The patient made an uninterrupted recovery. The growth proved to be a columnar-celled carcinoma.

CASE 4. *Carcinoma of the sigmoid simulating disease of the right uterine appendage.*—This case I also operated upon at the Chelsea Hospital for Women in September, 1908. Her age was 31 years, and her symptoms, which consisted of pain in the lower abdomen and back, had existed for three months. For the first two months of this period she had had frequent attacks of diarrhœa, but for the last month this had ceased and she had become very constipated. On abdominal examination there were tenderness and an ill-defined sense of swelling to the right of the middle line, and low down in the pelvis per vaginam a well-marked mass could be felt filling the right half of the pelvis and pushing the uterus forwards and to the left. A provisional diagnosis of inflammatory disease of the right ovary and tube was made.

When I opened the abdomen I found the tumour to consist of a loop of sigmoid colon at the flexure of which a large annular growth was situated. This was matted over with adherent small intestine and omentum and the whole conglomerate mass was attached to the back of the right broad ligament and the right lateral pelvic wall. The ovary and tube on either side were normal. Having separated the diseased intestine and removed the omentum, I resected the whole loop containing the growth together with some enlarged glands. The upper end of the bowel was then emptied of a large quantity of retained scybalæ and an end-to-end anastomosis was performed.

This patient also made an excellent recovery. The growth proved to be a columnar-celled carcinoma. At the present time the patient is quite well, I believe.

CASE 5. *Carcinoma of the sigmoid with secondary growth in the anterior rectal wall simulating a malignant ovarian tumour.*—In 1909 a patient aged 54 years was admitted into the Middlesex Hospital under my care as a case of malignant ovarian tumour. She was a miserably emaciated-looking woman with a degree of general abdominal distension but with no defined tumour to be felt from above. On vaginal examination a large mass lay between the back of the uterus and the front of the rectum and was apparently adherent to both. On rectal examination the tumour could be felt pressing on to the anterior rectal wall, which it had evidently superficially involved, but the mucosa of the bowel was unaffected. The history of the case was one of abdominal and pelvic pain for some months. For the last three weeks she had had diarrhœa.

I opened the abdomen in the middle line and found that the tumour was screened by a quantity of adherent omentum. It was apparently springing from the back of the right broad ligament, and I thought at first that I was dealing with some tumour of the ovary belonging to that side. I began to separate it, when a quantity of fæcal matter escaped into the pelvis and proclaimed the mass to be connected with the intestine. On separating it into its constituent parts and removing the diseased omentum I found it to be a large carcinomatous mass in the upper part of the sigmoid colon which had gravitated into the pouch of Douglas and then adhered to the anterior rectal wall which it had begun to infiltrate. I had torn through this mass while separating it from the rectum. I therefore resected the entire sigmoid colon, together with the upper part of the rectum, so as to include both areas of disease. Fortunately, owing to the extremely relaxed condition of the patient's mesenteries, I was able to pull the lower end of the descending colon down to the bottom of Douglas's pouch, and, obtaining sufficient free margin of the upper end of the cut rectum by freeing it from its peritoneal connexions and pulling it up, I was able to effect an end-to-end anastomosis. Before doing so, I emptied, as before, the colon of its retained fæcal matter, and as a considerable quantity of fæces had escaped into the pelvis owing to my tearing through the growth when separating it, the pelvis was carefully washed out with saline solution before I closed the abdominal wound.

The patient had a somewhat prolonged convalescence. The abdominal wound suppurated badly, but the line of anastomosis remained watertight although for some time she had a fæculo-purulent discharge from the anus. She left the hospital eventually in a very satisfactory state. The growth was proved to be a columnar-celled carcinoma.

These five cases are instructive from several points of view. The effect of gravity on tumours of the large intestine is seen to be very marked. In all of these patients the tumour mass had caused the affected portion of bowel to gravitate

downwards into the pelvis, to certain of the structures contained in which it had subsequently adhered. In Cases 2 and 5 this adhesion had occurred between the diseased bowel and the healthy bowel below it. In Case 2 actual short-circuiting had taken place and in Case 5 was about to take place. In Case 1 adhesion had occurred to the top of the uterus, in Case 3 to the front of the uterus and bladder, and in Case 4 to the back of the right broad ligament. It is therefore apparent that in growths of the large intestine one must not expect to find the position of the tumour necessarily corresponding with the normal anatomical position of the portion of gut involved, and that it is not safe to exclude from the diagnosis any portion of the large intestine merely on account of the position of the mass to be felt.

Another important fact illustrated by these cases is the large size of the palpable mass that may be produced as a result of a growth of the wall of the large intestine. This mass is a *conglomerate*—i.e., it is made up of several constituents. First amongst these is the omentum, which early becomes adherent and thickened. This is augmented by fusion of the primary growth with neighbouring coils of gut, swollen appendices epiploicæ, the uterine appendages or the uterus itself. Finally, the whole becomes rounded off by collections of organised peritoneal exudate, and the result is a tumour of large dimensions of which the primary disease forms but a small part.

When such a mass occupies the pelvis the simulation of disease of the uterus or uterine appendages may be, as these cases show, very close indeed, especially in the absence of symptoms pointing strongly to the bowel. Slight intestinal symptoms, such as moderate diarrhœa or constipation, are so commonly met with in bonâ-fide disease of the female genital organs as to be of little value in the differential diagnosis.

It will be seen that in four out of the five cases end-to-end anastomosis was performed (in Case 2 in two places). I am aware that certain authorities favour lateral anastomosis in the case of the large intestine on account of the larger aperture of communication that can be effected between the anastomosed segments of the bowel. End-to-end union has, however, in my hands proved very satisfactory. It certainly has the advantage over lateral junction of reducing the suture line to its smallest limit and in the large intestine, where so free an anastomosis exists between the vessels of the meso-colon, the danger of anæmic necrosis of the sutured ends is very slight.

I have always used three layers of sutures : the first, a continuous suture through mucosa and muscle; the second, a continuous suture through muscle and peritoneum ; and the third, a series of interrupted Lembert sutures picking up the peritoneum only. No doubt this involves the inturning of a considerable portion of the bowel wall, much of which subsequently sloughs off, but this is of small importance compared with rendering the line of junction watertight. I attach great importance to the emptying of the upper bowel before performing the anastomosis. It may be objected that this proceeding increases the risk of infecting the operation area, but I am of opinion that healthy fæcal matter, at all events, is very slightly septic, and that if the parts exposed by the incision are carefully packed off with sterilised gauze before the process and the bowel end thoroughly washed with saline solution after it, it may be carried out with great advantage to the patient.

Harley-street, W.

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# A CASE OF HENOCH'S PURPURA ASSOCIATED WITH ANGIONEUROTIC ŒDEMA.

BY ALEXANDER DON, M.A., M.B., C.M. ABERD., F.R.C.S. EDIN.,

SURGEON TO, AND LECTURER ON CLINICAL SURGERY AT, THE ROYAL INFIRMARY, DUNDEE.

A BOY, aged 8½ years, whom I saw on Feb. 8th, 1908, had been ailing for over a fortnight, but had always been able to be at school. His appetite had been very good, but he had swelling of the left knee and ankle and dysentery. A week previously there had been a swelling over the dorsum of the right foot. The left knee next became painful, and on examination his mother found that it was swollen. The elbow then became sore. This was his condition when I first saw

him. The knee and elbow contained fluid. The skin around both looked as if bruised, and on different parts of the body were what seemed like old bruises, especially a mark over the right trochanter major. Closer examination showed that many of these were really subcutaneous hæmorrhages. The patches varied in size from sixpenny-pieces to half-crowns, were irregular in outline, and were in all stages of absorption, some being bright red, others darker, and some only little more than a greenish-yellow stain. Other spots resembled fleabites and did not show the changes mentioned as they faded. One of these was on the right cheek, and others over the trunk below the umbilicus and on both legs, feet, and arms. These spots were distinctly worse on the legs and forearms. There had been diarrhœa for a week, foul-smelling and dysenteric—i.e., containing blood and mucus. There was no pain in the abdomen. The temperature was 99° F. and the pulse was 100 per minute. There was no cardiac symptom nor albumin. He was put on powders, one four-hourly, containing calomel ½ gr., salol 2 gr., and pulv. ipecac. 1 gr. Next day, the 9th, the penis was œdematous with a hæmorrhage at the frænum. It was quite free from pain and the œdema stopped abruptly at the trunk. The knee was slightly better and the elbow a good deal. There were some new purpuric spots. On the 10th the whole scrotum was livid red and œdematous, but the point of the penis was less swollen. The elbow was quite better, but there was a good deal of greenish-yellow staining down the forearm. The right hip had several erythematous patches, raised up like true urticaria, but not itchy. The diarrhœa was less frequent. The temperature was 99·6° and the pulse was 100. A sample of fæces was taken for examination. Professor Sutherland reported on this as follows:—

A. Films made directly from the specimen are examined in the fresh condition on the warm stage and after fixing with corrosive sublimate and staining in hæmotoxylin and eosin. Films are also stained in methylene blue, in carbol fuchsin, and by Gram's method. Examination for amœbæ is negative. The following organisms are recognised: 1. Bacillus coli. 2. A large Gram-positive bacillus tending to form filaments and to spore. This is not Shiga's bacillus of dysentery. 3. Gram-positive cocci in pairs and singly. Examination for tubercle bacillus is negative. B. The cultures obtained on agar are those of the above-mentioned organisms.

The œdema gradually disappeared from the penis and upper parts of the scrotum. The knee and elbow on the left side improved, and a swelling began to rise on the front of the right forearm, which pitted on firm pressure. There was pain in the right heel but no œdema. On Feb. 12th the fæces were again sent for examination, and the report is as follows:—

A. An examination similar to the last is made. No amœbæ are found. The organisms are less abundant. B. coli is present in distinctly smaller numbers. The larger Gram-positive bacillus is only present in very small amount. The majority of organisms are cocci—often in long chains. Examination for tubercle bacillus is again negative. B. Abundant growths are obtained on agar of the large Gram-positive bacillus. The B. coli and the cocci are apparently overgrown. The larger number of fatty catarrhal cells, the abundance of red blood corpuscles, and the scantiness of leucocytes in the material point in the direction of an extensive catarrhal rather than suppurative inflammation of the intestinal tract.

The patch in front of the right elbow increased in size during the next few days and then faded, leaving a greenish-yellow stain. There was great pain of a colicky nature over the descending colon, and a firm sausage-shaped tumour could be made out on palpation, though the patient winced a little and fixed the abdominal muscles on that side. The left knee and elbow were now painlessly moveable. No new hæmorrhages or swellings had appeared. Next morning, the 13th, he was a good deal better, but there was still pain along the descending colon which was less distinctly palpable. There had been no movement of the bowels. After my visit I heard by telephone that he had had a bad attack of diarrhœa with vomiting. He vomited twice, the second time quite green material. The bowels moved almost continuously, 13 or 14 times, and latterly pure blood with great tenesmus. After the last motion he was quite exhausted and dropped off to sleep. I ordered Dover's powder two grains. He slept again after the first dose. His milk was now peptonised. On the 14th he was better, the temperature and pulse being normal. The scrotum was now quite normal except at its most dependent part, where a little œdema still persisted. The only motion was of the muco-sanguineous type, with a good deal of pea-soupy fæces. There had been slight hæmorrhage from the nose. On the 15th the dorsum of the right foot and the

ankle were œdematous and pitted on pressure. There was no pain anywhere and he was quite cheerful. On the 16th, the right foot was pretty much as before. He complained very much of his back and on examination I found a new œdematous patch right over the centre of the lowest dorsal spines, which were very painful to touch. There had also been some swelling of the right ear, but it had almost disappeared, only a little remaining at the junction of the pinna with the head above. There was a little blood in the stool last night. He seemed much lower to-day. His pulse was feeble and about 130 per minute, but there was no fever. On the 17th the temperature was 99·8° and the pulse was 96. The patient was looking rather tired and cried readily. There was no more diarrhœa and no pain on palpation of the abdomen. The right knee was distended with fluid and the œdema extended up from the foot to the knee. The foot was not now swollen. The patch on the head had spread over the temporal bone, and was well defined and painful to touch. The swelling on the back was just about the same. On the 18th the knee was less painful, and the œdema was up as far as the middle third of the thigh. The greatest change was in the head. What was a small patch of the size of the palm over the right temporal ridge had spread all over the top of the head and down to the other ear, closing the right eye, and down to the supra-orbital ridge of the left. It was only slightly painful now to touch. The pulse was 110 and rather feeble. The heart sounds were quite closed in all areas, but not strong. The back had resumed its normal outline. The bowels had operated four times, once with a little blood. He felt quite comfortable, but was drowsy. On the 19th the pulse was 84 and the temperature was 99°. The swelling of the head had quite changed from where it was on the 18th. The right eye was open, and the left now closed. The swelling had travelled down the back of the head to the neck, and down the face on the right side to the ear, and on the left side to the zygoma. There were a few new spots of purpura over the legs about the knee-joints. The heart gave a slight systolic bruit over the apex. On the 20th the face was still swollen, especially over the cheeks and downwards. The right knee could now be bent slightly. The motions were dark, pea-soupy, with a little blood. He was very hungry. The pulse was still rapid. On the 21st he was much better. There was practically no swelling anywhere except on the left cheek at the angle of the lower jaw. He was feeling very well. The pulse was about 60 per minute, rather irregular, and intermittent. He had only one motion and it was more normal. The right leg was quite better. On the 23rd the stools were formed. The patient was very hungry. He was allowed a little ground rice and jelly. There was still a slight systolic murmur. The urine was very much clearer and there was no albumin. On the 25th the patient was improving. There was some dysentery yesterday, but it has ceased. There was no complaint of any kind except hunger. The improvement continued and he was able to sit up a little by the end of the month. He was advised to continue calomel and salol as disinfectants to the bowel and to prevent recurrence. This he did, and though he has at times felt out of sorts and bilious there has been no outbreak of the old symptoms during the last 14 months.

His personal history contains nothing of importance bearing on his symptoms. He was born in Australia. He had been subject to attacks of biliousness and was operated on for enlarged tonsils two and a half years ago. He was also circumcised, and at that time had an erysipelatous rash all over his body and was seriously ill. He had just then recovered from measles. His father and mother are alive and healthy. There was no history of any blood disease on either side.

This is the second case of angioneurotic œdema associated with purpura which I have met with, the first case [1] being less marked in its distribution and severity. The coexistence of these two symptoms, for one can hardly class them as distinct diseases, is mentioned by Butler,[2] and Osler[3] thinks that both may depend on "some poison—an alkaloid—possibly the result of some faulty chylopoietic metabolism, which in varying doses in different constitutions excites in one urticaria, in a second peliosis rheumatica, and in a third

1 Don: The Practitioner, June, 1908.
2 Butler's Diagnostics of Internal Medicine.
3 Osler: American Journal of Medical Science.
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a fatal form of purpura." Hyde and Montgomery [4] classify the purpuras among the hæmorrhages and angioneurotic œdema among the hypertrophies. Holt [5] includes the purpuras among blood diseases. Whatever classification is adapted the explanation given by Osler and others best fits in with the observed phenomena. There is nothing to support a vaso-motor neurosis. The swellings spread more like erysipelas or a transient cellulitis, the inflammatory adjuncts of heat and pain being often notably absent. Perrin [6] thinks that the toxins in the blood may so alter the walls of the vessels as to produce a blood stasis, with or without rupture, but if this were the only factor one would expect the condition to be more generalised. It is much more likely that the toxins act as general poisons, while the stasis is due to bacterial infection of the walls with thrombosis and rupture, [7] which would be more likely to occur in the slower circulation within the vessels of the extremities. This explanation would be supported by the pain which occurred in the right heel of this case two days before the œdema was observed, and is also quite compatible with drug eruptions, where the continued exhibition of the drug would so lower the vitality of the tissues as to allow of localised infections by toxin-producing microbes. It is extremely difficult to be certain from blood cultures that the organisms cultivated are really got from the blood, and more difficult still to exclude blood infection when no bacteria are grown. In cases of purpura and localised œdema there has been found a great increase of leucocytes, especially the polymorphonuclear cells.

The treatment varies according to the site of the infection. All inflammatory conditions must be treated locally as far as possible, such as conjunctivitis, rhinitis, tonsillitis, and pharyngitis. In acute œdema following any of these diseases surgical interference should rarely be necessary except where the air-passages are obstructed. In such cases adrenalin locally might give some relief. In those cases where the primary seat is in the bowel salol, ichthyol, calomel, and other antiseptics, with general tonics, are most likely to be useful, and as the symptoms of purpura and œdema are apt to recur periodically, as we should expect if the bowel condition is not treated or if the treatment is stopped too soon, these drugs should be continued for some months after all symptoms have disappeared. Surgical interference should rarely be necessary as the œdema of the bowel is transient, and there is no tendency to gangrene, but if the collapse with fæcal vomiting is extreme an opening into the bowel above the swelling should give prompt relief. In any case the extra risk is from the anæsthetic only. Dieting in such cases would seem to be of supreme importance, and should be such as to produce little residue, and to be easily assimilated. Rest in bed should be absolute as heart symptoms are apt to develop. Hæmorrhages into a cavity might lead to fatal collapse. Whether any vaccine might do good is rather uncertain. My own experience with vaccines has not been very encouraging. The causative organism might be isolated by the agglutinative test with the patient's blood-serum. Such vaccines were found harmful in some of Bruce's [8] mania cases and ineffective in others.

Dundee.

## ANTI-TYPHOID VACCINATION WITH ATTENUATED LIVE CULTURES.

BY ALDO CASTELLANI, M.D. FLORENCE,
DIRECTOR OF THE CLINIC OF TROPICAL MEDICINE, COLOMBO, CEYLON.

THE introduction of typhoid vaccines which have proved to be of practical importance is due to Wright in England and to Pfeiffer and Kolle in Germany. These vaccines consist of killed typhoid cultures—broth cultures as regards Wright's vaccine ; emulsion of agar cultures as regards Kolle's vaccine. Leishmann has made the important observation that the lower the temperature at which the cultures are killed the more powerful is the vaccine.

It is well known that in the lower animals, such as rabbits,

4 Hyde and Montgomery : Diseases of the Skin.
5 Holt : Diseases of Infancy and Children.
6 Perrin : THE LANCET, 1899.
7 Watson Cheyne : Brit. Med. Jour., Sept. 1st, 1883.
8 Bruce : Edinburgh Medical Journal, February and March, 1908.

the use of dead cultures for immunising purposes is far less efficacious than using live cultures, provided the live cultures be inoculated with certain precautions. In man it has been proved by Haffkine in cholera vaccination, and by Strong and Kolle in plague vaccination that the degree of immunisation obtained by using avirulent live cultures is far greater than that obtained by using dead cultures ; the same result was arrived at by me as regards typhoid fever.

*Preparation of the live typhoid vaccine.*—I now prepare the vaccine in the following manner. Tubes containing 10 cubic centimetres of broth are each inoculated with two loopfuls of a 48-hours old agar culture of a typhoid strain which has been kept alive in the laboratory for three years and is now avirulent.[1] The broth tubes are kept in the incubator at 35° C. for 24 hours ; they are then placed in a water-bath at a constant temperature of 50° C. for one hour ; after which the vaccine is ready for use. I always use it the same day I have prepared it. In this vaccine the typhoid bacilli are still alive as is proved by inoculating agar tubes in which they grow fairly well.

*Effects of vaccination with live typhoid vaccine.*—The objection to the use of live cultures for inoculation is that they may give rise to serious symptoms and may possibly transform the inoculated persons into typhoid carriers. The typhoid vaccine prepared according to the method I have described is, however, in my experience, devoid of any serious risk. Before using it on a fairly extensive scale, I inoculated (four years ago) myself and 15 of my clinic and laboratory attendants and servants who volunteered for the experiment. It is to be noted that the vaccine at that time was prepared by heating at 50° C. virulent cultures of typhoid and not avirulent ones as I do at the present time. None of us experienced any severe symptom and none of us has become a typhoid carrier. In one case after four days from the first inoculation a fever developed which lasted five days ; the microscopical examination of the blood proved it, however, to be of malarial origin.

The inoculation of the usual doses of live vaccine ($\frac{1}{2}$, 1, 1$\frac{1}{2}$ cubic centimetres) is followed by the local and general reaction, as is the case with dead vaccine (Wright's vaccine); in some cases the reaction is somewhat more marked. After three or four hours the region of the arm where the inoculation has been made becomes painful and red, and fever supervenes which generally does not last more than 24 hours and does not incapacitate one for work. In a certain number of cases (about 20 per cent.) the blood, after a few days, shows presence of agglutinins, whereas, personally, I have never seen any distinct production of agglutinins in man when using vaccines consisting of killed cultures. The director of the Chemical Laboratory, Professor Browning, kindly submitted himself to repeated inoculations of the live vaccine ; he received 1 cubic centimetre of live vaccine regularly once a week for several weeks. The first inoculation caused a little local reaction and a slight degree of fever ; the second inoculation induced a slighter local and general reaction ; the third, fourth, and fifth inoculations were practically not followed by any reaction either local or general. After the sixth and seventh the local reaction was very severe, and Professor Browning experienced a general malaise, though no fever was present. I stopped the inoculations for three weeks, after which he had another one which did not give rise to any local or general reaction. The blood was regularly examined for agglutinins. These began to appear three days after the third inoculation (1 in 20 positive, 1 in 40 bacilli immobilised, but no clumps). It reached its maximum four days after the fourth inoculation (agglutination limit, 40). After the fifth inoculation the agglutination limit was only 20, and after the sixth and seventh hardly 10. It increased again to 20 after the eighth inoculation.

*Experiments in animals.*—In rabbits and monkeys the inoculation of a single dose of live vaccine (2 cubic centimetres) induces the elaboration of a larger amount of agglutinins and immune bodies than the inoculation of the same dose of dead cultures. Very often a rabbit becomes highly immunised 8 to 15 days after receiving one single dose of live vaccine, while it may take several inoculations of dead vaccine to induce the same degree of immunity.

1 Previously I used peptone-water cultures, as the inoculation of such cultures is somewhat less painful than broth cultures.