organism under examination satisfies the essential cultural and biochemical characteristics of one or other of the dysentery bacilli is dangerous, particularly in the case of the mannite-fermenting group of dysentery organisms, for high titre serums prepared against this group are not specific in moderate dilution, and will agglutinate several kinds of coliform bacteria.

Innocence of this fact has led to much confusion in some military laboratories, as witness the discussion at the Medical Society of Vienna, April 30th, 1915, upon a paper by Falta and Kohn.⁵

From June to December, 1917, we made upwards of 1,200 efforts to recover dysentery bacilli from the stools of patients at various periods of their illness. The results of these attempts are arranged in Table II, in the relation to the time intervening between the onset of the disease and the examination. We have not included in the figures thus analysed the cases in which there was not clear evidence that the patient was manifesting or had manifested dysenteric symptoms, and all cases in which *E. histolytica*, either active or encysted, were discovered have been excluded.

TABLE II.—Results of 1,050 Efforts to Recover Dysentery Bacilli from Stools at Various Stages of the Disease, June–December, 1917.

Period of Disease.	No. of Examinations.	Positive Results.	Percentage Positive.
1st to 5th day ...	153	104	68.0
6th to 10th ..	161	28	17.4
11th to 15th ..	194	13	6.3
16th to 20th ..	162	5	3.1
21st to 30th ..	205	3	1.5
31st to 40th ..	104	3	3.0
41st to 50th ..	34	1	3.0
51st to 60th ..	14	—	—
61st to 70th ..	9	—	—
71st to 80th ..	5	1	—
81st to 90th ..	3	—	—
91st to 100th ..	6	—	—
Totals ...	1,050	158	—

Graph representing success in recovering dysentery bacilli from the stools at different periods after the onset of the disease (1,050 examinations).

CONCLUSION.

Our chance of recovering dysentery bacilli rapidly diminished after the first few days. This appeared to be the case whether the stools remained characteristically dysenteric or not.

The muco-pus and epithelial debris discharged in the milder pathological condition, and the necrosed coagulated superficial layers of the mucous membrane in the more serious is, except in the earliest stages of the disease, invaded by hosts of intestinal organisms, which soon overwhelm the dysentery bacilli originally present. This places a serious limit on the value of a bacteriological diagnosis of dysentery. If reliance had been placed on the results of one examination but 15 per cent. would have been discovered.

REFERENCES.

- ¹ Deut. med. Woch., 1916. ² Münch. med. Woch., December, 1915, p. 1768. ³ Zur Frage der Variabilität von Dysenterie Stämmen der Galizien-Russischen Epidemie Herbst, 1914, Wien. klin. Woch., 1915, vol. xxviii, p. 484.

TWO FATAL CASES OF ICTERUS GRAVIS FOLLOWING INJECTIONS OF NOVARSENOBILLON.

BY

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THE two cases here recorded are, we think, of distinct interest at the present time, when so many cases of syphilis are under treatment by arsenical drugs.

CASE I.

A soldier, aged 26, was admitted on March 22nd, 1917, with slight jaundice. He stated that he felt well, with the exception of a slight pain in the right hypochondrium, and only reported sick because he was told he looked yellow. He gave a history of recurrent attacks of abdominal pain for three years, occurring every three or four months and lasting three or four days.

On admission his skin and corneae were stained yellow. There was no abdominal pain or tenderness and no vomiting. The bowels were constipated; the urine contained bile in considerable amount, but no albumin or sugar. Liver dullness $4\frac{1}{2}$ inches in nipple line.

He had been under treatment for syphilis. Captain Brown, N.Z.M.C., in charge of V.D. section, reported that the man was admitted on January 22nd, 1917, with a large sloughing, discharging sore on right side of foreskin and also a small penile sore. There was some inguinal adenitis, but no rash; spirochaetes were present. The blood test was weakly positive. He was treated with novarsenobillon as follows: January 23rd, 0.45 gram; February 15th, 0.6; February 22nd, 0.6; March 1st, 0.9; March 8th, 0.9; March 15th, 0.6. He received also five mercurial injections. The sore had healed on March 1st. While in hospital he developed inguinal bubo, which was tapped twice. The result of the last blood test was negative.

The jaundice steadily increased, and on March 28th the liver dullness measured three inches. Vomiting began on April 1st, the jaundice grew more intense, the urine became almost black in colour, and the pulse slow and weak. He died on April 5th.

Post-mortem Observations.

A post-mortem examination was made by Captain E. C. Lowe, from whose report it appears that the heart was normal, save for bile staining of the valves and vessel walls and small petechiae on the walls of the left ventricle. The lungs were normal, except for hypostatic congestion, which was intense on the left side. The spleen was not enlarged and appeared normal on section. The intestines were not ulcerated, but the jejunum showed small petechiae and was deeply bile stained, and the duodenum, which contained a dark greenish bilious fluid, was markedly injected. The gastric mucosa was bile stained and injected, markedly at the pyloric end; there were no haemorrhages. The pancreas was slightly congested, but otherwise normal. Both kidneys appeared normal, save for bile staining. The meninges were bile stained, but otherwise the cranial contents were normal. The note upon the liver and gall bladder was as follows:

Liver.—Smaller than normal. Weighed 2 lb. 2½ oz., and was deeply bile stained. Some mottling over anterior surface, most marked on the right lobe. No unevenness of surface; edges sharp; no inflammatory adhesions; left lobe small. On section right lobe cuts easily and shows deep yellow degeneration in irregular areas mostly confined to anterior surface and anterior border for the distance of an inch inwards. The centre of the organ comparatively free, of yellow coloration, but showing a nutmeg appearance of central congestion and perilobular contrast. Left lobe shows much less sign of degeneration. Cuts normally. Slight sign of yellow degeneration. No nutmeg appearance.

Gall Bladder.—Normal. Contains a drachm and a half of bile. Ducts free and patent. No signs of gall stones or cholecystitis.

Microscopical Examination.

Captain F. L. Armitage reported as follows:

Liver.—Sections show marked excess of fibrous tissue throughout, especially round Glisson's capsule, but also spreading into the gland tubules. Islets of healthy liver tissue persist, with only a small amount of fatty degeneration in places. No active necrosis, but inflammatory changes are seen everywhere. It appears to be some variety of cirrhosis of the liver and not yellow atrophy.

Spleen.—Some excess of fibrous tissue in the trabeculae and pulp, but no gross change.

Kidney.—There is so much post-mortem change that it is difficult to say how much real lesion there may be. The consolidated tubules show marked necrosis, probably indicating a tubal nephritis. A few small cysts are present.

Note on the Histology.

By Professor F. W. ANDREWES, F.R.S. (Major R.A.M.C.T.).

The liver is partly bright green, partly deep red, and the appearances are different in the two areas.

Green Part.—Here the changes are less advanced than in the red part. There is a cirrhosis of multilobular type of fairly recent standing, but more than I should have thought possible in seven weeks. The young fibrous tissue is infiltrated with round cells. The hepatic cells show considerable degenerative change, with some fatty infiltration, but the material had been put in spirit, which spoiled it for Sudan III staining. There is a catarrhal cholangitis of the larger bile ducts.

Red Parts.—Here there is a little coarse cirrhosis, but the liver cells are almost completely degenerate, leaving only a loose fibrous stroma, with an interstitial inflammatory infiltration. Shrunken remains of the liver cells are seen. The bile ducts are better preserved. The red colour is due to extravasation of blood corpuscles in the centres of the lobules. This extravasation is extreme, masking the structure of the tissues, and is quite sharply defined, the periphery of the lobules being free. Instead of being due to dilated capillaries, as in ordinary nutmeg liver, the condition seems due to actual extravasation. I am unfamiliar with this appearance, which is very striking.

CASE II.

A soldier, aged 20, was admitted to hospital on January 24th, 1917, with left-sided pleurisy—not severe. At the end of February a suspicious ulcer appeared on the fraenum. A Wassermann test proved positive, and he was transferred to V.D. section on March 19th, when he had a round healed sore on the under side of the body of the penis, and general adenitis. The skin and mucosa were clear. The Wassermann reaction was “strong positive.” Captain Brown reports that he was treated with novarsenobillon, 0.45 gram, on March 25th, and 0.6 on March 27th. He received also two mercurial injections. The blood test on March 31st was double positive. He developed a second attack of pleurisy, and on April 19th the left chest was aspirated and 60 oz. of clear fluid removed. He improved in health, and on May 2nd it was decided to continue the anti-syphilitic treatment and he was given novarsenobillon (0.60) and a second dose (0.60). On May 9th he was placed on an iodide-mercury mixture. On May 15th the Wassermann test was double positive, and on the following day another dose of novarsenobillon (0.60) was given. No further injections were given. On June 1st he was slightly jaundiced; he was kept in bed and the mercurial treatment discontinued.

On June 3rd the liver measured 5½ in. in the nipple line. There was no improvement in the jaundice. The urine (specific gravity 1015) contained no albumin, sugar, blood, bile, or arsenic (Marsh's and Reinsch's tests). On June 5th the icteric tinge had slightly increased; the urine was free from blood and arsenic, but bile was present. The jaundice and the amount of bile in the urine had increased by June 12th, and on the following day he vomited. On June 15th there was swelling of the right parotid without rise of temperature. There was some slight improvement for the next few days, but on June 22nd it was noted that the jaundice was more intense, that he vomited once or twice nearly every day, and that the liver dullness now measured 2½ in. in the nipple line. The temperature was subnormal. The urine (specific gravity 1010) contained bile, albumin, and epithelial and granular casts. It contained neither tyrosin nor leucin. The jaundice deepened, anorexia became marked, and on June 27th the breath had a peculiar rancid odour. The tongue was clean; there was no tenderness over the liver, stomach, or spleen. The area of absolute liver dullness had diminished to 2½ in. The spleen was not enlarged. The pleurisy had cleared up, but the pleura on the left side was thickened. His condition fluctuated on the following days; he passed large quantities of dark urine. On July 5th there was no absolute note of dullness on percussion over the liver; the relative dullness in the nipple line was 2 in. only. Later he became delirious and vomited occasionally but not incessantly. On July 9th he was semi-conscious. He died early on the morning of July 10th. All the urine was collected from June 22nd till death; the quantity varied from about 38 oz. during the first week to 11 oz. during the later days of his life. The daily quantity was concentrated to about 50 c.cm., and submitted, with negative results, to Marsh's test, and on several occasions, on the advice of Mr. A. J. Ewins of the Lister Institute, to Norten-Koch's test. Arsenic was not detected in any one of the sixteen examinations, nor was it detected *post mortem* in the liver, kidney, lung, spleen, pancreas, or heart muscle. Two samples of urine were submitted to Dr. Hurlley (June 29th and July 2nd), who found no arsenic in either; he also examined a piece of liver without finding any trace of arsenic. Consultations with Colonel Davy, C.B., consulting physician in the command, were held on two occasions. Colonel Davy's note is as follows:

“I have seen — in consultation at Codford on two occasions—on June 7th and June 27th. He is suffering from jaundice, and has progressively become worse and worse, in spite of the most careful treatment. Some of his symptoms, especially first enlargement and then diminution of the liver dullness, rather look like acute yellow atrophy of the liver. Reviewing, however, the whole group of symptoms, they do not conform to the usual group found in this disease, and there is an absence of leucin and tyrosin, for which the urine has been carefully examined. It seems probable that we are dealing with a condition hitherto not recognized as any of the ordinary diseases, and the fact that he has had five injections of novarsenobillon raises grave suspicions that his condition is due to these injections.”

Post-mortem Observations.

A post-mortem examination was made by Captain E. C. Lowe, from whose report it appears that the external surface was

deeply bile stained. The peritoneal cavity contained bile-stained fluid, and the retroperitoneal gland was enlarged, pulpy, and bile stained. The heart was normal. The right lung was normal, but the pleura on the left side was adherent throughout, and the lung compressed, semi-solid, and friable. The intestines were normal, as was the stomach, except for a few areas of deep injection. The spleen (weight 10 oz.) was enlarged, showing definite sclerotic mottling on the surface, and a puckered scar near the posterior border. Its substance was less friable than normal. The kidneys were bile stained, and the cortex appeared fibrotic and dense. The right weighed 9½ oz., the left 10 oz. The gall bladder was normal and contained normal bile. The note on the liver is as follows:

Liver (weight 36½ oz.).—Transverse diameter, 7½ in.; vertical measurement, 6½ in.; antero-posterior measurement, 3½ in. External surface shows white fibrotic linings. No external adhesions. Organ irregular and nodular to touch. Extensive greenish-brown areas of necrosis were found over the upper third of right lobe, in a few places on the left lobe, and almost entirely involving the middle lobe. On section, these areas show extensive necrosis of liver tissue of a greenish-brown colour and of soft consistency, irregularly separated by dark red fibrotic areas of very dense consistency.

Report on the Histology of Organs.

By Professor F. W. ANDREWES, F.R.S.

Liver.—Small, tough, with extensive greenish staining involving almost the whole organ, here and there red fibrotic areas. Not nodulated as in ordinary cirrhosis. There is a well-marked cirrhosis, multilobular in type, throughout the green part of the liver. The connective tissue is young and cellular, with lymphocytic infiltration. The liver cells show only a moderate degree of degeneration (much less than in the green parts from Case I), and there is very little fatty change in frozen sections stained with Sudan III. There is marked bile staining, and amorphous masses of biliverdin, bright green in colour, are present in the substance of many of the liver cells, as well as in the bile capillaries. The red areas in the liver show much more complete destruction of the liver cells and more advanced fibrosis. The red colour is due to haemorrhage. As in Case I, it is difficult at first sight to believe that such advanced cirrhosis could have occurred in six or seven weeks, but the similar change in both livers suggests that this may have been the case. The cirrhosis is not of syphilitic type.

Kidney.—Very large and deeply bile stained. There is a good deal of vascular congestion, but there is no glomerular nephritis, though the glomerular capsules contain a coagulable exudate. The epithelium of the convoluted tubules is greatly swollen and vacuolated, but the nuclear staining is mostly preserved, and there is very little fatty change in Sudan III sections. Bile-stained casts and granules are numerous, green with biliverdin.

Heart Muscle.—Slight fatty change only, in the form of granules about the poles of the nuclei.

Spleen and Retroperitoneal Gland.—No striking changes found.

These two cases resemble one another very closely in their history, clinical manifestations, and morbid anatomy.

Briefly stated, after receiving five doses of novarsenobillon followed by an interval (of seven and fourteen days respectively), they became jaundiced. At first the symptoms were mild, but the jaundice gradually deepened, the liver became greatly reduced in size, persistent vomiting occurred, and the patients died twenty-one and forty days respectively after the onset of symptoms. Autopsy showed an acute cirrhosis of the liver. Both were cases of primary syphilis and showed no secondary manifestations. Case No. 1 gave a negative Wassermann reaction at the conclusion of treatment, but Case No. 2 gave a double positive reaction on the last occasion on which it was taken.

That the cirrhotic condition of the liver was due to syphilis appears to be almost out of the question, as shown by Major Andrewes's report. In Case II he remarks on the appearance of the liver: “I am unfamiliar with this appearance.” The clinical symptoms do not accurately agree with acute yellow atrophy of the liver, and the naked-eye and microscopical appearances of the liver are quite unlike what is found in this condition.

These two conditions being excluded, the question naturally arises whether these fatalities were due to chronic poisoning with arsenic. Inquiries were therefore made with a view to finding out whether similar cases had occurred at the N.Z.V.D. section or elsewhere.

Captain Falconer Brown, officer in charge of N.Z.V.D. section, states that he has treated 263 cases of syphilis with novarsenobillon, and the cases reported are the only ones followed by jaundice. Captain Robert W. McKenna, venereal specialist to 1st Western General Hospital, states that he has not met a single case of jaundice following treatment of syphilis by salvarsan and kharsivan, and

attributes his success to special precautions with regard to intervals between doses, etc.

Lieut.-Colonel Harrison, officer commanding Rochester Row Hospital, writes: "Jaundice occurs during treatment of syphilis with arsenical compounds in 0.6 per cent. of cases, and this symptom may last for four or five months."

In neither of the cases here reported was arsenic detected in the urine.

TOXIC JAUNDICE, WITH ATROPHY OF LIVER, FOLLOWED BY REGENERATION AND RECOVERY.

By BARBARA G. R. CRAWFORD, M.B., CH.B.

DURING the summer of 1917 I had the opportunity of seeing and treating three cases of toxic jaundice caused by trinitrotoluene. In all three there was profound illness, with jaundice, delirium, and marked diminution of liver area, and later recovery, with replacement of liver substance and function. During the course of the disease the patients were seen by one of H.M. Medical Inspectors of Factories, who confirmed the diagnosis and the diminished liver area in two of the cases (the third case, being convalescent at the date of his visit, was not fully examined), and who stated that in his opinion a fatal issue was to be expected.

The patients were workers on T.N.T. manufacturing processes, and were exposed both to fume and skin contact. C. B., male, aged 29, worked for four months in a corrugated iron building where the T.N.T. was washed, and then for eight weeks in the open air recovering T.N.T. from waste water gullies. T. M., male, aged 22, worked for three months in the T.N.T. process, and then for five weeks on the outside laundries (as the gullies are called) at the same work as C. B. B. C., female, aged 19, worked for six weeks in the T.N.T. packing house. One patient had thus been in contact with the T.N.T. for six months, and one for four months; both of these had been employed in the open air for many weeks before the onset of illness; the third had worked in T.N.T. for six weeks only, and had been free from contact for thirty-eight days before the jaundice was observed; during that time she had been attended by her own private doctor for "sore throat." The hands of all three were stained orange yellow, as is common among T.N.T. workers.

In each case the health had not been satisfactory for some weeks before the onset of jaundice, the complaints varied greatly and can hardly be regarded as definite prodromal symptoms: B. C. complained of sore throat, T. M. of faintness, C. B. of tightness of chest (and a fourth case, referred to later, of weakness of the eyes).

On investigation, however, it was ascertained in each case that the worker had felt weak, with poor appetite, slight nausea, and a tendency to headache (one case, C. B., came to the surgery asking for his discharge, as he did not feel able for his work). Cyanosis was not observed in any of these cases, and the patients had never suffered from T.N.T. dermatitis.

The first definite sign was yellowness of the conjunctivae, quickly followed by general icterus; at the beginning the patient did not appear to be seriously ill, but shortly afterwards became suddenly worse with vomiting, delirium, incontinence of urine and faeces; rigors were frequent and were associated with severe epigastric and hepatic pain; the stools were paler than normal but never entirely clay-coloured; the urine was heavily bile-stained, normal in quantity and specific gravity, acid in reaction, and containing small traces of blood and albumin (in one case tube casts and epithelial debris were present); leucine, tyrosine, and T.N.T. were absent.

In all three cases the disease ran a similar course, the patient becoming steadily worse; the liver area decreased and drowsiness and delirium persisted. In one case the patient was more or less unconscious for over three weeks, passing his evacuations under him and having to be fed by hand. In this case an inexperienced nurse placed the clinical thermometer in the patient's mouth, and a moment later recovered part of it with difficulty, the lower end having been bitten off and swallowed by the semi-conscious

man. Fortunately the thermometer end was passed later with a globule of liquid mercury in the stools.

Extreme emaciation occurred in two of the cases, the third lost weight but did not emaciate to the same extent as the others. The temperature was normal as a rule, rising occasionally for a day or less at a time to 100° F.; the pulse-rate was normal though feeble at the height of the illness. The breath was foul and had a characteristic odour; the tongue and lips were furred and bled slightly; the colour of conjunctivae and skin became dark yellow; small raised petechial spots appeared on the limbs, chest, and face; there was no itching. Vomiting was troublesome and the bowels tended to be constive; in response to an enema or an aperient slimy pale stools were passed which stained the draw-sheet pink round the edges of the soiled area; during this time no T.N.T. could be detected in the urine. Perspiration was scanty, the skin being harsh and dry.

Whenever the patient was sufficiently conscious he complained of constant pain over the liver region, and the liver dullness steadily diminished until in the two most severe cases one to one and a half inches or less could be made out in the nipple line.

The treatment was necessarily somewhat empirical, the symptoms being alleviated as far as possible as they arose. The skin was encouraged to act, the bowels kept free by a mild aperient (white mixture) and enemata; nourishment was given in small quantities at frequent intervals—milk and soda water, meat juice, thin broths, barley water, etc.; meat extracts were well tolerated, while fruit and fruit juices disagreed and caused vomiting. Injections of 6 oz. of a saturated solution of sodium bicarbonate were given by the rectum twice daily at the height of the illness, and the same salt by mouth also in a mixture and in milk to the amount of 2 drachms daily; whenever this was discontinued the patients became worse. All three cases slowly rallied, and in the fifth or sixth week of the illness began definitely to improve; delirium ceased, the vomiting and pain became less frequent, appetite better, colour less deeply jaundiced, and the stools became normal in colour and consistence; the area of the liver increased, and its function returned with remarkable rapidity; in one case (C. B.) in five weeks the liver dullness from being less than one inch increased to two and a half inches.

Convalescence, however, was slow and slight relapses frequent, the patient becoming drowsy and sick, and having recurrence of epigastric pain if allowed to do much at first, or if excited by friends or visitors. When the patients were allowed up oedema of the legs and to a less extent of the body was troublesome, and persisted for weeks after the urine was clear of albumin; the jaundice was slow in subsiding, a yellow tinge remaining after ten weeks. The liver dullness, after having almost disappeared in two of the cases and having greatly diminished in the third, returned practically to normal. The petechial spots persisted as small raised papules, with no itching, especially on the face, long after the patients had otherwise recovered and the jaundice had completely disappeared.

The three cases were eventually discharged home and returned to work, T. M. as a miner, C. B. as a sanitary worker, and B. C. on the factory traffic gang. The length of treatment in hospital averaged ten weeks, and the duration of illness until the patient was fit for work again was nearly twice that period. I have recently heard from the patients, and all report themselves well and at work at the present time, six months after recovery. In the third case, B. C., which was the least severe, blood examination revealed no pathological change, cell and haemoglobin ratios being normal. Menstruation was missed for three periods during her illness, but has occurred normally since.

In a fourth case, a girl of 18 years, who worked for four months on the outside laundries, and was seen on several occasions but not treated by me, the symptoms and course were the same—full recovery and regeneration of the liver taking place after a serious and prolonged illness of many months, in which the liver area diminished to less than half its normal size. In this case also sodium bicarbonate was given freely throughout.

The chief points of interest appear to be: (1) The regeneration of the liver after very extensive destruction. (2) The beneficial result of the exhibition of sodium bicarbonate¹ in what seemed to be hopeless cases. (3) The absence of T.N.T. in the urine when it was being excreted by the bowel.