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MEDICO-SURGICAL SUGGESTIONS

Vol. XVI.

JUNE 1947.

No. 6.

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XVI

JUNE 1947

No. 6

LIVER ABSCESS

R. SUBRAMANIAM, BSC., M.D., M.R.C.P. (Lond.),

Asst. Physician, Govt. General Hospital, Madras.

Liver abscess is the commonest complication of amœbic dysentery. Though in a large majority of cases the diagnosis is very easy, at times the symptoms and signs are misleading. One must be on guard not to miss the possibility of liver abscess in such obscure cases.

In my opinion the predisposing factor in abscess liver seems to be an alcoholic habit. In the series of my cases which I have studied for this paper, out of 32 cases I came across two cases of liver abscess in non-alcoholics. Even at the expense of being considered as overstressing, I should like to say that I consider liver abscess—case proved by aspirating chocolate coloured pus—is exceedingly rare in a non-alcoholic. Alcoholic habit seems to devitalize the liver resistance to amœbic invasion. I am quoting three cases just to show the importance of alcoholic habit. In my first case liver abscess was diagnosed in an old man. We aspirated him once and put him on Emetine. In spite of that he was sinking. Finding that he was not improving, we asked him as to what he wanted. He wanted a pot of toddy to drink and he was given the same as his general condition was too poor. In a day or two he died and partial autopsy showed a big liver abscess containing a small amount of pus and the rest of the abdominal visceral healthy. In the second case a man was admitted with abscess liver. He was aspirated 18 years ago and we aspirated again typical chocolate coloured pus. The liver had shrunk and he was afebrile. At this stage he took leave to attend his daughter's marriage, went out, drank heavily at the wedding and in a week's time he was back in the hospital with the recurrence of symptoms and liver again palpable four fingers breadth below the costal margin. We again aspirated about 10 oz. of pus and warned him not to indulge in alcohol. He was reporting himself once in a way for two or three years when he was found to be maintaining his health. Later he joined the Military in 1942 and by 1945 started to take alcohol and

in 1947 reported sick with hepatitis. This time we did not strike any pus and the hepatitis responded to Emetine treatment.

I have come across liver abscess only twice in women. In the second case which occurred in December last year when I inquired for a 'coholic' habit the women actually said brandy was very welcome. This woman was aspirated twice and she was a heavy alcohol addict. It is well known that liver abscess is comparatively infrequent in women. Even amoebic dysentery is less common in women than in men. This might be due to the more sheltered life that they have. But the liver abscess as a complication in women is almost a curiosity. I presume it is so because they do not indulge in alcohol. For the same reason liver abscess is very rare in children. The youngest age recorded is by Bigram A. G. in 1932 of a case of amoebic dysentery in an Egyptian child three months of age who had also amoebic abscess of the liver. Child died of broncho-pneumonia and autopsy showed amoebic ulcers in the bowel.

Pathology of liver abscess.—*Entamoeba histolytica* reach the liver from the dysenteric ulcers in the colon through the portal vein in large numbers. At this stage it can be compared to an army on the march and amoeba are scattered in the liver and cause a diffuse inflammation or hepatitis. At this stage if a needle is put into this enlarged liver only blood is drawn. This condition improves dramatically with Emetine. If the amoeba meets with devitalised liver cells and gets a hold it multiplies and by a process of co-agulative necrosis causes destruction of the liver. This occurs in various centres and these spread, and by a confluence lose their individuality and constitute a large abscess. Thus the pus inside is actually a liquefied liver and not due to suppurative process as in a coccal infection. Hence culture of this pus is always sterile unless secondary infection has taken place. The abscesses may fail to coalesce and then we get multiple liver abscesses. The pus when secondarily infected is no longer chocolate coloured but is greenish or yellowish depending upon the organism. The commonest secondary organism seems to be *B. coli*.

The abscess may slowly work its way to the surface and may even rupture into the adjacent portion as into the pleural cavity, pericardial cavity into the peritoneum or rarely into the surface by a sinus. In chronic abscesses the pus may be well walled off by a wall of connective tissue. In these cases, signs and symptoms are apt to be misleading. If as a result of treatment, the amoeba are destroyed, calcification of the abscess wall may take place. Amoeba themselves are not usually seen in the liver abscess pus. They are only seen in the scrapings from the wall of the abscess cavity. Cysts are never found in the liver abscess pus.

Liver efficiency tests are likely to show greater deficiency of the liver in the hepatitis stage, and in a chronic abscess liver in

which the abscess is well walled off, the liver efficiency may be normal.

Symptomatology.—There are few diseases with such varied symptomatology. Even the best of clinicians have missed abscess liver and diagnosed one when it was not there. In a typical case patient complains of pain over the side of the chest over the liver area or over the shoulder. The pain is fairly severe, with fever coming on in the evenings. At the onset of the fever, there may be rigor but there may or may not be further rigors but occasionally there may be daily rigor. On examination there is bulge on the right side of the chest over the liver area and also over the right hypochondrium. The liver is enlarged and tender. The enlarged liver is smooth and not nodular. It may be moderately firm or even very hard. Quite a few cases have even been misdiagnosed as cancer liver because of the hardness of the liver that might occur in some cases. In most of the cases over the right base of the lung percussion note is impaired and the breath sounds may be feeble or even absent with fine rales. This may be due to either the upward enlargement of the liver in the right upper quadrant or associated pneumonitis in the right base or to pleurisy with or without effusion in the right side. This pleural effusion may be clear straw coloured fluid showing that the pleura is being irritated or in some cases the liver abscess may burst in the pleural cavity. When liver abscess bursts into pleural cavity—if the lung itself is not adherent to the diaphragm—it may behave like pleural effusion due to any other cause. If, on the other hand, the lung is adherent to the diaphragm, then the patient may cough out liver abscess pus, and the liver might suddenly shrink. I can now recall a case. A wandering Sanyasi was admitted with what appeared like an oval tumour filling up the right hypochondrium, right loin and almost reaching the right iliac fossa. No definite diagnosis could be made. The tumour was found to be moving with respiration and looked as though in continuity with liver dullness. The man gave a history of dysentery some years ago and was an alcoholic. He was complaining of pain and was also running a temperature between 102° to 103°. Though we were not certain of the diagnosis we put the patient on Emetine I. M. daily and on the 2nd day the patient said he was feeling giddy and vomited about a pint of chocolate coloured pus and in the course of the next few hours the tumour disappeared under our very eyes. He was spitting bile stained saliva for a few more days and this man made an uneventful recovery.

In a typical case the abscess may actually point in various parts of the chest or even in the back. In one of my cases, our surgeon even thought it might be abscess of abdominal wall. In another case the abscess had worked its way into the anterior abdominal wall and presented as a small ball-like structure in the

anterior abdominal wall. Only on the table it was realised that it was a case of liver abscess which had worked its way into the rectus sheath. In another case the abscess had worked its way into the small of the back and was diagnosed as perinephric abscess. This case again was properly diagnosed only by operation. In another case a man came complaining of pain over the area of right kidney and intermittent type of temperature. Fever used to be coming on with rigor. There were not positive clinical findings except slight tenderness over the small of the back on the right kidney region and very slightfulness. Urine did not show any change and urine culture was sterile. All the same he was put on alkaline diuretic mixture for a few days with no benefit. One day the patient complained of a severe pain and said that something had given way deep in his chest and in a few minutes he was in a state of shock with profuse perspiration and fast and feeble pulse. Clinical examination showed signs of pleural effusion right base and a chest picture taken in the next few hours confirmed the diagnosis. In view of the fever and the abrupt onset of effusion liver abscess bursting into the pleural cavity was thought of and a needle was put into the pleural cavity and chocolate coloured pus was aspirated. Patient was immediately started on Emetine therapy with considerable improvement. In this case the liver abscess must have been situated posteriorly and pressed upon the kidney, causing a slight amount of fulness over the loin and stimulated pyelitis.

Jaundice does definitely occur in the course of liver abscess. Failure to bear this possibility in mind has been the cause of missing at least quite a number of cases by clinicians. In one of my cases a man came with jaundice, enlarged spleen and liver and intermittent type of fever. Jaundice was of the obstructive type. He gave a history of alcoholic habit and also of having had dysentery some years ago. We put him on a course of Emetine and aspirated about 8 ozs of pus and the jaundice promptly cleared. A few days later he was admitted again with jaundice. He was aspirated again and the jaundice cleared within a day or two. In this case jaundice showed unmistakable relationship to the abscess liver. In another which I happened to see was in an old man past 55 or even more. This man was toxic and deeply jaundiced with a very big liver which was nodular and very hard to the feel? Primary carcinoma liver was the diagnosis made. At the autopsy it proved to be a case of liver abscess and the nodularity felt in the wards turned out to be due to the abscess wall bulging through the healthy liver. In this case the age of the man, the nodularity of the liver and the hardness of the liver completely misled everybody and but for the autopsy this would have been completely missed. So it is worth bearing in this factor in mind. An enlarged liver with fever and

jaundice means the possibility of a liver abscess. Another of my case, again an old man, was admitted with what looked like a case of congestive heart failure. The patient had oedema of the legs and arms with slight puffiness of the face. He was deeply jaundiced and an abscess pointing in the anterior abdominal wall. It looked as though the abscess would burst any minute. I put him on Emetine and showed him to our surgeon. He was operated on immediately and about a pint of pus was drained. Left to me I would not have advised operation at that stage but my surgeon was afraid that the abscess might burst and thus might become an emergency. He had to be aspirated two or three more times before he recovered completely. In this case by the 3rd day the oedema of the legs and arms cleared up and in a week's time the jaundice also cleared up but he developed broncho-pneumonia for which he was put on Sulphathiazole and was fully recovered at the time of discharge. In this case there were several features which were misleading in arriving at a diagnosis. The patient having congestive failure symptoms and abscess pointing almost like a tent in the anterior abdominal wall and deep jaundice. My chief called my diagnosis a bold one. This case illustrates the type of cases that come with symptoms of congestive heart failure. I have seen another case with symptoms of heart failure and generalised scabies. In this case for a time at least the liver abscess was missed. Text books do not mention this type of cases. The problem in this type of case in Emetine therapy. I am of opinion that the heart failure is only secondary to abscess liver and it can only be cured by drainage of the abscess and Emetine therapy. I advocate Strychnine or Coramine or any other cardiac stimulant may be given along with Emetine. I will refer to this point later when I come to the treatment.

In only a very small group of cases we get the abscess liver and dysentery being present at the same time. In my series of cases in only two cases were the amoeba seen in motion. Motion examination may more advantageously be done for cysts but it is not easy to spot them. In the analysis of 32 cases in only two cases were E. H. seen. It is easier to look for such indirect evidence as thickening of the ascending or sigmoid colon. It is very exceptional for the transverse colon to show any evidence of thickening.

Rarely it is the complication that occurs in the course of the abscess that is likely to draw attention to the existence of the liver abscess. The abscess might burst into the neighbouring structures. By far the common sites for rupture of the abscess are into the pleural cavity and peritoneal cavities. I have seen one case in which the abscess burst on to the skin. The case in which it burst into the pericardial cavity was a middle aged man. He was first seen by me in a mild state of shock with

thready pulse and cold sweat. He complained of severe pain in the epigastric region. Examination showed liver enlargement two fingers breadth below the costal margin. I admitted this case as hepatitis. In the wards he got over the state of shock and was quite all right in about three hours time. At this stage he gave a history of periodic attacks of pain coming on two or three hours after food and being relieved by taking a little food. In view of the history I thought I was dealing with a case of duodenal ulcer. Fractional test meal showed low acid and barium meal series failed to reveal any defect in the duodenal cap. I thought of the ulcer with perigastric adhesions. By this time again for no reason while he was at perfect rest he went into a mild state of shock. This only further favoured my suspicion of perigastric adhesion causing sympathetic disturbance and our consulting surgeon suggested that it might be only liver abscess and took over the case. He put the patient on Emetine $\frac{1}{2}$ gr. I.M. daily. After three injections were given patient again developed a state of shock but this time it ended fatally. At autopsy it was found to be a liver abscess that had burst into the pericardium. In this case we had two misleading features. One was the periodicity of pain in relation to food simulating duodenal ulcer (subsequently I have elicited such a history in a number of cases). Probably it is the distension of the duodenal cap pressing on the inflamed liver that causes the pain). The second misleading thing was periodic cold sweat and a state of shock from which the patient recovers in the course of a few hours. Very rarely the abscess might burst into the perinephric tissues.

The aids to diagnosis are examination of blood, a skiagram of the chest and finally aspiration of the enlarged liver.

Blood shows leucocytosis in the hepatitis stage and in the acute stages of the liver abscess. In some of the chronic cases when the abscess is well walled off by fibrous leucocytic does not occur. In one of the cases leucocytic count done three times showed only 4,000 per cm m. The liver was enlarged to such an extent as to almost completely fill the entire abdomen, leaving only a very small area free between the margin of the liver and symphysis pubis. On opening the abdomen was occupied almost completely by the liver and on incising the liver $7\frac{1}{2}$ pints of pus was drained and scrapping from the wall showed motile amoeba. This patient was put on Emetine with complete recovery. A few days later at the time of discharge liver was only just palpable.

X-ray of the chest is a very valuable procedure. It may not be of any value when the abscess enlarges downward or is situated in the left lobe. It is of the greatest value when the abscess is situated in the right upper quadrant. In a few cases in which effusion right base is suspected X-ray chest has shown only raising of the dome of the diaphragm without any displacement of the heart. In

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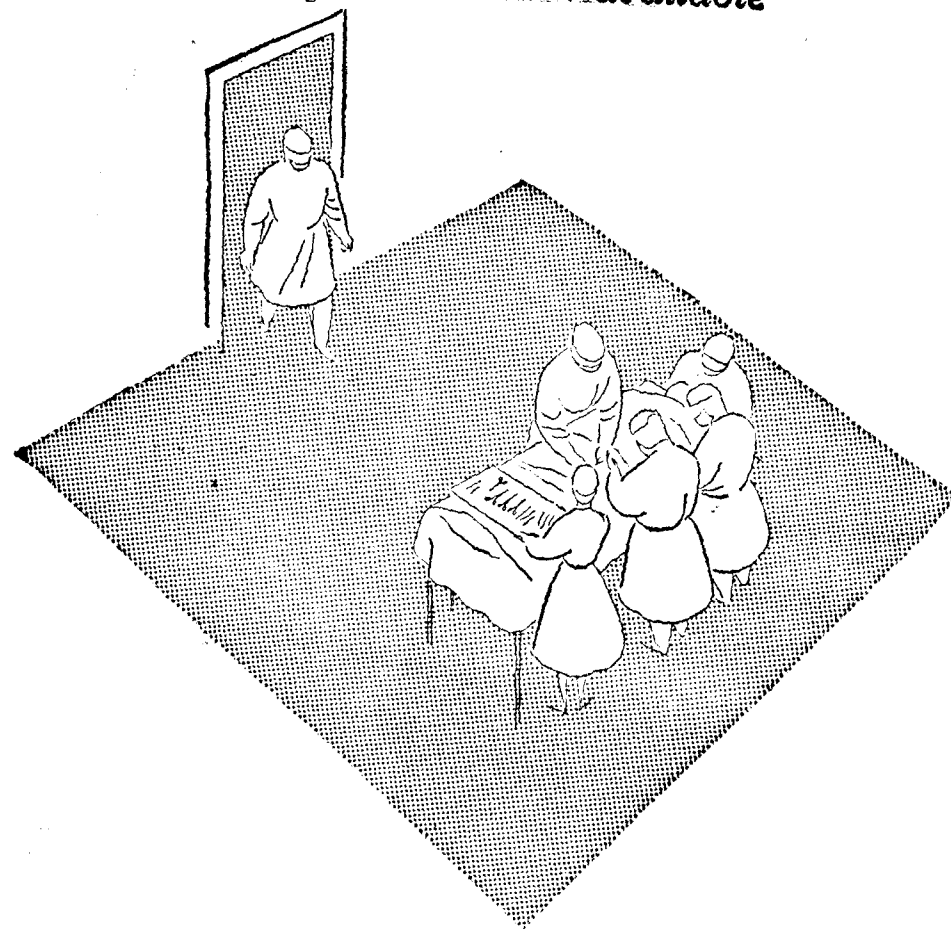
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two cases where the patients were very markedly emaciated and complained of pain in the abdomen with doughy feel they were suspected in one as tuberculous peritonitis with a just palpable liver and in the other as tuberculous pleural effusion right side. In both cases X-ray chest showed that we were dealing with liver abscess. Screening shows absence of diaphragmatic moving on the right side in a large number of cases but where the abscess does not progress in the upper quadrant diaphragm might freely move with respiration.

Aspiration of the liver clinches the diagnosis and is also part of treatment. Once a needle is put in and pus is drawn, aspiration should be done straightway. I very well remember a physician putting in a needle and demonstrating to a batch of students the presence of pus in the morning. By night the patient developed acute abdomen and laparotomy showed nearly a pint of pus had collected into the peritoneum. In the liver abscess the pus is under tension and a needle track affords sufficient passage for the pus to leak.

Differential diagnosis in liver abscess.—As I said at the very beginning a number of conditions may be mistaken for liver abscess. The common conditions which have to be differentiated are primary carcinoma liver and a liver riddled with secondaries. The liver that is the seat of malignancy has many factors that are likely to present misleading features. It is likely to show a low temperature, hard liver which might also be tender and moderate leucocytosis and skiagram may also show elevation of the right dome of diaphragm. Aspiration might show blood stained material and if the needle passed through a portion of the liver bearing malignant deposit or malignant changes, then the aspirated material shows malignant cells as in one of my broncho-genic carcinoma cases with extensive secondary deposits in the liver. In another case, with primary growth in the gall bladder, with plenty of secondaries in the liver, it failed to show any malignant cells. Therapeutic response to Emetine may also be tried.

The other conditions to be thought of are pneumonia right base; pleural effusion right base, tuberculous peritonitis, peptic ulcer, typhoid and other long continued fevers, gumma of the liver, hydatid of the liver, perihepatitis occurring in cases of kala-azar and malaria cholecystitis both acute and chronic and also adenocarcinoma of the gall bladder. Perinephric abscess and pyelitis and malignant tertian malaria and early cases of cirrhosis liver. I do not say I have completely exhausted all the possibilities. There are many conditions not mentioned by me but I have mentioned the common ones.

A Hindu, male, aged 16, was admitted for pain in the legs and abdomen and night blindness of two months duration.

Previous history:—History of dysentery 4 years ago. History of venereal sore 5 years ago. Habits: Occasionally takes alcohol, non-vegetarian.

History of present illness:—Two months ago patient had fever for ten days. This was followed by pain in the right hypochondrium.

This patient was an emaciated young man with oedema of the feet. Pigmentation of the palate, sclera and icterus. Abdomen: liver enlarged, more the left lobe and soft. No tenderness, palpable—3 fingers breadth below the right costal margin and 5 fingers breadth in the epigastrium. The other systems were normal.

Blood W.R. was positive strong. Total W.B.C. 6,000 per cm.m. By liver aspiration through the right 8th inter-space only blood was drawn. No pathogenic organisms were seen. X-ray chest showed moderate elevation of right dome of the diaphragm.

Patient was admitted as amoebic hepatitis. He was given a course of Emetine 1 gr. I.M. daily with no benefit. Since the left lobe was enlarged and only blood was drawn in the aspirating syringe left lobe abscess was diagnosed and the case was transferred to surgical side. Under local anaesthesia laparotomy was done. Liver was not adherent to the peritoneum. Liver surface was smooth. Aspiration of left lobe also yielded blood only. Peritoneum stuck to the liver surface and packed with gauze.

In this case patient had no fever to start with and at the end of 7 injections started having fever. After the laparotomy on the 8th day patient started having fever and this responded to iodide by mouth. Eight months later patient developed ascities. He was given mercurial diuretics and milk diet and ascites cleared. In view of the history of dysentery and enlargement of the liver and emaciation amoebic hepatitis was diagnosed. This should have been revised in view of the left lobe being much more enlarged, leucocyte count being only 6,000 per cm, and the absence of response to Emetine. As a matter of fact the temperature started going up on the 8th day of Emetine injection. With the history of sore on the penis five years ago, blood W.R. should have been done at the very first instance. This type of diffuse involvement of the liver by a syphilitic process is not common and is likely to be mistaken for an abscess liver.

For every one of the conditions that has to be borne in mind can cite illustrative cases and I am sure you would also have seen cases of a similar nature.

Treatment in this condition, that I adopt as a routine is to put the patient on Emetine 1 gr. daily I.M. for 9 days. If there is no urgency then I prefer to aspirate at the end of course but where the pain is severe and abscess is bulging and threatening to perforate I aspirate at the end of 3 grains of Emetine but where the symptoms are very urgent and where delay might mean rupture of the abscess any minute I aspirate immediately after giving 1 grain of Emetine. But I always prefer if conditions permit to allow the patient to have at least three injections of Emetine 1 grain each daily, before I aspirate. This much of Emetine is enough to kill the active forms at the surface and aspiration tract is not likely to act as a passage for the amoeba to spread.

Most of the symptoms clear up by the third or fourth injection. If a patient is markedly emaciated and general condition too poor, I do not prefer to give a lower dose of Emetine but I give Emetine gr. 1 and Strychnine or Coramine along with Emetine. If the patient is febrile he becomes afebrile by this time. I do not find any advantage in putting Emetine locally into the abscess cavity and I do not adopt that procedure. The aspiration with potains aspirator is the method of choice when the abscess is in the right side of the liver to let out the pus. I have aspirated by this procedure in two of my cases as much as 64 ozs. But where the abscess is aspirated in the left lobe open operation is the ideal method. Even for this a preliminary premedication with Emetine is of great value in avoiding post operative complications. Aspiration is done if necessary more than once at intervals 4 or 5 days. Where there is urgency I aspirate at the end of three grains of Emetine and repeat the aspiration at the end of 9 grains of Emetine.

After a course of Emetine the patient is put on E.B.I, 2 grains at bed time for 12 nights.

I prefer to have the bowels regular and from the start I put my patients on Oleum Recini emulsion. By the time they have had about 6 grains Emetine I shift over to Shark Liver Oil emulsion so that these emaciated patients may put on some weight.

Prognosis in these cases is good if the abscess is aspirated or drained well and if the patient has not gone down in general condition too far. It is surprising how even very advanced cases respond to aspiration and Emetine.

In my analysis of 32 cases only 2 deaths occurred. Abscess liver is likely to recur if the patient takes to drinking alcohol again. This is one of the few conditions where under our very eyes with proper treatment a patient gets remarkably better in the course of a few days. (*The Antiseptic, May 1947.*)

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The incidence of this serious infection was high in 1914—1918. Even in desert campaign, the incidence of anaerobic myositis was 3.4 per 1,000 (Madden 1944), in Tunisia 6.7 per 100.

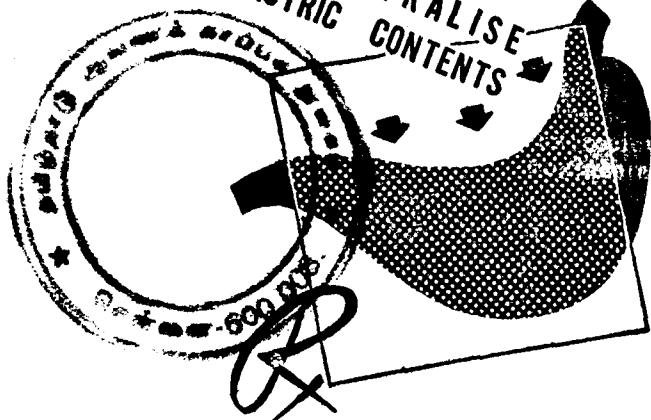
The Value of Penicillin in Surgery: Penicillin has a great value as a prophylactic of wound infection. During 1945 war casualties had marked absence of severe sepsis and incidence of all wound infections. The most dominant factor in this was the use of penicillin. This fact was confirmed by bacteriological investigations as well. In the 1942 Middle East Campaigns "no growth" reports on the first wound swabs, taken after admission of casualties to hospital were most uncommon, a positive culture was obtained in a series of 100 cases at one centre. In the N. W. European (B.L.A.) campaign of 1944—5, "no growth" reports were common and phyogenic infections were relatively uncommon (Porritt and Mitchell), 1946. *Sterptococci* were isolated only in 5 per cent of cases in B.L.A. casualties as against 68 per cent in M. E. F., *Staphylococci* in 25 per cent as against 58 per cent, *Clostridia* 2 per cent, as against 28 per cent, coliform 10 per cent, as against 6 per cent, and in Italy not less than 10 per 1000 (Jeffre and Thompson 1944). In N. W. Europe the incidence in Allied troops (Porritt and Mitchell 1945) was only 1.5 per 1,000. The death rate in the N. W. Europe was exceptionally favourable, being 21.5 per cent.

Prophylactic Use: In minor wounds local application alone is usually adequate. Penicillin powder 5,000 units of penicillin per gramme, the diluent being sulfonamides or powdered plasma; is used. It is dusted on the wound at the first examination. In serious cases local and par enteral use (15,000—100,000 units per injection are used at 3 hourly, 6 hourly intervals) is needed. The dose and frequency of administration depend on the severity of infection.

Value of Penicillin Therapy:—Penicillin treatment by curing sepsis made secon dary sutures, grafts and plastic procedures safe for the patient. Lot of time and suffering of the patient, material and attendance of hospital staff were saved. The work of Florey and Cairns (1943) and others showed that many wounds could be closed safely under the protective action of penicillin. Prophylactic use of penicillin made at least 9 out of 10 wounds clinically clean and secondary sutures could be performed successfully in such case.

G. A. G. Mitchell reviewed the results of wound sutures in 4,432 cases treated with various methods. Penicillin therapy gave results with success in 80.86 per cent of cases, success and partial success in 95.98 per cent of cases. These results with sulphonamide therapy locally and parenterally were 62.41 per cent and 83 per cent, with local sulfathiazole and proflavine mixture 54.09 per cent—81.97 per cent. The highest percentage of success was in cases treated

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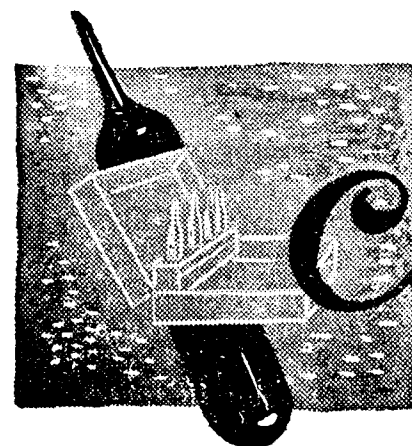
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with parenteral penicillin only. Briefly speaking, success in penicillin cases was about 81 per cent as against about 63 per cent in other cases, success and partial success was about 94 per cent in penicillin cases as against about 84 per cent in other cases.

Results of penicillin therapy will appear still far better when it is realised that penicillin therapy especially the parenteral was given to serious and major types of wounds.

B.M. J., G. A. G. Mitchell,
January 11, 1947. (Pages 41-45.)



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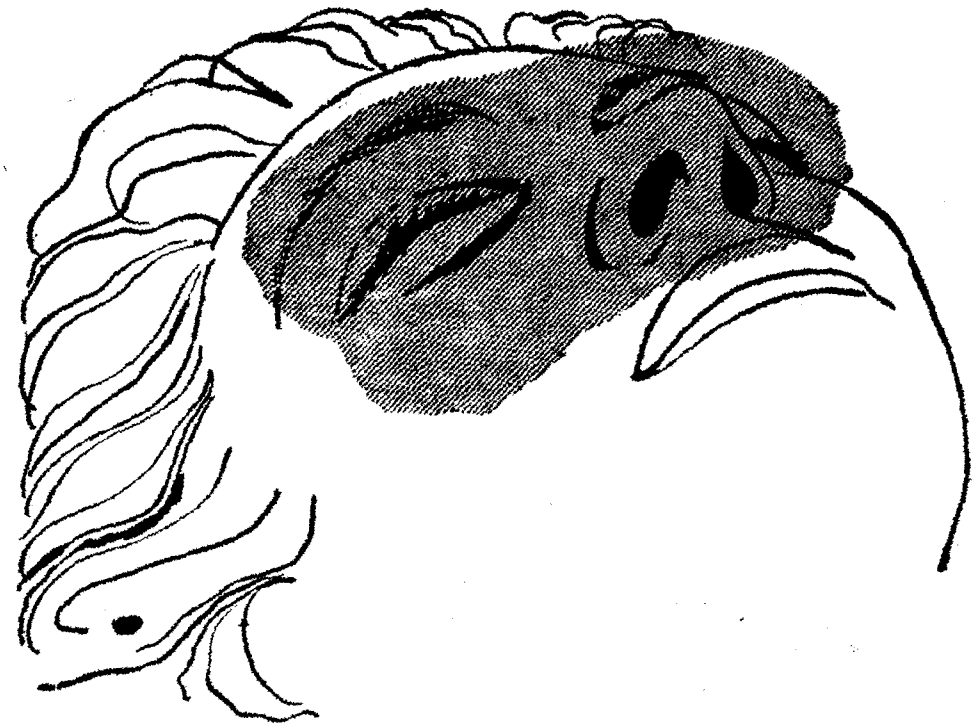
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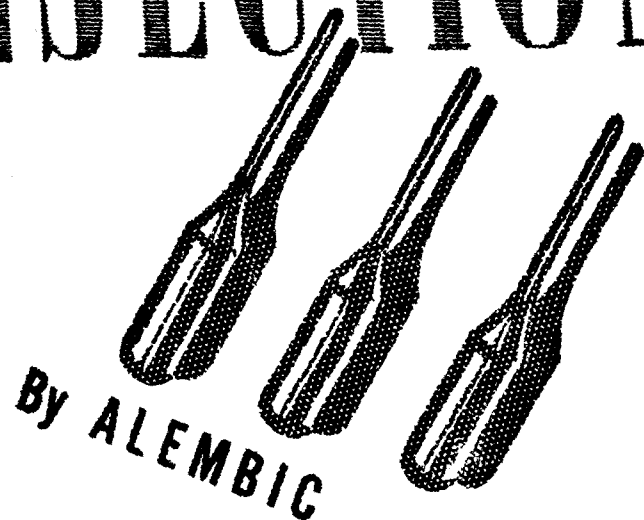
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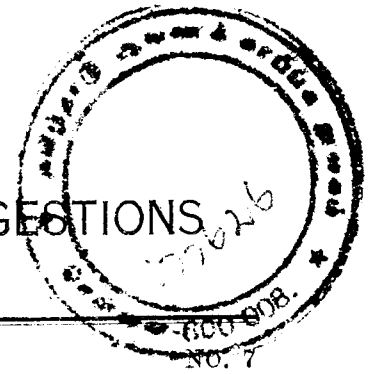
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JULY 1947



THE VALUE OF THE STAINED VAGINAL SMEAR IN GYNECOLOGICAL DIAGNOSIS

BY HERBERT F. TRAUT, M.D.

San Francisco, California.

The history of gynecological diagnosis has been divided and the characteristics of the successive eras have been shaped by a series of discoveries, inventions, and methods. The vaginal speculum, the uterine sound, bimanual pelvic examination, the uterine curette and other tissue sampling techniques, bacteriological examination and tubal insufflation with x-ray visualization, all have added to the possibilities of observation and deduction. Each has made a contribution appropriate to its sphere of application. The essential usefulness of each contribution has required many years to assay, and not infrequently new methods have, in the course of events, modified the importance of older ones.

The purpose of this paper is to describe what we know of a new method of diagnosis as it may be applied to the field of gynecology as a whole. The stained vaginal smear as a laboratory entity is not really new. for Papanicolaou has been studying it for many years, first in animals and more recently in the woman; however, in its interpretation and in its readiness for practical application it is new, for it has only been in the last few years that the effects of pathological processes have been sufficiently shifted from the normal variations of the cells to make application of the procedure of practical value to the diagnostician. Either fortunately or unfortunately, we have been led to think of the vaginal smear chiefly from the point of view of the diagnosis of uterine cancer. This may be justifiable, because the record of the method in revealing early cancer lesions cannot be approached by any other means. However, this interest in cancer has seemed to hide the fact that the procedure can reveal many other normal and pathological processes occurring in the utero-vaginal tract. Our experience in New York, and more recently in San Francisco, has led us to feel that it should become a part of the routine gynecological examination almost, if not quite as essentially, as the use of the speculum or manual palpation. Certainly it is more important than routine blood examinations, urine analyses, or Wassermann tests. The

variety of information it is capable of giving should place it at the top of all laboratory-involving procedures as far as the gynecologist is concerned, for it reflects normal physiological states, as well as the pathological, with a fidelity which would seem to indicate it as indispensable. The only close analogy to it from the general clinical point of view is the study of blood smears. Hematology has become an indispensable adjunct to internal medicine. The study of vaginal smears can become an even more important asset to the gynecologist. It would seem almost certain that, in time, this procedure would become as definite a part of the routine of gynecological diagnosis as bimanual palpation. For this reason we feel that this method should be brought to the attention of all physicians caring for women patients. We have learned to anticipate and have learned to interpret the results from blood examinations; indeed, no physical examination is considered complete without such a study. The same attitude should prevail with regard to the more specific gynecological examination.

Principles of the Vaginal Smear Technics

Exfoliation of cells from the epithelial surfaces of the endometrium, endocervix, portio and vagina occur normally as an expression of the hormonal stimuli of the ovarian secretions. These cells drift downward and collect in the fornix of the vagina, where they remain for sufficient periods of time unless artificially disturbed so that one may recover them and by placing them upon a glass slide can study their characteristics. The size, shape, intracellular characteristics and staining reactions of the cells change with the various ovarian stimuli of lack of them, to which they have been subjected, so that one can tell the preovulatory phase from the postovulatory, the menstrual and post-menstrual almost as surely as though one were examining an endometrial biopsy. And of course very much more easily and simply, for the vaginal smear can be an office procedure without invasion of the uterine cavity. In like manner catamenial changes, the menopause and even pregnancy may be suggested by evidences of considerable certainty.

In abnormal states such as infections of the endometrium and endocervix, trichomonas and monilia vaginitis, hyperplasia of the endometrium, uterine polypi, as well as cancer, the vaginal smear exhibits cellular characteristics which are not only suggestive but more and more often diagnostic. The cervical mucus acts as an albuminous adhesive and attaches the cells to the glass slide upon which they are spread. One should attempt to distribute the cell mass somewhat evenly over the surface of the clean glass slide, although great care in achieving thinness is not essential. It is more important to make the smear quickly and then plunge it before it has had a chance to dry into the fixing solution. This solution consists of equal parts of 95 per cent alcohol and ether. In

it the slides may be stored for days without danger of deterioration. It is well to place a paper clip on each slide to prevent rubbing against one another and thus prevent marring of the smear. The paper clip is also useful in attaching small piece of paper with essential data, such as the name and date, to the slide.

It is well to remember when securing material from the vaginal fornix that any procedure which effects a dilution, such as bleeding, douching, vaginal examination or coitus, should be compensated for by making multiple rather than single smears. Of course a few hours' delay, if practicable, would be even more efficacious thus allowing a reaccumulation of cellular material.

Staining of the smears is a very important matter, and one to which a great deal of attention has been given. Perhaps unfortunately, what we have to say about diagnostic possibilities of the vaginal smear can only pertain to the properly stained one. Because of the mucus present in the material, translucency can only be obtained by use of alcoholic stains. Watery solutions produce clogging and obscure cellular detail. A good nuclear stain is essential, particularly for cancer diagnosis. In addition, the cytoplasm and its inclusions must be allowed to react to acid as well as alkaline dyes. These staining requirements though not complex are definite and must be met if success is to be realized. Several good stains, already compounded and in solution, are available on the market. As the staining is of greatest importance and should be uniform, it is well to carry out the process, staining several slides at a time in small metal racks. This also serves to cut down the total time consumed and will serve to remove one of the chief technical obstacles to the method. In the ordinary office a nurse attendant can easily be trained to carry out the procedures. If later one trained to microscopic diagnosis can afford to spend some time in scrutiny of the slides, both the physician and the patient will benefit.

Study of the stained Smear Preparations

This is a time-consuming process and usually requires a trained cytologist with some experience for ultimate diagnosis, although much can be done by self-training on the part of any interested physician. The average slide should be accorded at least five minutes' study, and some will require twenty or more. Thoroughness is the keynote of success. The work, therefore, should be done by those having had training and who may be given adequate time for the purpose. This will usually mean a pathologist with a central laboratory to which preparations may be sent for staining and study. In all probability it will only be exceptionally that the gynecologist will have the training and the time to stain and study the smears.

A detailed description of the various types of cells to be found under changing circumstances together with their significance

cannot be entered into here. To learn to recognize them is a matter of training at the microscope. However, some indication can be given briefly, referring those seriously interested to the literature and the atlas already available.

Normal Menstrual Cycles

Preovulatory phase: the large cells are essentially flat and discrete, do not tend to agglutinate. The individual cell has a cytoplasm which has an affinity for the acidophilic stain and contains toward the end of the phase, small round granules which we think from their size and number may be an expression of the degree of estrin influence. The nucleus is relatively small and is basophilic.

Postovulatory phase: the cytoplasm tends to become basophilic; the inclusion granules disappear. The edges of the cell tend to crinkle and the individual cells adhere to one another as though sticky. The nuclei are generally paler in their reaction to the basophilic stains and are much increased in size.

These changes are marked and with a series of vaginal smears taken at different stages in the cycle, at four or five day intervals or weekly, serve to give a reliable record of ovarian function. Combined with basal body temperature records the two sources of data form the most reliable basis for the study of utero-ovarian relationships.

The post-menstrual phase, as also the premenstrual and menstrual, have definite cellular responses which are recognizable and may be of importance in any complete study of individual cases.

Anovulatory Cycles

These cannot be discerned except by following a series of smears at weekly intervals over the whole month or a succession of months. Because the woman of normal intelligence can easily be taught to make smears from her own vagina, fix them and bring them to the laboratory, such a study becomes an easy and relatively inexpensive method of following the fundamental reproductive processes of an individual.

The first anovulatory cycle is expressed in the vaginal smear by a persistence of the various criteria which have been outlined for the preovulatory phase. That is, the cytoplasm of the cell remains acidophilic beyond the time for normal ovulation; viz., fourteen days before menstruation, and the cells gradually become pyknotic as menstruation approaches. There is little or no tendency for the cytoplasm to become basophilic and the agglutinative tendency of the ovulatory cycle does not appear.

With the second anovulatory cycle the cytoplasm becomes more acidophilic, that is it takes the eosin or fuchsin dye (red) in greater degree. More of the brown inclusion bodies may be noted and the nucleus remains relatively small and densely basophilic.

When three anovulatory cycles occur successively, the vaginal smear approaches what one observes in association with cystic glandular hyperplasia of the endometrium. It is an expression of unopposed estrin influence, without much shedding of the endometrium and without adequate progestin or corpus luteum influence. In the vaginal smear this is represented by an abnormal affinity toward acidophilic strains, smaller individual cells of discrete nature, many of which show keratinization, and in addition the cytoplasm includes large brown, round bodies. The nucleus remains small and densely basophilic.

Cystic Glandular Hyperplasia or Hyperestrinism

The description just given for the third anovulatory cycle is apt in depicting what may be observed in the vaginal smear under these circumstances. Hyperkeratinization of discrete cells may be a fair summary of the findings. In our experience the degree of acidophilic response of the cells in hyperestrin states is only approached by the cells in trichomonas vaginitis infections. Many patients checked by both vaginal smears and curettage biopsy have taught us that the diagnosis is as clear in the interpretation of the vaginal smear as upon curettage—an important application of the procedure to office gynecology.

Amenorrhea

In primary, as in secondary amenorrhea, the cellular response as reflected in the vaginal smear, is one of degree. In the individual who has a marked pituitary or ovarian lack the smear may more or less nearly approach that of the postmenopausal or senile woman.

In scanning smears from the vagina of such individuals, one will observe many small basophilic cells with nuclei disproportionately large. The individual cells have a round or oval appearance and have a uniformly homogenous cytoplasm. The nuclei show a normal chromatin content, but relatively few nucleoli. One can judge of the degree of ovarian or pituitary suppression by a comparison between the larger or more mature cells and those of a small, atrophic appearance.

In following various attempts at therapeutic correction, the vaginal smear is an indispensable index as to the efficacy of such treatment. For with stimulation of the gonads by the use of gonadotropins—when it rarely occurs—one can observe a response in the appearance of the more mature forms of cells in the vaginal smears. Or if one chooses to use estrogens, one can quickly observe the appearance of cells of such a cell pattern as we have described under preovulatory phase of the normal cycle; that is, large, well formed, flat, discrete, acidophilic cells. In this way the effects of therapy can be evaluated. In addition, as most often happens, the persistence of the cells characteristic of preovulatory phase, without the advent of basophilic change plus crenation and agglutination

of the cells, serves as a caution to the therapist that he has fallen short of the objective—*viz.*, normal ovulation, and thus may be used as an indication and guide for progestin therapy in combination with the use of estrins.

Pregnancy

In our experience the vaginal smear is of little or no assistance in the diagnosis of early pregnancy. However, pregnancy after the second or third months shows a profound change in the character of the cells which are observed in the vaginal smear. The individual cells are about one-half the size of those of the normal menstrual cycle and tend to be more basophilic. They undergo a marked change in form also, in that they are clumped and are boat-shaped as to cellular outlines and as to nucleus.

Vaginitis

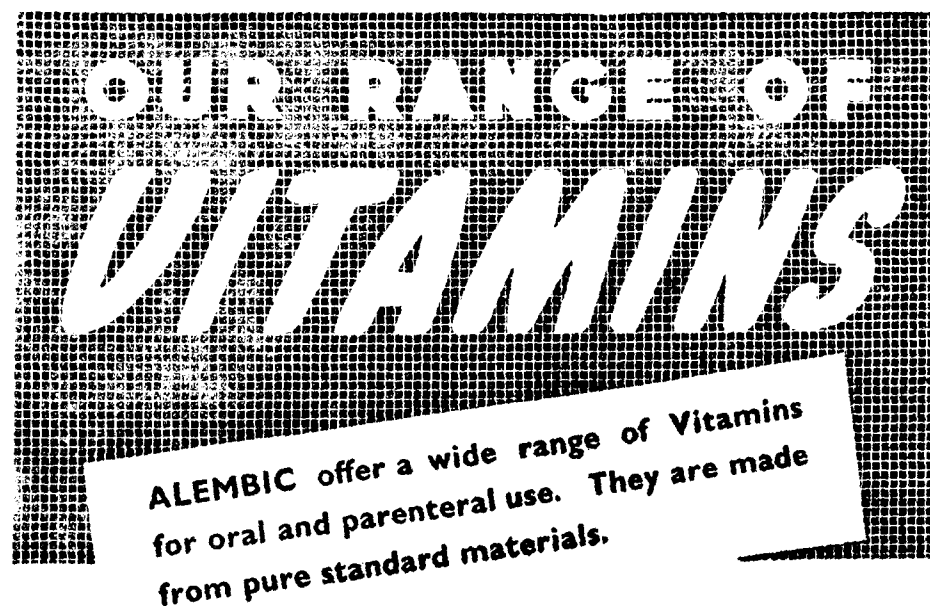
The various forms of vaginitis, that occurring during the reproductive period of life and that seen in the postmenopausal period, are characterized by definite findings in the vaginal smear.

In trichomonas infections one may see the stained trichomonads and in addition there is a most advanced and marked degree of keratinization to be observed in the cells of the vaginal smear. Because of the keratinization one should be careful to differentiate between hyperestrin keratinization and that due to the trichomonas flagellate. The latter produces clumped, often anuclear cells which take the acid stains excessively. Having observed these forms one should at once look for the small basophilic trichomonads. Finding them clinches the diagnosis. In hyperestrin states, as has been said, the cells are large, discrete, acidophilic and contain numerous brown, round inclusion bodies in the cytoplasm.

In monilia vaginitis one sees the branched yeast forms surrounded by large basophilic epithelial cells. The picture is in marked contrast to either of the foregoing clinical entities. Inasmuch as the therapy of these infestations is quite different, these smear pictures lead toward a specific therapeutic approach which cannot be equalled except by means of extensive and expensive laboratory techniques.

Menopause

The menopause is characterized by declining pituitary and gonadal function. This is reflected in the cells of the vaginal smear by the presence and gradual increase in the numbers of small round or oval, increasingly basophilic cells of the atrophic type, in many ways analogous to those in the smears of amenorrheic individuals. One can follow the gradual subsidence of ovarian function by occasional smears. The cellular picture is a most graphic and reliable index of ovarian function. Our studies in hundreds of women have taught us that contrary to common thought the decline in ovarian function in normal woman begins about the age of 35 and continues



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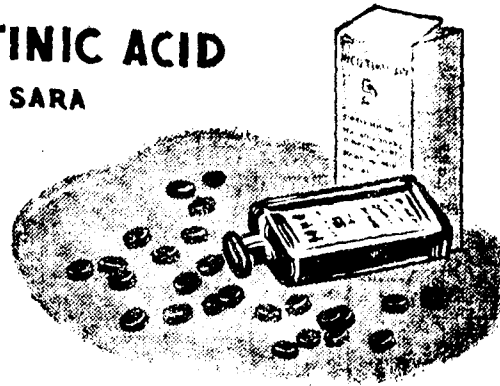
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gradually until the age of 52 or 53. Thus the physiological menopause is seen to be a much longer period of time than has been usually thought, almost twenty years being the usual course.

When emotional disturbances intervene, as they frequently do in our modern urban-dwelling women, the vaginal smear forms a most useful means of directing estrin therapy. When estrins have been given to a point where the preovulatory type of cell has replaced the small atrophic cell forms, one can be sure that adequate therapeutic intervention has been realized. Estrin medication beyond this point is seldom indicated, unless perhaps it might be in the control of migraine, although this indication is dubious. Thus the estimation of cellular response as based upon the vaginal smear content may be a most useful guide toward the treatment of the menopause syndrome.

Cancer of the Female Genital Tract

Carcinomatous lesions of the endometrium endocervical and portial epithelium are characterized by exfoliative tendencies even in the earliest lesions. As the cancer cells show typical abnormalities in their nuclei, scrutiny of the vaginal smear becomes the best means we now have for the early diagnosis of cancer in the female generative tract. Because even the intraepithelial lesions which cannot be detected by the eye or by the Schiller test exfoliate cells, the routine examination of vaginal smears becomes an obligate duty of every physician until such time as a better method has been attained.

The recognition of the characteristics of malignant cells, whether of cervical or endometrial origin, is a matter requiring experience. The pathologists look at tissue preparations obtained by local biopsy and come to a conclusion by observing individual cells, but also by the relationships of other cells, invasion, mitoses, etc. The vaginal smear diagnosis is based upon the evaluation of individual cells, sometimes in clumps, but more often scattered individually over the surface of a smear preparation. Because of the inherent difficulties, which are real but often over-estimated, we have always taken the attitude that the smear diagnosis should be seconded by a positive biopsy preparation. Most often this is eventually possible. But nothing in cancer diagnosis is more illuminating—and we may say disillusioning—than the frequently necessary repeated attempts at biopsy demonstration in the presence of continuously positive smear preparations. The biopsy is necessarily selective, whereas the vaginal smear is diffuse and all-inclusive. The latter requires careful search as compared to the former. However, because early lesions may be found by the smear studies, it has an advantage beyond that of biopsy technic.

The characteristics of cervical cancer as reflected in cell preparations—smears—pertains principally to the nucleus. Cancer

is a disease of the nucleus and visually may be detected there in the changes in size and form and in the chromatin organization of that part of the cell. As has been said, experience is necessary in attaining skill in evaluating these variations. But this should not be over-emphasized, because many resident house staff physicians under our system of training have attained proficiency. This should mean that any pathologist, without a mental block and possessed of a real desire to learn, can achieve the requisite judgment.

Endometrial carcinoma is more difficult because the cells are smaller and are nearly always shed in clumps. They stain densely and hence require a good preparation for recognition. But here, too, experience leads toward success, and we have repeatedly diagnosed lesions so early that repeated curettage failed to substantiate a smear diagnosis, which was subsequently proved correct.

It should be emphasized that the smear preparation and its evaluation should be backed up by biopsy findings in the corroborative sense before radical therapeutic procedures are resorted to. However, experience has shown that sometimes the biopsy fails repeatedly. In these instances, when the smears are repeatedly positive over a period of time, it may be well to apply the appropriate surgical approach. In doing so, in carefully selected cases we have been rewarded, not only in curing a patient in the most susceptible phase of the disease, but have learned in addition that cellular smear diagnosis may occasionally be, in good hands, more reliable than biopsy techniques.

Training Necessary for Vaginal Smear Diagnosis

Any interested physician with a good microscope and a laboratory to adequately stain routine smears can achieve some of the most important features as we have outlined them. He should be able to recognize all phases up to and including the menopausal characteristics. Many will in addition at least attain the proficiency necessary to make them suspicious of malignancy.

However, the chief benefits from scrutiny of vaginal smears will come only when routine smears are taken, not only upon the occasions when a woman presents herself voluntarily, but when such presentations are dictated by a public health policy operating in an enlightened community. If ever we give our women the followup care which the dental profession has established, then we will be approaching what our present knowledge is capable of affording in gynecological matters. Such smears usually should be processed through a central laboratory and submitted to thorough scrutiny. General pathologists may easily be trained to this form of service, though they have been somewhat resistive because they have lacked confidence in the method on one hand, and on the other it takes longer to search a vaginal smear adequately than it does to

look at a tissue biopsy. Histologists are more easily trained because they are usually more amenable to the scrutiny of individual cells, upon which the vaginal smear as well as the blood smear is based. In teaching hospitals where resident staff physicians are rotated in their course of training through the pathological laboratory one can because of his proximity to the patient as well as his association with the laboratory, be rapidly convinced and taught. Physicians having this type of training will ultimately prove the bulwark against many gynecological diseases and in their practice do much to ameliorate many of the diseases peculiar to women.

This necessarily brief outline is merely an indication of the possibilities of the vaginal smear technic in gynecological diagnosis.

(*Rocky Mountain Medical Journal*, May 1947.)

MEDICAL ASPECTS OF MALIGNANT LESIONS OF THE ANUS, RECTUM AND COLON

E. G. Wakefield, M. D., Division of Medicine: Diagnoses of malignant lesions of the anus, rectum and colon are made by the proctologist, the roentgenologist or the general surgeon at the time of surgical exploration. These diagnoses are confirmed by study of the tissue by the pathologist. A diagnosis of a malignant lesion should not be recorded on the history without a pathologic report which would substantiate such a diagnosis.

The treatment of uncomplicated malignant processes of the anus, rectum and colon is prescribed by the surgeon. In a few cases the treatment is then executed by the proctologist, but generally, however, by the surgeon. As an adjunct to treatment or solely as a palliative measure, irradiation with radium or roentgen rays may be employed. Malignant lesions of the anus, rectum and colon may be employed by the existence of other diseases in various regions or systems of the body, or they may have complications as results of themselves—that is, extension or metastasis.

The complicating diseases which may prove hazardous to the patient while the surgeon is carrying out his procedures commonly are the results of acute or chronic infections of the respiratory system, disease of the heart or kidneys, diabetes, hyperthyroidism, gout or any other diseases characterized by chronicity, with a tendency to relapse or recur after operation. A great number of patients in the age groups in which malignant lesions of the anus, rectum and colon occur have hearts, blood vessels or kidneys which are not capable of full functional activities. Generally, however, no special preoperative preparation is made for these patients unless there is some objective manifestation of decreased functional activity in these organs. If there is evidence of decreased functional activity in these organs, it is well to observe the patient long enough to be able to evaluate the limitations of function, and

perhaps to administer appropriate amounts of digitalis, insulin, antibiotic agents or to carry out other appropriate supportive measures such as the intravenous administration of fluids, if dehydration or hyperazotemia is present. Phlebitis or thrombophlebitis is a common occurrence. In such cases rest and bandaging and elevation of the part until the acute phase of the process has subsided are indicated.

The complication of the malignant process itself which is of prime importance is metastasis, and in by far the greater number of cases, metastasis from malignant lesions of the rectum and colon occurs in the liver. It should always be kept in mind, however, that an enlarged liver does not necessarily indicate that metastasis has occurred. If there are no evidences of metastasis other than a slightly enlarged liver, it is generally well to proceed with surgical exploration.

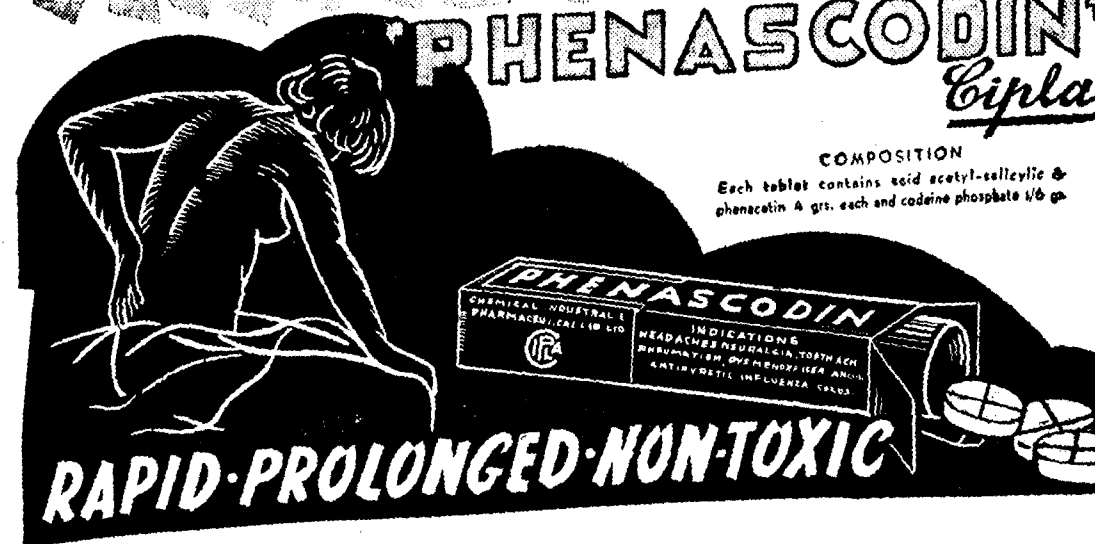
In lesions of the colon, and especially of the right half of the colon, which have been present for a long time without symptoms, a constant loss of blood may be followed by rather severe hypochromic anemia. Such a type of anemia is related to the chronic loss of blood, rather than to any sort of toxin produced in the colon. Anemia of this type is amenable to blood supplied by transfusion.

All patients before operation are hospitalized for a few days to a week for preparation for surgical operation. This preparation consists in the administration of a saline laxative agent, such as a saturated solution of sodium acid phosphate, which is administered once or twice a day. It is not necessary to administer enough of the saline laxative to make the patient too uncomfortable. The whole aim of the saline laxative is to produce a liquid or semiliquid stool which can be readily removed by colonic irrigation. Colonic irrigation is carried out twice a day during the preoperative period. It is usually continued until the return flow is clear. In the hospital these patients receive a high carbohydrate diet. This diet is not adequate and should not be prolonged if for any reason surgical treatment is postponed.

In cases in which the malignant process itself has produced local complications, such as small degrees of intestinal obstruction lowgrade perforations, very little change is made in the routine preparation of the patient. Where the malignant lesion is so situated, or is of a configuration such as to produce intestinal obstruction, then alterations in preparation of the patient for surgical operation are necessary. In such cases, nasal suction is instituted and hot abdominal stupes are applied. In some cases the administration of a saline laxative agent through the nasal tube will help to relieve the obstruction. Of course, the tube should be clamped after introduction of the laxative. The colon is again irrigated twice a day. Sometimes, beneficial results may be obtained by

carrying out the irrigation while the patient is not in knee-chest position. It is essential to administer fluids intravenously every day that the nasal suction tube is in operation. Every attempt should be made to replace, by intravenous administration, the volume of fluids that is removed through the nasal tube. It must be realized, however, that the intravenous administration of fluids will not replace all the electrolytes that are lost through nasal suction. Prolonged nasal suction is undesirable, and as soon as it is clear that the intestinal obstruction is not going to be relieved by the so-called conservative methods, surgical treatment should be resorted to immediately. The surgeon is not pleased by having to operate on a patient who has obstruction of the rectum or colon which has not been relieved by medical means, because operations in such cases usually are only palliative, and although they may be lifesaving, the patient in the end is subjected to an extra operation.

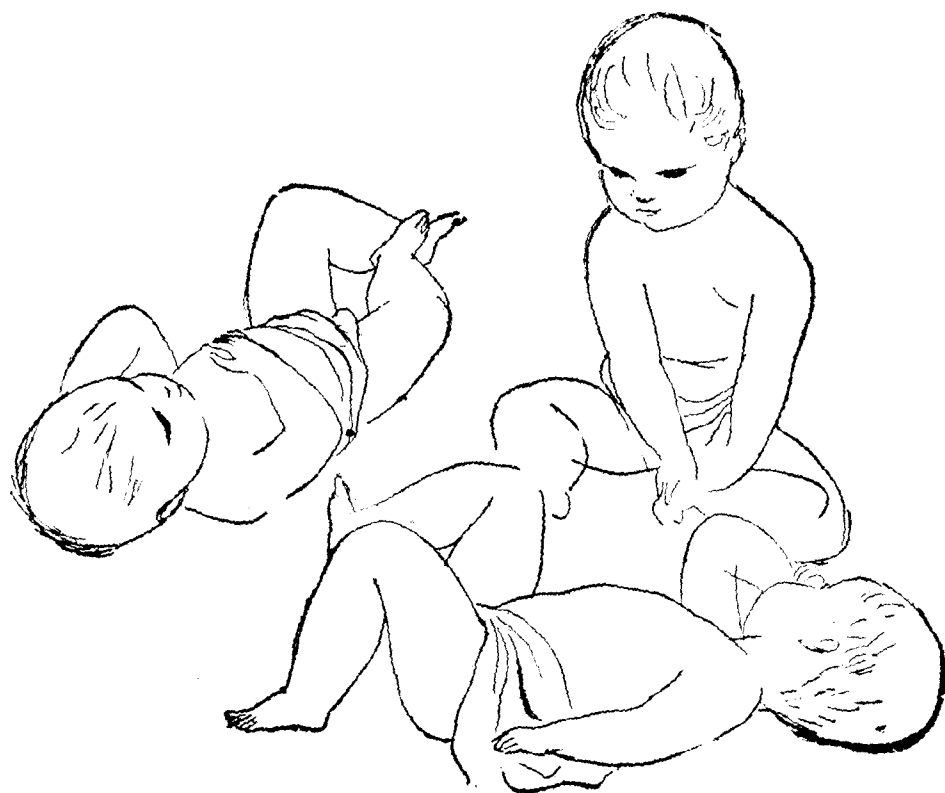
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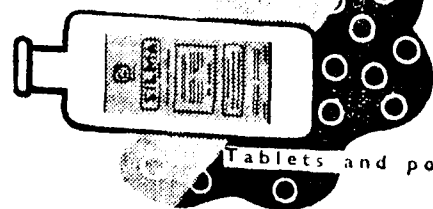
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[illegible]

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