. He remained very somnolent for four days, although he could be aroused promptly by mild stimuli. The nystagmus, the dysnergia on the left, and the pyramidal tract signs on the right remained constant, although the conjugate eye movements to the left did begin to return somewhat. Eleven days after operation, the patient's general condition was much improved, he was out of bed daily, his cerebellar signs were beginning to lessen, and his

* We are indebted to Dr. Philip Hadley and his staff in the Department of Bacteriology of the Western Pennsylvania Hospital for the very numerous and extremely helpful bacteriologic studies in both of the cases reported.

headaches had disappeared. In another week still further gains were made, and at the time of his discharge, one month after operation, only very slight awkwardness of the left extremities was present.

Follow-Up.—Examination three months postoperative disclosed no evidence of intracranial pathology. The patient was symptom-free with two exceptions: (1) His parents reported occasional periods of irritability and sulkiness; (2) the boy had observed that if he extended his head far backward, he became dizzy. He had noticed no impairment of coordination and could run, play golf, and ride a bicycle.

SUMMARY.—Left otitis media followed in five days by headaches, awkwardness of left hand, stupor. Left cerebellar abscess drained two weeks after initial ear infection. Sulfanilamide begun immediately. Twenty-six days later drainage ceased, and tube was removed. Follow-up examination three months later showed no evidence of cerebellar pathology.

Case 2.—J. G., white, female, age 10. Hospital No. 9312. Admitted March 30, 1937. Discharged June 4, 1937.

History.—After suffering with a draining left ear for several months, the patient began to complain of headache. Within three days it was observed by the family that she tended to keep her head and eyes turned to the right. Two days later, she became stuporous and was referred to us by Dr. Roger E. Phillips of Philipsburg, Pa.

Examination.—On admission, the child appeared extremely ill. She was deeply unconscious, quite dehydrated, had a temperature of 105° F. by rectum, pulse 144. There was a purulent discharge from the left ear. The head and eyes were fixed to the right. The neck was stiff, and Kernig's sign was very definite on both sides. The left pupil was smaller than the right. No papilledema was present. The patellar reflexes were hyperactive, and ankle clonus and Babinski reflexes were present bilaterally. Lumbar puncture showed a pressure of 10 Mm. of mercury (in the horizontal position), the fluid containing 300 white cells per cmm., but showing no organisms.

It was felt that the patient had a left cerebellar abscess, and that both because a generalized meningitis seemed imminent and because of the high intracranial pressure (presumably the spinal pressure was low because of a posterior fossa cerebrospinal fluid block), drainage of the abscess should be carried out without delay. She was given 500 cc. of a 20 per cent sucrose in physiologic saline intravenously, prontosil 5 cc. hypodermically, and prontosil grains ten by rectum, preoperatively.

Operation.—As a preliminary diagnostic measure, both lateral ventricles were tapped and found to be enlarged. The left cerebellar hemisphere was then exposed through a bone opening 4 cm. in diameter and a similar opening in the dura mater. In spite of the previous drainage of 20 cc. of cerebrospinal fluid from the ventricular system, there was a marked increase in pressure in the posterior cranial fossa. Gentle palpation with a brain canula revealed a sense of resistance 3 cm. beneath the surface. An attempt was made to expose the abscess, using the Bovie loop to remove the overlying cerebellar tissue, but as in the previous case, the small size of the bone opening rendered this impossible. It was then thought that the lesion might be allowed to herniate toward the decompression for 24 hours or more. At this point, however, the child became slightly restless, and cyanotic, her respirations slowed markedly, and the veins of the cerebellum in the operative field became very congested. As it seemed probable that serious medullary damage might occur very soon unless the pressure in the posterior cranial fossa were reduced, the margins of the dural opening were coagulated, and a small drainage tube was introduced into the abscess. Between 20 and 30 cc. of very foul smelling pus escaped at once under considerable pressure. The tube was sutured to the side of the skin opening and the wound loosely closed over a small amount of gauze packing. The signs of medullary embarrassment disappeared promptly after the drainage of the abscess.

Sulfanilamide Therapy.—The early smears of the pus disclosed a considerable variety of organisms, but on culture it was apparent that the predominating one was of the

Friedländer group. Since the meager data in the literature concerning the effect of sulfanilamide upon the Friedländer bacillus were at least partly favorable, and since Streptococci were present in the pus as well, the drug was continued for 35 days, grains ten being given twice daily for two weeks and then grains five twice daily for the next three weeks.

Course.—The drainage tube was shortened slowly, beginning on the ninth post-operative day, the rate of withdrawal being governed by the amount of discharge, the bacteriologic studies (Table II), and the clinical condition of the patient. On the twelfth postoperative day, cerebrospinal fluid began to drain from the wound around the drainage tube. This continued for 48 hours before the ventricular and spinal drainages, which were instituted immediately, resulted in a sealing-off of the leak. Several examinations of the cerebrospinal fluid at this time showed a normal cell count and no growth on culture. The tube was removed entirely 24 days after operation, and the wound then healed rapidly.

TABLE II

RESULT OF SERIAL SMEARS AND CULTURES FROM ABSCESS IN CASE 2

Date	Smear	Culture
3-31-37.....	Abscess drained. Streptococci, Staphylococci, fusiform bacilli	Gram-negative bacillus of Friedländer group
4-2-37.....	As before	As before
4-5-37.....	Few Streptococci. Friedländer type predominating	Friedländer type only
4-11-37.....	As before	Friedländer type with few Streptococci
4-12-37.....	Gram-positive diplococci (mostly phagocytosed). Number about the same	Friedländer type only
4-16-37.....	Gram-positive diplococci (mostly phagocytosed). Number less than on previous examination	Friedländer type only
4-19-37.....	Gram-positive diplococci (phagocytosed in large numbers). Few gram-negative bacilli	Friedländer type only
4-21-37.....	Very few gram-positive diplococci	Negative after 48 hrs.
4-23-37.....	Drainage tube removed	

For 24 hours the patient remained semi-stuporous, though she could be aroused. She slowly reached a normal level of consciousness during the next six days. The conjugate eye movements returned to normal within the first ten days after operation. The left-sided dysnergia, which was quite marked at this time, began to lessen slowly, and by the time the drainage from the abscess had ceased, was almost entirely absent. For some weeks the patient displayed a peculiar, shy, sullen mental attitude which seemed in part attributable to her intracranial pathology.

Cultures from the left ear showed an organism of the Friedländer type, and otoscopic examination disclosed several polypi in the external canal and a large perforation of the drum. On roentgenologic examination, the left mastoid showed no air-containing cells and a small area of decreased density suggesting some bone destruction. May 30, one week after the healing of the cerebellar abscess, a partial radical mastoidectomy on the left was performed by Dr. L. L. Darsie. Culture from the mastoid again showed the Friedländer organisms. The patient's convalescence was uneventful, and the drainage from the ear subsided steadily during the next few weeks. At the time of her discharge from the hospital, June 4, 1937, the mastoid and cerebellar wounds were well healed,

there was only a small amount of exudate from the left ear, and neurologic examination was entirely negative.

Follow-Up.—One month after discharge the patient was symptom free and showed no evidence of intracranial pathology on neurologic examination.

SUMMARY.—Chronic left otitis media for three or four months, followed by progressive headaches and stupor within one week. Drainage tube inserted into left cerebellar abscess. Sulfanilamide begun before operation and continued for five weeks. Recovery from abscess with removal of tube 25 days after operation. Mastoidectomy one month after admission. Symptom-free one month after discharge.

COMMENT.—From the neurologic standpoint, these two cases of left cerebellar abscess had several interesting features in common. Both patients showed a conjugate deviation of the eyes to the side opposite the lesion, and an inability to carry out conjugate movement to the left. It seemed probable that this symptom was the result of pressure from the lesion upon the superior colliculi, since it disappeared in each instance following drainage of the abscess. Such a finding, however, is certainly not a common result of cerebellar disease, and its occurrence in two successive cases seems worthy of remark. We were impressed, too, by the mild but definite mental symptoms, consisting principally of negativism and irritability, displayed at times during their convalescence, by these patients. Such changes have been observed, of course, in cases of cerebral abscess and of cerebellar tumor, so that their occurrence following cerebellar abscess is not surprising. The complete recovery of coordination within two months following extensive cerebellar damage was also most striking.

The surgical problem was primarily that of preventing death from medullary compression and, at the same time, avoiding a generalized meningitis as the result of premature drainage of an early abscess with very little capsule formation. In each instance, despite repeated withdrawal of ventricular fluid and a certain amount of decompression directly over the lesion, the development of dangerously high pressure in the posterior cranial fossa forced the insertion of a drain within ten days of the onset of intracranial symptoms.

The fact that under these conditions meningitis did not develop seemed to be partly attributable to the sulfanilamide, although there is little evidence in the literature to substantiate this action of the drug. In Case 1, the Type V pneumococcus was the predominant organism. While the effects of sulfanilamide upon other pneumococcal infections seem definitely established,^{2, 3, 4} there have been no reports concerning pneumococcal brain abscess, and only two rather inconclusive references to pneumococcal meningitis.^{2, 3} It is true that antipneumococcal serum was used in Case 1, but in previous similar cases these sera have not proven effective.

In Case 2, meningitis seemed an almost certain complication. The high cell count in the cerebrospinal fluid before operation suggested an impending meningeal involvement, the drainage was carried out in one stage with little chance for protective adhesion formation, and beginning on the twelfth post-

operative day cerebrospinal fluid drained freely from the wound for 48 hours. Again the sulfanilamide may have aided in preventing spread of the infection—although little is known about the effect of the drug upon the Friedländer bacillus. Thus, Levaditi and Vaisman⁷ obtained no protection with prontosil (insoluble) in mice infected with this organism. Buttle, *et al.*⁸ demonstrated a limited degree of curative action with sulfanilamide in mice infected with the Friedländer bacillus. Bürgers⁹ was unable to demonstrate such action with prontosil (soluble) in similarly infected mice.

Finally, the rapid subsidence of the middle ear infection while the brain abscess was progressing in Case 1, and the healing of the cerebellar abscess, in spite of the persistent mastoid and middle ear infection, in Case 2, indicated that in these patients at least, the two lesions had no constant direct connection capable of transmitting the infection, and that the elimination of the source of infection is not always a prerequisite to the successful treatment of an intracranial abscess.

SUMMARY

(1) Two cases of cerebellar abscess successfully treated by continuous drainage and the use of sulfanilamide are reported.

(2) The rapidity and completeness of the patients' recovery, despite their extremely critical preoperative condition, and the early stage at which drainage was of necessity carried out, suggest that the sulfanilamide played an important part in the therapy used, and warrant its further trial in this field.

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SPONTANEOUS RUPTURE OF THE UTERUS
DUE TO HYDATIDIFORM MOLE

REPORT OF A CASE COMPLICATED BY CLOSTRIDIUM WELCHII SEPSIS

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IN A review of the reported cases of spontaneous uterine rupture associated with destructive hydatidiform mole, one is impressed not only by the infrequency of the condition but also by the attendant high mortality. It has long been recognized that an apparently benign mole may occasionally assume a malignant invasive propensity. After eroding the endometrium this type will further involve the myometrium and finally perforate the peritoneal investment of the uterine body.

The dissecting or penetrating mole, *mola hydatidosa destruens*, represents a pathologic alteration of the ovum which has intrigued clinicians and pathologists for many years. It is rather generally agreed that serious uterine damage such as perforation resulting from hydatid moles which are not distinctly neoplastic is extremely rare. The occurrence of a case complicated by a *C. welchii* sepsis was considered unusual enough to warrant reviewing the subject and reporting a personal experience.

Classification.—Ewing⁸ groups the entity of hydatid mole under the heading of *choriomata* and then postulates three histologic variations:

- (1) Chorio-adenoma destruens—the invasive type of growth which is also known as *mola hydatidosa destruens*.
- (2) Highly malignant metastasizing chorio-epithelioma.
- (3) Syncytioma.

Inasmuch as our case is of the first, nonmalignant variety, we shall confine our discussion to that group alone.

Grossly, the contents of the uterus vary with many circumstances. When the mole remains in situ, it presents the usual bulky tumor adherent over the implantation site and altered by hemorrhage and suppuration. Hemorrhage, infection and the site of implantation will govern this appearance.

The microscopic appearance is quite specific and in the invasive type the villous structure is less marked and the islands or clusters of Langhans' cells are more numerous. The Langhans' cells in this instance are found in irregular masses instead of being confined to a layer or single row while the syncytial cells are increased in size and number (Figs. 1 and 2).

Among the earlier reported cases which were uncomplicated and which recovered following supracervical hysterectomy is that of Waldo,²² in 1910. In his description the hemorrhage was stated to have been controlled by a fringe of omentum, and the mole was regarded as a benign growth.

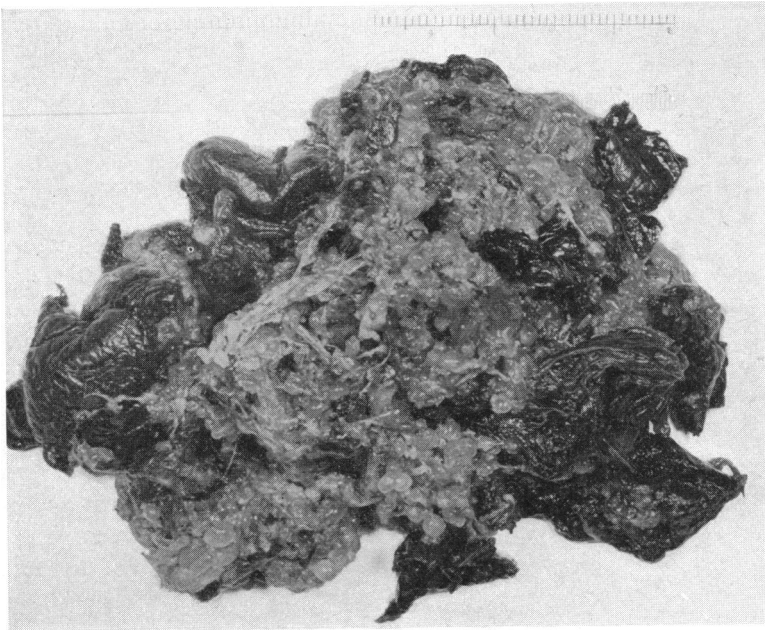


FIG. 1.—Pathologic specimen No. 3416—Extruded Hydatid Mole: Gross examination of the extruded specimen shows it to consist of many masses of thin-walled cysts 2 by 8 Mm. These cysts contain a clear seromucinous material and are arranged in clusters resembling bunches of grapes. A few blood clots are present in addition to the grape-like masses of cystic material. In its retracted form, the entire mass measures approximately 18 by 18 by 18 cm.

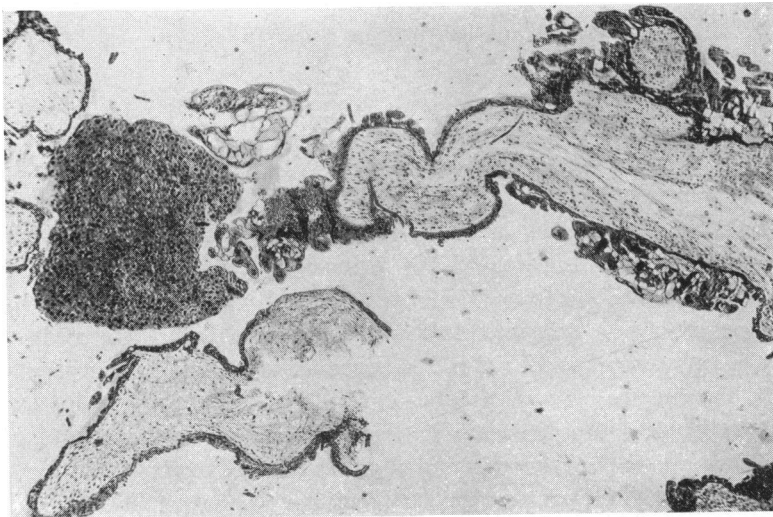


FIG. 2.—Pathologic specimen No. 3416: Photomicrograph of a section of the hydatid mole showing many large chorionic villi. These are composed of an edematous stroma and a hypertrophied Langhans' layer. The layer of syncytial cells is also hypertrophied. The stroma is very edematous and is infiltrated with a few lymphocytes and polymorphonuclear leukocytes. The Langhans' layer in some areas is composed of several islands of heaped-up cells.

Krellenstein,¹⁴ in 1924, reported a case of spontaneous uterine rupture due to hydatid mole, with recovery following supracervical hysterectomy. At the same time he reviewed four other cases: Those of Seitz, in 1904, which resulted fatally; Lord's case, reported in 1868, which also died; and that of Harkness who reported a case, in 1921, that recovered following a hysterectomy, and reviews Waldo's case, of 1910, which also recovered.

Mazet,¹⁶ in 1926, reported a successful result following a hysterectomy, and Johansson,¹² in 1929, details an unsuccessful result with death following operation. Both of these authors stress the difficulty of the preoperative differential diagnosis of perforated uterus due to a hydatid mole from that of ruptured ectopic pregnancy. It is also interesting to note that in the cases of Mazet and Johansson, both patients were multiparae and under 25 years of age. Bland,² in 1927, reported a case of perforation of the uterine wall which resulted fatally.

McClure,¹⁸ in 1935, reported a case of spontaneous uterine rupture by hydatidiform mole and emphasizes the rare occurrence of the condition. In his review of the literature he was only able to find seven cases which had been previously reported. The case cited occurred in a patient age 24, who was admitted in shock with the preoperative diagnosis of ruptured ectopic pregnancy. At operation a perforation was found in the left side of the uterus along the course of the uterine artery, and a few vesicles from the hydatid mole were in the process of being extruded into the pelvis through the rent in the wall of the uterus. Panhysterectomy plus a transfusion resulted in complete recovery. The perforation in the thinned-out uterine wall was sufficiently large to admit the index finger. In his case the cervical os was tightly closed—a fact which would rule out criminal abortion. In his report he remarks about the markedly cystic condition of both ovaries and discusses the frequency of occurrence of this finding in association with the condition of hydatid mole. In two of McClure's cases, which were subjected to celiotomy, marked cystic ovarian changes were noted.

There is no agreement among observers as to the incidence or frequency of this finding. McCallum¹⁷ believes it occurs in a high percentage of cases and Munro and Kerr¹⁹ state that while it is a common finding it is by no means an invariable one. In the appended case report the ovaries presented no cystic changes.

The exact relationship between hydatid mole and the occurrence of lutein cysts in the ovary has not as yet been definitely established but there seems to be some reason to believe that the excess production of hormone by the hyperplastic trophoblastic elements stimulates the development of lutein cysts. Experimental injection of placental suspensions produces marked lutein changes in the ovaries of rabbits. Zondek suggests that lutein cysts are produced by the action of the excessive amounts of gonadotropic hormone on the ovary. These facts would account for the disappearance of the cysts, which sometimes follows successful removal of the mole.¹¹

Brews³ report, in 1935, on the subject of hydatid mole, was based on

72 cases of this condition and is of particular interest to us chiefly because of Blaikley's¹ discussion of the paper, as he reports an instance of hydatidiform mole, without perforation, but which also had an acute *C. welchii* infection with recovery.

Case Report.—B. B., female, age 51, Italian, was admitted to the Surgical Service, Gouverneur Hospital, January 26, 1937, with the complaint of cramp-like abdominal pain associated with nausea and vomiting for the preceding week, which was not related to the ingestion of food but occurred regularly morning and evening.

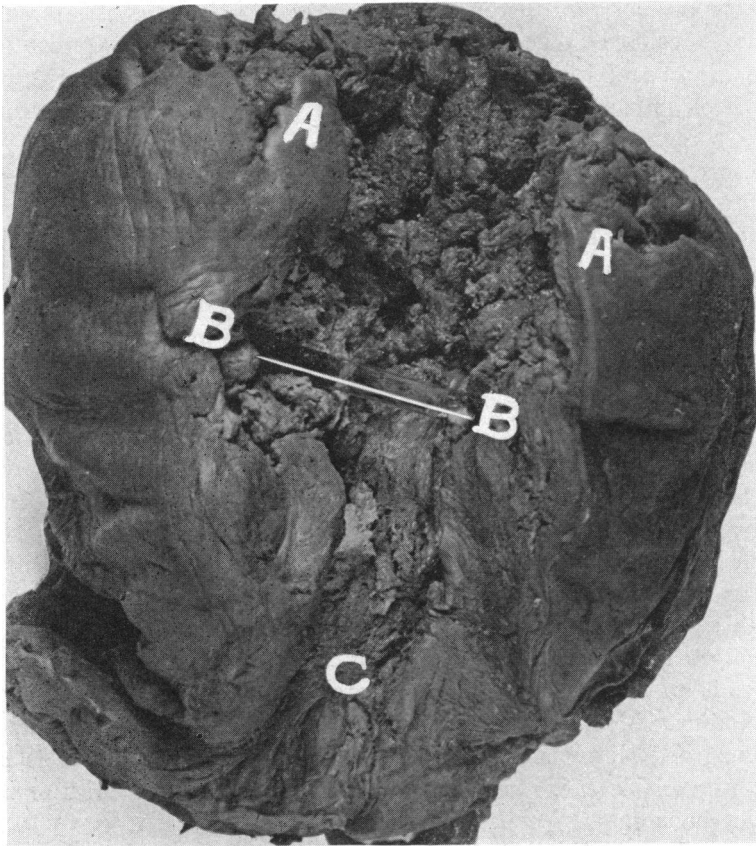
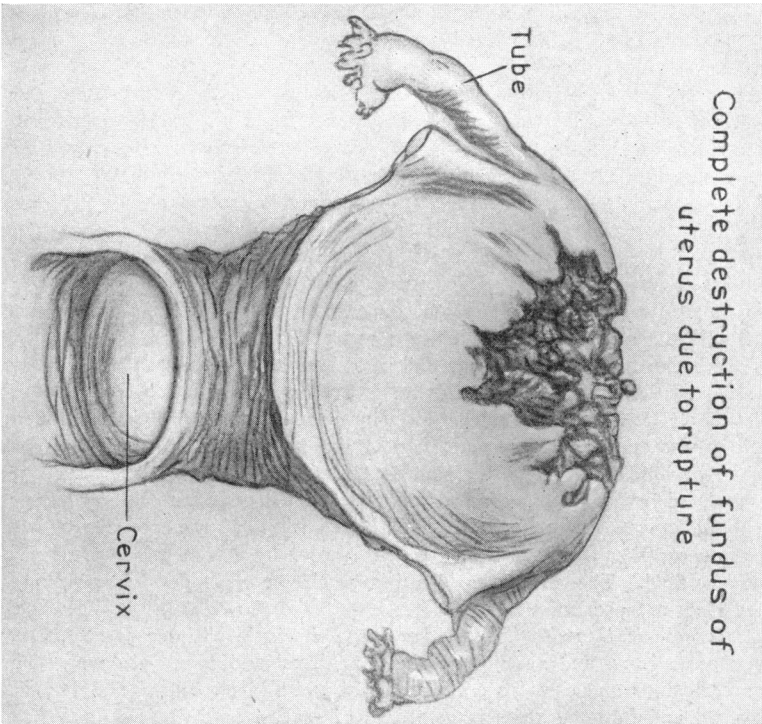


FIG. 3.—Autopsy specimen No. 113: Photograph of the uterus removed at post-mortem which has been opened longitudinally to demonstrate the erosion of the fundus of the organ by the destructive hydatidiform mole. Uterus was found to measure 15 cm. from the internal os to the fundus. The perforated area indicated by the points AA' measures roughly 6 by 8 cm. and indicates how complete was the destruction of the fundus uteri. The wall of the uterus is greatly thinned as one approaches the fundus uteri. The midportion of the organ is held apart at points BB' by a rule. The cervix is indicated by the point C.

She had had irregular periods of amenorrhea for the past four years. Three days prior to admission she passed a large blood clot per vaginam and bled moderately for the next two days. This episode occurred after a two month period of amenorrhea.

Her past history was irrelevant. Marital history revealed her to have been Para. VII, Grav. V, the last pregnancy having occurred eight years ago (1929).



Complete destruction of fundus of uterus due to rupture

Fig. 4.—A drawing demonstrating the appearance of the uterus as seen at postmortem examination before opening the organ (Fig. 3). The fringe of omentum surrounding the fundus uteri has been removed and the area is shown as it appeared following the perforation due to the destructive hydatidiform mole. The ruptured area measures approximately 6 by 8 cm.

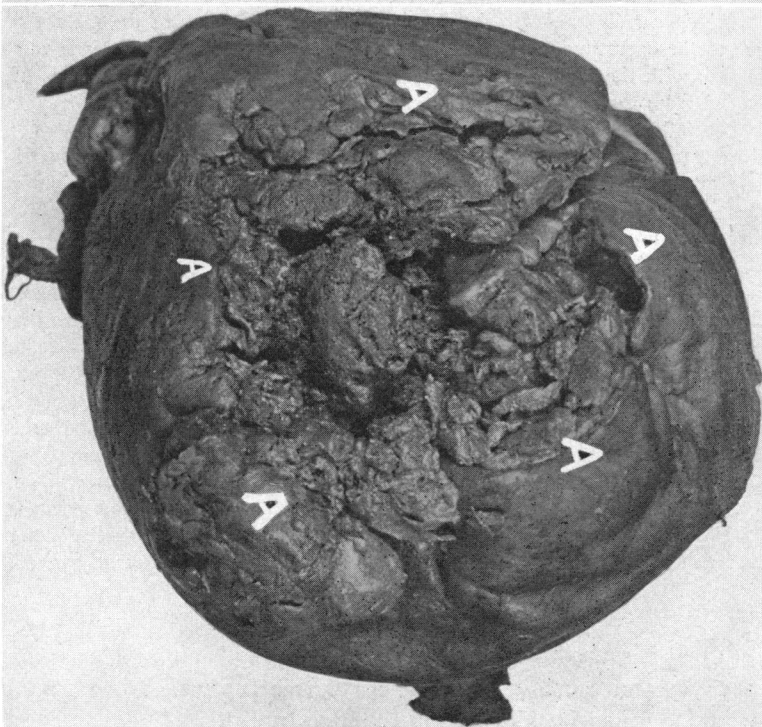


Fig. 5.—Photograph of the ruptured uterus from its superior aspect. This view is taken looking from the fundus towards the internal os and again illustrates the entire destruction of the major portion of the fundus uteri. The points marked AAAAAA indicate the outline of the perforated area.

Physical Examination disclosed a well nourished, white female who appeared acutely ill and complained of abdominal pain. Bimanual pelvic examination revealed an old lacerated, patulous cervix which would admit one finger. There was a large abdominal mass occupying the central portion of the abdomen which extended one finger's breadth above the umbilicus. It appeared to be the uterus, which was freely movable and very tender. No additional masses were palpable in the fornices. There was also present a cyst of the right Bartholin gland about the size of a large lemon.

Diagnosis on Admission.—Fibromyomata with degeneration.

Laboratory Data.—Temperature, 99° F.; pulse, 100; blood pressure, 132/84, blood chem., N.P.N. 24; sugar 95; Wassermann, negative; uranalysis, negative, except for one plus albumin. Aschheim-Zondek test, positive.

On the day following admission, January 27, 1937, the patient's temperature rose to 102.2° F., the pulse remaining between 110 and 120; blood pressure, 90/52. The next day she began to bleed per vagina and passed several small blood clots.

Shortly thereafter a large, flabby mass was extruded from the cervix which resembled a large cluster of grapes. The bleeding became quite profuse and for that reason pituitrin was administered to arrest the uterine hemorrhage. In addition the patient was given morphine and treated for shock. General condition at this time was fair. The diagnosis of hydatidiform mole was obvious from gross examination of the specimen.

Pathologic Examination.—No. 3416. Gross: "Shows the specimen to consist of many masses containing many small thin-walled cysts 2 by 8 Mm. which contain a clear seromucinous fluid. The mass resembles a large cluster of grapes. In addition, a few large blood clots are present" (Fig. 1).

Microscopic Examination.—"Many large chorionic villi are present, composed of an edematous stroma and an hypertrophic Langhans' and syncytial layer. The stroma is very edematous and contains a few red and white blood cells. The Langhans' layer is thickened and in some areas is composed of several layers" (Fig. 2).

Subsequent Course.—On the day following the extrusion of the mole, the patient was taken to the operating room and examined under anesthesia. The uterus was still greatly enlarged, with the fundus at the level of the umbilicus. Two small pieces of tissue were removed from the cervical canal but no curettage was performed.

The following morning, January 30, 1937, her temperature was 103° F.; pulse, 120; and her general condition reported as poor. At this time a beginning jaundice was noted. Blood pressure, 90/56; icteric index, 21; white blood cells, 20,000; polymorphonuclears, 90 per cent. She was given three transfusions of 350 cc. each and in spite of these supportive measures the patient expired on the sixth day after admission to the hospital.

Repeated blood cultures were reported as negative.

Autopsy.—A postmortem examination was performed and the entire fundus of the uterus was found to have been the site of a necrotic process and to have been eroded by the destructive hydatidiform mole. The protocol states: "The uterus is found to be soft, large, friable and boggy. The omentum is found to be adherent to the uterine fundus. From the internal os to the fundus measures 15 cm. From cornu to cornu, the viscus measures 10 cm. The fundus, for an area 6 by 8 cm., is necrotic, hemorrhagic and diffusely ruptured (Figs. 3, 4 and 5). A fibrinopurulent peritonitis is also present.

Microscopic Examination of sections of the liver show formation of gas bubbles in the parenchyma of the organ (Section No. 113) and colonies of gram-negative *C. welchii*.

Pathologic Diagnosis.—(1) Perforation of uterus due to destructive hydatidiform mole; (2) *C. welchii* sepsis; (3) acute generalized fibrinopurulent peritonitis.

SUMMARY

(1) It is exceedingly rare that an apparently benign mole assumes invasive propensity and causes a spontaneous uterine rupture; up to 1935 only seven cases were found by McClure in the literature.

(2) In those cases which were operated upon and recovered, the preoperative diagnosis was almost always confounded with ectopic pregnancy.

(3) There is no agreement among observers as to the frequency of cystic ovarian changes associated with the condition of hydatidiform mole. In the case herewith reported, the ovaries were entirely normal.

(4) In our case, the entire fundus of the uterus was destroyed by the massive rupture due to the invasion of hydatidiform mole.

(5) One other case of hydatidiform mole associated with *C. welchii* sepsis is reported in the literature, with recovery. In that instance, however, there was no complicating uterine rupture.

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THE CAUSE OF THE PUTRID ODOR OF PERFORATED
APPENDICITIS WITH PERITONITIS

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THIS paper is presented to correct a prevalent but erroneous impression that *B. coli* is responsible for the putrid odor of the pus in perforated appendicitis. The numerous references to "*B. coli* odor" that can be found in the literature and the uniform impression among the staff members, both senior and resident, of this clinic that *B. coli* causes this characteristic odor, lead us to assume that this belief is generally held. We have been unable to trace the origin of this idea.

During the past two years the pus obtained at operation in 100 cases of acute perforated appendicitis with abscess formation or peritonitis has been cultured both aerobically and anaerobically at this clinic. The results of this bacteriologic study are to be found in the ANNALS OF SURGERY, 107, 517-528, April, 1938. In working with the bacteria isolated from these cases, the uniform fetid odor of anaerobic cultures, and likewise the consistent absence of this odor in the aerobic cultures, was noticed. This observation led to our investigation of the rôle played by *B. coli* in the production of the "*B. coli* odor" in instances of perforated appendicitis.

It was elected to use sterile human pus as a culture medium in this experiment in an effort to approach as closely as possible the conditions found *in vivo*. We have been uniformly unsuccessful in attempting to produce peritonitis in rabbits with pure cultures of *B. coli*. This pus was obtained from two different sources: (1) A tuberculous pleural empyema; and (2) a pyarthrosis of a shoulder joint.

Twelve tubes each containing 8 cc. of tuberculous empyema pus were inoculated in the following manner: (1) Four tubes were used as controls, two being incubated aerobically and two anaerobically.

(2) Four tubes were inoculated with *B. coli*, three of which were incubated aerobically and one anaerobically.

(3) Four tubes were inoculated with anaerobic *Streptococcus putrificus* and anaerobic *B. melanogenicum*,¹ all of which were cultivated under anaerobic conditions. These two organisms were chosen from the numerous types of anaerobic bacteria composing the bacterial flora of appendicitis peritonitis because of their greater prevalence. The former was present in our series in 66 per cent of the cases, and the latter in 93 per cent. In addition, these two organisms were usually found growing in symbiosis and were extremely difficult to separate. All 12 tubes were incubated for four days at 37° C., and then examined for growth of organisms and production of odor. The control tubes were all negative for growth of organisms and production of odor. All tubes which had been inoculated with *B. coli* showed good growth of this bacteria but gave no evidence of a putrid odor. On the other hand,

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in all the tubes of the third group a heavy growth of the anaerobic bacteria had occurred, and these tubes gave off the marked, penetrating, putrid odor characteristic of the pus in cases of perforated appendicitis. This experiment was repeated, using the sterile pus obtained from the case of pyarthrosis, and the same results were obtained.

From the above experiments it is evident that the *B. coli* is in no way responsible for the production of the putrid, so-called "*B. coli* odor."

Further proof is to be had in the fact that the typical "*B. coli* odor" was found in 12 cases of appendicitis peritonitis from which *B. coli* was not isolated.

It has been impossible for us to produce a fatal peritonitis in guinea pigs or rabbits with intraperitoneal injections of the *B. coli*. The peritoneal fluid of these animals three and five days after injection of the *B. coli* has no putrid odor. Inoculation of mixed peritonitis cultures without *B. coli* produces a fatal peritonitis in rabbits, the exudate having the characteristic putrid odor.

We are unable to explain the origin and prevalence of this erroneous conception of the ability of the colin bacillus to produce putrid products during their growth in pus. The ability of anaerobes to produce foul odors, however, is recognized especially among German authors. Fraenkel² has stated that the putrid odor of pus in any given lesion bespeaks the anaerobic nature of its infecting agent. This has also been our experience.

Heyde³ (1911) published a careful study of the anaerobic flora of appendicitis, concluding that *B. coli* played a subordinate etiologic rôle. He did not believe this Bacterium had the ability to form putrid products within the animal body. This opinion has apparently been generally overlooked or disregarded.

Brütt⁴ (1923) found the anaerobic Streptococcus in 45 cases out of a total of 107, emphasized the putrid nature of the pus produced by the anaerobic Streptococcus, and made the observation that the odorless seropurulent pus was probably due to *B. coli* alone. Based upon his personal experience, the ability of *B. coli* alone to produce pus having the characteristic foul odor so frequently encountered in appendicitis was doubtful. He believed that this fetid odor was the result of infection by the colon Bacillus in association with the anaerobic Streptococcus.

In addition to the more frequently encountered anaerobic *Streptococcus putrificus* and the *B. melanogenicum*, other anaerobic organisms capable of producing putrid odors during their growth were recovered by us from the pus of appendicitis peritonitis. These organisms included members of the Clostridium group, the *Streptobacterium fetidus*, and other forms of gram-positive and gram-negative unidentified Bacilli.

CONCLUSIONS

(1) *B. coli* are not responsible for the putrid odor present in cases of perforated appendicitis peritonitis, generally designated as "*B. coli* odor."

(2) When inoculated into sterile pus and incubated, *B. coli* exhibits no ability to form putrid products.

(3) The characteristic putrid odor of appendicitis pus is caused by the presence and growth of anaerobic bacteria, chiefly the *B. melanogenicum* and anaerobic Streptococci.

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**A POINT IN THE CLINICAL DIAGNOSIS OF URETERAL
CALCULUS**

A PRELIMINARY REPORT

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SOME years ago the writer made the observation that in certain cases of calculus in the lower third of the ureter, that is, below the brim of the bony pelvis, there was one point in the abdomen where tenderness was more marked than elsewhere. After further observation it was found that this point, whether on the right or on the left side, was located just below the one described by McBurney¹ as being the site of maximum tenderness in acute appendicitis. McBurney described this point in the adult as "one and a half to two inches inside of the . . . anterior superior spinous process of the ilium on a line drawn to the umbilicus." He also stated that it was "not enough to compress with the whole hand the region of the iliac fossa" but that pressure must be made with the finger-tip "to determine that the most sensitive point is a definite one in most cases."

A similar point of maximum tenderness will be described, which may be elicited by employing the same procedure. It can be found with great accuracy by first locating McBurney's point. One then moves the finger-tip downward and inward one inch from this point and in a direction at right-angles to the line on which McBurney's point lies (Fig. 1). By pressure with the finger-tip the patient will show evidences of very definite pain, sometimes even with only moderate digital pressure. There is generally no spasm unless deep and vigorous pressure is made. As in McBurney's observation, it is not enough to press with the entire hand over this area, as while there may be more or less tenderness, there may be none at all. In no instance has there been any evidence that hyperesthesia of the skin is a factor. Having located this point, on one side or the other, concentric circles can be drawn around it as shown in the diagram. In a typical and well marked case, finger-tip pressure around the most distant circle may elicit no tenderness; as the finger moves from one circle to the other, toward the center, tenderness becomes more and more marked, until its maximum is found to be at the point indicated.

The phenomenon has now been sought for in 115 cases of proved ureteral calculus. Positive findings were obtained in 47 instances, or 40.8 per cent,

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URETERAL CALCULUS

occurring both on the left and on the right side, and about equally divided between men and women. In probably a majority of these cases the ureter was no more than slightly or moderately dilated, nor was infection present in any great severity in more than a few cases. It has not seemed to make any difference in the findings whether the stones were single or multiple, large or small, or whether they lay just outside of the bladder or just below the bifurcation of the iliac vessels. In a few instances it has been found that after the removal of the stone, either by spontaneous passage or by operation, the tender spot could no longer be demonstrated. McBurney stated that in acute

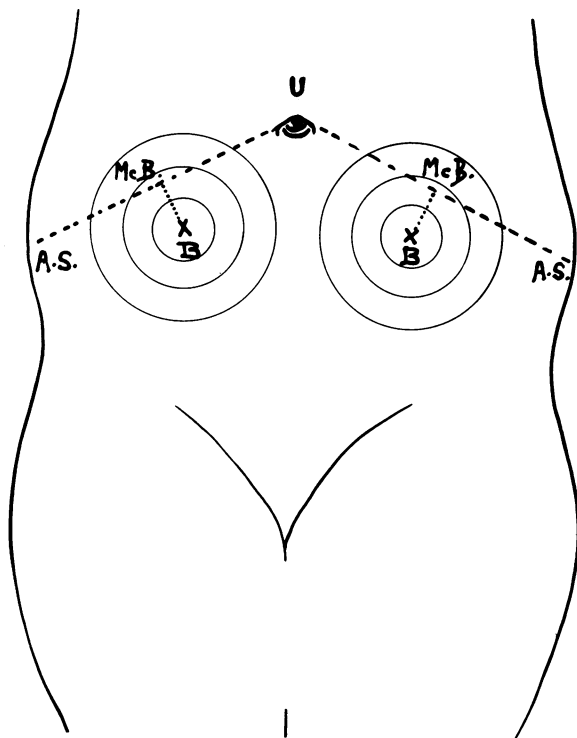


FIG. 1.—Diagram of point of maximum tenderness in stone in lower ureter. U—Umbilicus. A.S.—Ant. Sup. Spine. McB.—McBurney's Point. B—Point of maximum tenderness. This point lies downward and inward one inch below McBurney's point and at right angles to it. It is found in over 40 per cent of cases. Tenderness increases around concentric circles to point B.

appendicitis "from the first hours of the disease even up to the end of several days, this sign may be clearly made out in every case." The writer acknowledges that he has no evidence as to how long this tenderness may persist in the presence of a stone, nor does he claim that it is present in "every case." The observation is described in the belief that it may, in certain cases, help to clear up an obscure diagnosis. It is known that about 4 or 5 per cent of stones in the lower third of the ureter cannot be roentgenographically demonstrated, either because the stone is composed of uric acid, or because it has the same density as the sacrum against which it lies. In these cases the diag-

nosis would doubtless eventually be made by cystoscopic study and perhaps, especially, by the passage of a wax-tipped catheter.

A case related to me personally by Dr. Edward L. Young, Jr., illustrates some of the observations made in this communication. The patient, a male, age 40, without previous urinary or abdominal symptoms, was seized with sudden, severe pain in the right lower quadrant. There were no urinary symptoms, but there was nausea. Temperature, 99.2° F.; white blood count, 23,000. Urine sediment showed an occasional white cell, no reds. Marked tenderness, but no spasm (until deep pressure was made), was found on the right side at the point which has been described. There was no costovertebral tenderness. In the belief that this was a case of acute appendicitis preparations were made for operation. During this time, and on the chance that there might be an ureteral calculus present, cystoscopy was performed. A small stone was seen protruding from the right ureteral orifice. It was removed by rongeur forceps. The pain disappeared almost at once and the tenderness had subsided by the time the patient was returned to his bed. There were no further symptoms.

When it comes to an explanation of this point of tenderness, the writer finds himself somewhat at a loss. Certain observations made on the ureter at various times, while of interest, do not seem to throw much light on the question. Some years ago the writer saw an elderly lady who had had both ureters brought out on her back just below the costovertebral angles. About two inches of normal-looking ureter protruded beyond the skin on either side. The ends of these ureters could be snipped with scissors or crushed with a clamp without causing any sensation to the patient. Nor did she realize it when a crochet needle was inserted into the ureter and moved vigorously up and down in its lumen, producing considerable bleeding by trauma of the hook. When, however, a small clamp was inserted into the ureter and then opened, thereby dilating its lumen, quite severe renal colic was produced, which subsided promptly, however, when the tension was released. From these observations it may be deduced that renal or ureteral colic is produced, not by the roughness of a stone but by the dilatation of the ureter or renal pelvis which it causes.

More recently, and inspired by the work of Dr. Chester M. Jones, I have tried the effect of dilatation of the intact ureter. A Dourmashkin catheter was passed up the ureter, first on one side and then on the other, in three female patients. In two, both ureters were normal, in one there was considerable dilatation on one side but none on the other. The bag surrounding the tip of the catheter was dilated to what appeared to be its maximum extent (using about 2 cc. of 12 per cent sodium iodide solution) when the catheter was in the ureter at 25, 20, 15, 10 and 5 cm. A series of roentgenograms, in one of these patients, showed that the bag was dilated laterally and that it had not been merely elongated in the lumen of the ureter. Two of the women had no pain or tenderness at any time, or in any place, when the bag was dilated. The third patient experienced a little momentary pain in her

normal left ureter when the bag was dilated at about 10 cm., but there was no tenderness. This experiment with the ureter has, therefore, failed so far in producing the pain and tenderness which Jones has been able to elicit by the inflation of a bag at various points in the gastro-intestinal tract.

Aid in the solution of this problem has been sought at autopsy. In two bodies, long, sharp, and rather heavy steel pins were driven through the abdominal wall on either side at the point under discussion, until they were fast in the bone. The abdomen was then opened, care being taken not to dislodge the pins. On exposing the ureters by retroperitoneal dissection, and without disturbing their position, they were found in both instances to lie almost an inch to the medial side of the pins. It would seem, therefore, as if pressure with the finger-tip did not compress either the ureter or the stone lying within it. It undoubtedly does impinge upon both layers of the peritoneum, upon the coils of intestine lying beneath and upon the muscles of the abdominal wall and of the pelvis. That none of these structures is the seat of pain is obvious from the fact that in the absence of stones, and even in the presence of 60 per cent of stones, the phenomenon is not elicited.

The work of various investigators has shown that the ureter is very richly supplied, and in a most intricate manner, by the sympathetic nervous system. Wharton² has shown that the ureter is supplied by nerves from the lowest renal ganglion at the head of the spermatic and ovarian plexuses and from the aortic, hypogastric and pelvic plexuses. Not only this but it is in close contact with "the rich network of fine nerves which course through and directly beneath the peritoneum." Wharton has shown: (1) That these nerves can be divided without interfering with ureteral function; and (2) that clinically, the patient is relieved of the ureteral colic. This is "rather strong evidence," Wharton says, "that at least one of the functions of these nerves is to convey sensations of pain—in other words that they contain afferent or sensory fibres." It is probable that further observations following the same lines as those resulting from the painstaking research by Wharton will throw light on the problem which has been presented.

In the present state of our knowledge this work does not make clear *why* the point of tenderness under discussion is situated *where* it is, or why it is not present in all cases. Neither does it explain why if it is absent at this point which has been described, it is not likely to be present elsewhere. Possibly these variations indicate that the location or arrangement of the ureteral sympathetic nerve supply varies with different individuals, thus accounting for the discrepancies observed.

Further observations, both clinical and experimental, may help to elucidate the question. There is no doubt that any procedure, or observation, which will help toward the solution of a difficult and obscure diagnosis is worth while.

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