tube before the body was raised and it continued to do so as the body was raised as before, ceasing by the time the body was raised to 45 degrees. About 600 c.c. were collected, probable waste 40 c.c. With syringe and catheter nearly 250 c.c. were recovered from the right loin ten minutes after the body had been replaced in its original position.

Experiment 10.—In the abdomen of a male body a small incision was made in the median line just above the umbilicus and with syringe and catheter 500 c.c. of water were introduced into each loin. A loop of small bowel was withdrawn and a catheter fastened into its wall. Air was now pumped into the intestine till the abdomen was moderately distended. An incision 1 inch long was made in the median line above the symphysis and the body slowly raised. Water began to escape from the lower incision before the body had been raised more than 20 degrees and continued to do so till from 60 to 70 degrees was reached. About 500 c.c. were recovered, waste 30 or 40 c.c. About 150 c.c. were recovered from the pelvic cavity with syringe and catheter and less than 10 c.c. recovered from the right loin, none from left.

Experiment 11.—500 c.c. of water were introduced as before and the body turned on its right side, just more than mid-way between pronation and supination. An incision 1 inch long was made just below and internal to the right anterior superior iliac spine. Some water escaped at once. The usual tube was inserted. More water flowed. The body was now slowly raised as before, water continued to flow from the tube until the body was elevated to from 40 to 45 degrees. Barely 735 c.c. were recovered, waste 30 or 40 c.c., and it was impossible to recover any with the syringe.

Experiment 12.—Experiment 11 was repeated, turning the body on the left side. The amount of water recovered from the tube inserted just below and internal to the left anterior superior iliac spine was only slightly more than 500 c.c. and more could not be made to flow out, no matter how high the body was raised. On lessening the distention, about 120 c.c. were recovered from the right loin.

CONCLUSIONS

The experiments showed:

1. The pelvic cavity could not be completely drained of water by raising the supine body even to 90 degrees "bolt upright."
2. The pelvic cavity could be completely emptied of water by turning the horizontally placed body just more than mid-way between pronation and supination.
3. Water found its way from the left loin to exit just below and internal to the right anterior superior iliac spine with body raised to 45 degrees in the right lateral position.
4. With a distended condition of the intestines, although water gravitated less readily, practically the same results were obtained.
5. Although water found its way from the left loin, as above stated, it did not so easily find its way from the right loin to exit just below and internal to the left anterior superior iliac spine; no matter how high the left laterally lying body was raised a quantity remained in the right loin.

I wish to express my thanks to Professor Terry in the Washington University Medical School and to Professors Eycleshymer and Shoemaker in the St. Louis University Medical School for their great kindness and courtesy, and to Dr. H. McClure Young for valuable assistance.

Metropolitan Building.

Health Insurance.—I am in favor of compulsory low-wage insurance, and believe that it will come sooner or later in some form and that it is our duty to keep awake that we be not the loser but be benefited by the arrangement. All of which means complete organization.—J. N. Davis in *Journal of Kansas Medical Society*.

CLINICAL ASPECTS OF SYPHILIS OF THE LIVER *

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An error in diagnosis gave me the incentive for reviewing this subject. I had occasion to observe a patient for a period of one and a half years. He had what I considered to be fairly typical symptoms of gall-stones, whereas the operation showed that the clinical picture was due to multiple gummata of the liver. The general literature of this topic gave me the impression that the keenest clinicians frequently failed to suspect the syphilitic process in the liver since it mimics, as Arthur R. Edwards¹ puts it, a great many diseases of the liver and gall-bladder.

HISTORY

Syphilitic jaundice was known as far back as Paracelsus, Matthiolus and Francois de la Boë Sylvius. French writers, among them Lancereaux,² Cornil and Mauriac, have emphasized the relationship between icterus and syphilis. Werlhof (1732), J. Frank (1821), and Yvarres (1854) had a knowledge of fever in lues. Guntz first recorded syphilitic fever by a thermometer. Frerich³ in 1861, Bäumler⁴ in 1872, and Hirschberg and Raichline⁵ in 1894 called attention to the fever accompanying syphilis. Bäumler⁴ reported seven cases of syphilis, mostly joint cases, all having a hectic type of fever. The names of Lancereaux in France and Virchow in Germany are closely connected with the study of syphilis of the liver, both as an anatomic and as a clinical entity.

During a period of eighteen years thirty cases were diagnosed during the patients' lives at the Johns Hopkins Hospital.⁶ Among 2,500 necropsies in the same period there were forty cases of gummata or scars and fifteen syphilitic cirrhoses. An analysis of 5,088 post-mortems by Flexner at the Philadelphia Hospital showed forty-two cases with interstitial changes, twenty-two gummata, sixteen cases of perihepatitis, seventy of amyloid degeneration, and thirty-eight of specific scars. The post-mortem records of St. George's Hospital, London, for a period of forty-two years, showed that among 11,629 post-mortems, there were thirty-seven cases of gummata and twenty-seven of syphilitic scars.

PATHOLOGY

The *Spirochæta pallida* is, of course, the primary etiologic factor of the disease. Additional factors put the liver in a state of *locus minoris resistentiæ*, thus favoring a pathologic process in that organ. Gastro-intestinal disorders, especially those in which ptomaines are in excess in the intestinal tract, throw more work on the liver, which, as we know, has among other functions, that of destroying ptomaines. This is the view entertained by Hirschberg and Raichline. Alcoholism, trauma, malaria, preexisting jaundice, which lessen the resistance of the liver, are predisposing factors. In a case of Pitt, the syphilitic process developed on the site of an old hydatid cyst.

* Read before the Chicago Medical Society, Oct. 28, 1911.

1. Edwards, A. R.: *Am. Jour. Med. Sc.*, 1910, cxi, 527.

2. Lancereaux: *Syphilis hépatique*, *Union Méd.*, 1889, No. 40.

3. Frerich, Th.: *Klinik der Leberkrankheiten*, 1861.

4. Bäumler: *Deutsch. Arch. f. klin. Med.*, 1872, ix, 397.

5. Hirschberg and Raichline: *Bull. gén. de thérap.*, June 30, 1895.

6. Quoted from "A System of Syphilis," D'Arcy Power and J. Keough Murphy, iii.

It is the belief of many that syphilis of the liver is seldom associated with parasyphilitic diseases of the nervous system. A. R. Edwards, however, alludes to two cases in which the persistence of pain, after the subsidence of gummata under specific treatment, was in all probability due to the associated mild tabes.

The majority of the histories I have read show that the clinical manifestations appeared about ten to fifteen years after the initial infection. In very exceptional cases, gummata were found in the livers of fetuses or still-born children.

Pathologic changes in the liver occur either congenitally or during the secondary and tertiary stages of acquired syphilis. Congenital syphilis may assume the type of interstitial hepatitis or the gummatus type. The acquired variety may also be interstitial or gummatus. In the first form, the organ is frequently divided by strands of connective tissue into several lobes, forming what is known as *hepar lobatum*. A case of syphilis of the liver that came to post-mortem contained sixteen lobes. The organ may be covered by adhesions, mostly diaphragmatic, leading to what is usually described as *perihepatitis fibrosa adhesiva*. Gummata may be single or multiple, and are situated usually in the periphery of the organ, the region of the suspensory ligament, the edge of the liver and the region of the gall-bladder and the common duct. They are less frequently situated in the depth of the organ. J. L. Allen collected eighty-six cases of gummata of which eleven were single.

A gumma may attain a very large size. A specimen in St. George's Hospital museum (Series IX, 183g) shows a voluminous gumma of the right lobe of the liver, perforating the diaphragm and involving the lower lobe of the right lung.

This brief description of the pathology assists us in the explanation of several of the clinical manifestations. The perihepatitis accounts for the pain, but I found no plausible explanation in the literature for its periodicity, although the perihepatitis is persistent. The presence of gummata in the depth of the organ, on the posterior surface, or any other part which is not readily accessible to the eye or the exploring finger of the surgeon, may escape his notice, thus accounting for those curious cases in which the symptoms continue in spite of the apparently negative anatomic findings.

Gummata situated in the region of the common duct explain the mechanical type of syphilitic jaundice.

The symptoms of syphilis of the liver are both subjective and objective. Pain, fever and, less commonly, jaundice, are the foremost symptoms. The pain may be continuous for a period of days, weeks or months, or it may be periodic. It may be mild, or intensely colicky in character. One day I found my patient rolling on the floor in an attack, and morphin did not lessen its intensity. It is usually local, occasionally referred to the back, exceptionally to the shoulder. Primary nocturnal pain or nocturnal exacerbations of diurnal pain are suggestive of a syphilitic process. Pell considers the localization of pain in the left lobe as pathognomonic.

Fever may occur during secondary or tertiary syphilis in all its forms. It may be continuous or intermittent. It may resemble the typhoid curve, the hectic fever of pulmonary tuberculosis or pyemia and occasionally that of malaria. It is frequently preceded by chills and often associated with sweats. It is rather irregular in its periodicity and atypical in its aspect. There is one case on record which had an irregular fever for eight years. According to Klemperer and a majority of

writers, the fever is due to the absorption of toxic elements resulting from broken-down gummata. Bristowe,⁷ Rolleston,⁸ Lilienthal⁹ and others believe that the fever is due to secondary infection of gummata. The sterile blood-cultures in a number of cases speak against this view (Klemperer).

Jaundice is of less frequent occurrence. It may manifest itself in the early secondary stage, or be one of the symptoms of tertiary syphilis. It usually appears five to six weeks after the initial lesion and frequently in conjunction with the cutaneous manifestations. Lancereaux collected twenty-one cases of icterus associated with the secondary stage of syphilis. This relationship was first emphasized by Gübler in 1853. The percentage of jaundice in syphilis is higher in the French records than in the German. In S. Werner's collection of 15,799 cases of syphilis, jaundice was present in only fifty-seven cases or 0.37 per cent., which is a much lower figure than the percentage given in French statistics.

As a whole, jaundice is less frequent than the other symptoms and is of a mild character and short duration. Its cause has been variously interpreted. Gübler considers it as due to an exanthem of the intestines and the mucosa of the bile-tracts, a sort of specific cholangitis; Lancereaux and Cornil as due to pressure from enlarged lymph-nodes on the portal vessels. In a series of fifty-seven cases of syphilitic jaundice there was enlargement of the superficial lymph-nodes in forty-one. Virchow ascribes it to pressure of gummata on the bile-tracts, while Bierner and Frerich attribute it to perihepatitis.

A great many cases of lues of the liver have a long latent period, characterized only by occasional gastro-intestinal symptoms of a vague nature. Marcuse believes that two-thirds of patients with gummata of the liver have early digestive disturbances. In another group of cases pain, fever and jaundice may subside for a time during which the patients may have only atypical gastro-intestinal symptoms, thus adding to the confusion of the clinician.

The spleen is often enlarged. The urine contains, in some cases, albumin. The leukocyte count is either normal or deviates within small fractions above or below the normal. A number of patients had leukopenia, which in conjunction with a continuous fever and large spleen suggested typhoid. Neusser found a slight increase in eosinophils in several cases.

The physical findings do not seem to be pathognomonic, judging from the number of errors committed. It is usually asserted that the liver is most frequently enlarged. It may, however, be normal or even smaller than normal. The organ may be irregular in shape and distinctly lobulated. The left lobe is sometimes atrophied or separated by bands of connective tissue from the right lobe. Occasionally a fair-sized gumma can be palpated. Adhesions may so fix the liver as to restrict the respiratory excursion of the organ.

DISEASES FOR WHICH HEPATIC SYPHILIS MAY BE MISTAKEN

The diagnosis of syphilis of the liver is difficult and at times impossible, as it simulates closely almost every hepatic disease, gall-stones and carcinoma in particular. At times the clinical course resembles that of several febrile diseases. While bedside experience teaches us that classical or text-book cases are not common, still we have to admit that we must have a number of suggestive

7. Bristowe: Brit. Med. Jour., 1880, I, 878.

8. Rolleston, H. D.: Diseases of the Liver, 1905, Phila., p. 348.

9. Lilienthal: Ann. Surg., 1902, xxxvi, 132.

symptoms, grouped in a definite manner, in order to make an ordinary diagnosis. With syphilis of the liver we are more or less helpless in the interpretation of clinical manifestations, and logic and experience count for little in its diagnosis. Whenever a patient exhibits a symptom-complex suggesting a disease of the liver, in which the clinical history is atypical, the order and the character of the symptoms unusual, one ought to think, among other possibilities, of syphilis of the liver. A definite history of syphilis, a positive Wassermann reaction and a rapid improvement under the influence of specific treatment are the only means of making a definite diagnosis. The affection may simulate the following diseases:

1. *Cholecystitis, with or without Stones.*—The greatest number of diagnostic errors is reported by Riedel,¹⁰ who speaks of several patients operated on for what was thought to be gall-stones, but proved to be gummata of the liver. Joseph L. Miller¹¹ reports six cases of syphilis of the liver in which the diagnosis of cholecystitis was made once, and that of stones twice. Frank Billings¹² relates a typical history of gall-stones. The patient was operated on by Christian Fenger, and the case proved to be one of gumma. The latter surgeon had another similar experience shortly after. He believed that whenever gummata are situated in the region of the gall-bladder, the differential diagnosis cannot be made. A case of Howard Lilienthal imitated suppurative cholecystitis, although lues was thought of. Exploration revealed a suppurating gumma. Of ten cases of biliary colic reported by Riedel there was icterus in seven. One patient had attacks for fifteen years. The difficulty becomes still greater when the patient really suffers from cholecystitis with or without stones in addition to gummata. This association was present in the collection of Charles H. and W. J. Mayo¹³ in four cases, two only having stones. While the histories of the cases reported are suggestive or even classical for cholecystitis, a closer discrimination usually reveals that the pain is not always colicky in character; that it may extend over long periods with irregular remissions; that it is more or less limited to the right hypochondrium, and that it does not radiate toward the shoulder. The fever is capricious in its type and the jaundice, if present, is very mild and of short duration.

2. *Carcinoma.*—Virchow¹⁴ states that he has seen the best clinicians mistake gummata of the liver for carcinoma. Joseph L. Miller speaks of a case diagnosed clinically as carcinoma which was apparently confirmed by exploration, yet in which specific treatment resulted in cure. Syphilis of the liver may exhibit some of the typical symptoms of carcinoma—pain, tumor of the liver, cachexia, ascites, gastro-intestinal symptoms, even blood in the vomitus and feces and absence of free hydrochloric acid from the gastric juice. Fournier holds the view that ascites is rather uncommon in syphilis. A patient of William E. Morgan, as mentioned by Arthur R. Edwards, was extremely emaciated and had enormous ascites in connection with gummata. Prior to the operation a diagnosis of carcinoma was made. Splenic enlargement and albuminuria are absent in carcinoma. The hepatic tumor, if palpable, is never so large in syphilis as it is in carcinoma. Syphilis extends over a longer period of time and usually attacks younger people.

3. *Liver Abscess.*—Two brief histories will illustrate the point. In the first one, a case reported by G. Klemperer,¹⁵ the patient had for several months pain in the region of the liver, chills, followed by an irregular temperature, enlarged liver and icterus. He was to be operated on for liver abscess. At the suggestion of Renvers the patient received intramuscular injections of corrosive sublimate. The whole clinical picture cleared up after fourteen injections. The second case is reported by Lesage. The patient had marked epigastric tenderness, chills and fever extending over a period of nine months, 21,000 leukocytes, and lost 40 pounds. At first a diagnosis of liver abscess was made. After one week of mixed treatment, however, all the symptoms disappeared and never recurred. One is more apt to confuse syphilis with liver abscess in tropical countries.

4. *Septic Pyelophlebitis.*—The patient of Dr. Arthur R. Edwards had all the earmarks of septic pyelophlebitis of the portal vein. The diagnosis was based on the sudden tenderness over the portal region, large ascites, irregular temperature, preceded by chills and fever. Subsequently a cure was effected by mixed treatment.

5. *Pulmonary Tuberculosis.*—Cases in which there is loss of weight, night sweats, afternoon temperature and cough may resemble pulmonary tuberculosis. Such cases were reported by E. G. Janeway,¹⁶ Joseph L. Miller, Bäumlér, and others.

6. *Typhoid Fever.*—A continuous fever with vesperal exacerbation, leukopenia, and splenic enlargement may suggest typhoid. Hirschberg and Raichline report the case of a patient who, after twenty years from the initial lesion, developed a febrile disease with evening exacerbation, some gastro-intestinal symptoms, diarrhea in particular. A diagnosis of typhoid was made. Later, antisyphilitic treatment administered to this patient was followed by a prompt cure. Similar cases were reported by Bäumlér and others.

7. *Malaria.*—This was diagnosed in a number of cases by very competent clinicians on account of the intermittent type of temperature preceded by chills and accompanied by splenic enlargement.

8. *Echinococcus Cyst.*—This diagnosis was made in several cases.

9. *Splenic Anemia.*—This condition may be suggested by splenic enlargement, in the presence of a normal-sized liver, leukopenia and anemia of the secondary type.

A splenectomy was performed in a case of Coupland for what was supposed to be splenic anemia. The patient improved shortly after the operation but subsequently died from hematemesis and ascites. A post-mortem examination disclosed syphilis of the liver. Several similar cases have been reported by Osler.

10. *Atrophic or Hypertrophic Cirrhoses.*—The differentiation from these conditions is often impossible. Syphilis of the liver differs somewhat from the atrophic type in that the liver is usually large, irregular, and ascites is not so common. The general nutrition is not necessarily impaired. Hematemesis and melena are usually absent. It differs from the hypertrophic type in that the liver is large but irregular instead of smooth. The jaundice if present is very mild. It never amounts to an icterus gravis.

11. *Movable Kidney.*—A lobulation of the liver may resemble the kidney.

In order to appreciate how easy it is to mistake all the conditions enumerated for syphilis of the liver one must

10. Riedel: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1904, xiv, 1.

11. Miller, J. L.: Illinois Med. Jour., 1905, viii, 240.

12. Billings: Philadelphia Med. Jour., 1900, vi, 671.

13. Quoted from Keen's Surgery, iii, 980.

14. Virchow: Die Krankheiten Geschwülste, ii, 428.

15. Klemperer, G.: Therap. d. Gegenw., 1903, v, 41.

16. Janeway, E. G.: Am. Jour. Med. Sc., September, 1898, p. 251.

read in detail the individual histories. It is also striking that practically all the cases reported in the literature emanate from the pen of clinicians of repute.¹⁷ One is almost tempted to say that whenever we do not know definitely what is the matter with the patient presenting vague or atypical symptoms referable to the liver, it would be advisable to put the patient on a rigid antisyphilitic treatment for two or three weeks. Rosenbach¹⁷ is not in sympathy with this method of diagnosis simply based on the therapeutic test.

COMPLICATIONS

Gummata may disintegrate and subsequently suppurate. They may break into the general peritoneal cavity or into neighboring structures or organs. Two cases of peritonitis from this cause were reported by S. Wilks¹⁸ in 1877, and by Griffith¹⁹ in 1888. Newbolt reports a case of empyema of the right chest resulting from rupture of a suppurating gumma situated on the posterior surface of the right lobe. Gummata may calcify and, if numerous, may calcify the entire liver.

TREATMENT

Mixed antisyphilitic treatment has a remarkable influence on syphilis of the liver. It is almost impossible to believe the reports of some cases. Patients suffering from the most intense symptoms for years are reported permanently cured within a week or two, under specific treatment. As far as I know, salvarsan was never used for the cure of gummata of the liver. In my case I deemed it wiser to put the patient on the usual mixed treatment and not to inject salvarsan until some later date. I reasoned that if salvarsan were effective in destroying so many spirochetes, enough antitoxin would be liberated to hazard the patient's life. The case reported by Floyd Burke Riley²⁰ had a slight fall in the temperature, which was continuous for two months, under the influence of atoxyl. Occasionally, a gumma was removed for diagnostic purposes. In some cases a suppurating gumma was curetted and the cavity packed with iodoform gauze. Keen reported in 1899 twelve cases of resection of the liver for gumma. Cumston²¹ in 1903 added fifteen cases to that list.

CASE REPORT

History.—H. C., aged 35, about 18 months prior to this report experienced epigastric distress shortly after meals, which continued almost daily up to the time of examination. At times he had a sense of fullness and distress an hour after eating, frequently associated with nausea, but not with vomiting. This feeling lasted from one to two hours. Occasionally, he was awakened after midnight with sharp epigastric pains. These symptoms were often mild in character; at times, however, they were quite distressing. In addition, the patient had had in the previous year and a half sudden severe attacks of pain in the right hypochondrium, radiating toward the back, sometimes to the tip of the right scapula. These attacks would last from three to seven days. I saw the patient during several attacks and, on one occasion, as mentioned, I found him rolling on the floor with pain. The attacks were severe enough to require morphin. Every attack was usually associated with a chill followed by a rise of temperature. The patient was never jaundiced. He always had a certain degree of tenderness under the right costal arch even when free from attacks. His appetite was poor most of the time and he was frequently nauseated about a half hour after eating, but never vomited. He was chronically constipated. He had no genito-urinary

symptoms. He was of nervous temperament. During his illness he lost 20 pounds. He had never been ill before except fourteen years previously when he contracted syphilis while a soldier in the army. The lesion was typical and was followed by equally typical secondary symptoms. He was treated for four months by deep intramuscular injections of mercury. One year later he was again treated for a period of six months by injections with mercurial ointment. He had married about three years prior to examination. His wife had no miscarriages; one pregnancy was carried to full term. The child was 13 months old and had no stigmata of syphilis.

Examination.—The patient was admitted to the Presbyterian Hospital, Sept. 4, 1911. Two days previously he had had a severe attack as above described. His temperature, the day of admission, was 101.4 F., dropped to 99.4 the second morning and rose to 101 in the evening. His leukocyte count was 10,300; hemoglobin, 75 per cent. The urine was normal. Physical examination revealed generalized adenopathy, the individual lymph-nodes being painless and movable. The integument was distinctly anemic. The bulbar conjunctivæ were subicteric. He had a marked alopecia. Otherwise the physical examination was entirely negative. Prior to the operation I made a diagnosis of cholecystitis, possibly with stones.

Diagnosis.—The epigastric distress coming on after meals and covering a period of eighteen months compelled me to think also of the possibility of a gastric or duodenal ulcer. On Sept. 7, 1911, I made an incision through the rectus muscle with the purpose of exploring the pylorus and duodenum and also the gall-bladder. I found the stomach and the duodenum normal. The gall-bladder was normal in size and appearance and emptied readily on pressure. The convex surface of the right lobe of the liver and its border were studded with numerous, small, whitish-gray nodules. There were similar tumors along the common duct and also at the neck of the gall-bladder. From the gross appearance I could not identify the nodules. I excised two small nodules for diagnostic purposes. The histologic sections showed the typical picture of gumma.

Treatment.—On the second day after the operation I instituted the mixed treatment and have continued it to the present. There was a sudden drop in temperature from this day on and it remained normal afterward. The patient made an uneventful recovery, the wound healing by primary intention.

At the end of the week the patient was entirely free from symptoms. He remained well and at the end of two weeks had gained 14 pounds.

CONCLUSIONS

1. The clinical statistics underestimate the frequency of syphilis of the liver. The Wassermann reaction will increase the number of cases.
2. The symptom-complex of syphilis of the liver is not pathognomonic, as it simulates almost every hepatic disease; occasionally it simulates febrile diseases.
3. Whenever the diagnosis is uncertain, resort should be had to the therapeutic test as well as to the Wassermann reaction.
4. Mixed treatment has a striking effect on lues of the liver frequently, regardless of the time it has existed.

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Conscription for Japanese Military Service.—According to statistics recently published in Japan, 7,941 of 436,343 conscripts examined last year had trachoma and 11,593 venereal disease. The average of educational acquirements is constantly rising, but still there were 4.3 per cent. who were unable to read and write. There were 551,924 young men of the conscript age, but 83,602 were excused on account of attendance at school or college; 35,538 are residing elsewhere than in Japan, and 26,678 could not be located or were in jail and 696 were convicts, while 8,383 were excused on account of sickness. About 70.3 per cent. averaged well physically. *Journal Royal Army Medical Corps*, 1911, xvii, 112.

17. Rosenbach: *Therap. d. Gegenw.*, 1903-1904.

18. Wilks, S.: *Tr. Path. Soc. London*, viii, 2401; *Lancet*, London, Dec. 8, 1877.

19. Griffith: *Lancet*, London, 1888, i, 220.

20. Riley, Floyd Burke: *Tr. Chicago Path. Soc.*, Feb. 1, 1911.

21. Cumston: *Ann. Surg.*, 1903, No. 37.