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MEDICO-SURGICAL SUGGESTIONS

Vol. XIII.

JANUARY 1944.

No. 1.

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MEDICO-SURGICAL SUGGESTIONS

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XIII

JANUARY 1944

OSTEITIS FIBROSA CYSTICA

BY S. N. DEBOO, M.B., M.R.C.S.

Hon. Radiologist, G. T. Hospital, Lecturer in Radiology for
D. M. R. Bombay, at the G. T. Hospital Institute of Radiology,
Examiner for D. M. R. Bombay.

Hyperparathyroidism was probably first described in 1899 and its effects and association with osteitis fibrosa reported in 1901. It is well known that as a result of increased production of hormone in hyperparathyroidism, the blood content of calcium is increased, whilst that of phosphorus may be decreased. In the urine however the secretion of both these elements is increased.

Clinical features:—It is a disease usually seen between the ages of 35 and 55, although in one case it was seen in a girl of 12 years. It is a disease quite different from focal osteitis fibrosa. It is sometimes mistaken for osteitis deformans (Paget's) but where as Paget's remains symptomless for 10 years or more, and rarely influences the general health, and gives rise to very few troubles beyond pain and deformity, generalised osteitis fibrosa progresses with pain, fractures, disabling deformities and if untreated is usually fatal. The symptoms of the disease are hypotonia, constipation, bone tenderness and pain. Bone tenderness and pain are invariably present and are usually the first to draw the attention of the attending physician. Sometimes there are severe arthritic symptoms, and the type is known as arthritic type. In some cases the earliest evidence is the appearance of a tumour in the mandible-like an osteoclastoma.

Frequency:—The disease is rather uncommon and I have seen only 4 cases. The first case was seen by me some years back, where it was first diagnosed as a case of secondary carcinomatosis. On careful examination of the various bones, and the blood examination it was diagnosed as osteitis fibrosa.

Radiographic appearances:—Generalised osteitis fibrosa produces characteristic radiographic appearances. Frequently, as happened in the case mentioned above, the appearances are not appreciated if one area alone is radiographed. But when the extremities, skull, spine have been X-rayed, the appearances at once suggest the diagnosis.

Radiographic appearances are usually five. They are:

- (1) Osteoporosis general or localised.
- (2) Absorption of the compact bone.

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- (3) Formation of large cysts and giant cell tumours in the bones.
- (4) Pressure deformities.
- (5) Fractures.

Radiologically, the most striking difference between this and the focal osteitis fibrosa is generalised decalcification throughout the bone of the skeleton. The cortex of the bone usually is seen as a thin linear shadow, and the cancellous bone fades or tends to fade entirely or almost entirely.

Skull:—Shows a finely mottled or stippled appearance with small areas of bone of normal density surrounding areas of relative translucency. This is well seen in the outer table. The outline of the outer table is less defined than the normal. There may be numerous cystic areas in the skull. The sinuses may expand. The outline of the sella turcica and other basal structures may be ill-defined.

Spine:—The vertebrae may be biconcave like fish-vertebrae, and they may be flatter and smaller due to pressure. Satisfactory radiograms are at times difficult to obtain due to the fact that like osteomalacia the density of the bones is not much greater than that of surrounding soft tissues. There is very little tendency to wedging in the cervical region of the spine.

Pelvis:—The pelvis may be distorted, and shows pressure deformities due to thrust inwards of the heads of the femora. Cyst like areas are common in all pelvic bones. The femora may show coxa vara deformity.

Extremities:—All the bones may be affected, even the phalanges of the hands and feet. Marked bending of the long bones of the extremities may occur.

Chest:—On radiographing the chest and neck, a parathyroid tumour may be seen. In my 4 cases not once was the parathyroid tumour seen either in the mediastinum or the neck.

Kidneys:—The excessive excretion of calcium may give rise to calculi in the urinary tract, and therefore in all cases urinary tract should be examined. It is said that multiple calculi may occur not only in the urinary tract, but also in the biliary tract and in the salivary and pancreatic ducts.

Accessory methods of help in the differential diagnosis.

Gill and Stein state that blood studies in this condition show that the blood calcium is elevated from 9 to 15 milligrammes. The blood phosphorous is lowered from levels of 3.5-5 mgs. to 2 mgs. The chemical findings are the deciding factor in the differential diagnosis.

DIFFERENTIAL DIAGNOSIS.

Sometimes instead of bone tenderness and pain, or arthritis, attention of the physician may be directed to the bone because of an

abnormal bending of the limb, or because of a spontaneous fracture. Radiographs of other bones, the skull, pelvis, etc., may establish the diagnosis.

(1) *Osteomalacia*:—In certain cases it is difficult to differentiate between the two. Here the presence of cysts especially large and many would favour osteitis fibrosa. Blood calcium study would also be helpful.

(2) *Osteitis deformans (Pagets)*:—The radiological picture is quite definite, with marked magnification of cancellous tissue. In osteitis fibrosa the cortex is merely an uneven linear shadow, and the cancellous bone tends to fade almost entirely.

(3) *Multiple myelomatosis*:—This is sometimes difficult owing to widespread osteoporosis. The serum calcium is usually normal but occasionally is raised.

An interesting case of this type was a child of 12 years, and was referred for X-ray examination for a deformity of left hip. The previous history was that the patient had a fall about five years back, and the fracture was set. Two years back the girl was seen and some medical treatment was given. Three months back she developed a deformity in the left hip.

Left hip radiograph:—The radiograph shows great lack of calcium, the cortex has lost its ivory character, and is reduced to a thin uneven linear shadow. The cancellous bone has faded almost entirely. There are cysts in the neck of the femur, which shows marked coxa vara. The upper shaft of the femur has somewhat expanded. The shaft of femur in its lower third also shows cysts.

Pelvis:—Shows pressure deformity, shows cysts in the left innominate bone and in the left ala of the sacrum.

Skull:—Shows a mottled appearance in the frontal bone, also in the occipital bone with small areas of bone of normal density surrounding areas of relative translucency. The most peculiar and interesting appearance in the frontal bone which has expanded considerably, and shows a mottled bone structure between the two layers of the diploe. This is most marked in the outer table. Another peculiarity not usually seen in osteitis fibrosa is that the sphenoidal sinuses and the neighbouring region of the middle fossa are dense and bony. This is the characteristic appearance in the lateral view. The anteroposterior view shows the right maxillary antrum quite opaque and dense, left antrum is normal. The density in the right antrum is bony and is not of the type of chronic maxillary sinusitis.

Chest:—Shows nothing abnormal except scolioses. No parathyroid tumour was seen in the mediastinum.

Left leg:—Shows a big cyst in the fibula and two small cysts.

Spine:—The spine here did not show the classical biconcave fish bone appearance. The cervical spine was normal. The dorsal spine showed marked scolioses, and cysts were seen in the twelfth dorsal.

The lower dorsal vertebrae were deformed, probably pressure deformity, but the vertebrae were not exactly biconcave. The lumbar spine showed a marked scoliosis, and some cysts.

Ribs:—Only one rib namely the seventh rib showed cysts.

Urinary tract:—No calculi were seen in the kidneys, ureters or bladder.

Blood chemistry:—The blood report showed 11.8 milligrams of blood calcium. Somewhat higher than normal.

Differential diagnosis:—Osteomalacia, Osteitis deformans and multiple myelomatosis were easily ruled out. Gee's disease or Coeliac rickets were ruled out, as there were no gastro-intestinal symptoms. The skull appearance was not of the type of renal rickets (renal dwarfism) and the epiphyseal changes of renal rickets were completely absent. The diagnosis was given as that of osteitis fibrosa. Blood calcium of 11.8 mgms also supports it.

However there were three peculiar features, which were difficult to co-relate. (1) This disease was seen in a girl of 12 years whereas the usual age is between 35 and 55. (2) The peculiar changes in the skull, where, in addition to the cystic changes, the skull showed increased density of the sphenoidal sinuses and of the right maxillary antrum. (3) That with such marked cysts all over the body, no calculi were seen in the urinary tract.

Treatment:—The disease if untreated is usually fatal. The number of recorded cases which have been arrested or cured by removal of a parathyroid tumour is now more than fifty. This operation brings about dramatic changes. Usually the pain in the bone goes immediately. In many cases polyuria is promptly abolished. Often there is disappearance of gastrointestinal symptoms. Patients gain in weight and strength, and they resume work. Decrease in the size of the cysts of the bone has been recorded within a few weeks of operation on the neck, and as a rule the level of serum calcium and the plasma phosphorus, and the excretion of calcium in urine are restored to normal. The progress of the disease should be checked radiologically after removal of a parathyroid tumour.

The other method of treatment of interest from the radiological point is the irradiation therapy.

RADIATION VERSUS SURGERY.

Advantages of radiation over surgery are (1) its painless character, (2) ability to treat even a very irritated hyperparathyroid.

Surgical operation (1) may prove a failure and no tumour may be found, (2) surgical removal of too much parathyroid may result in tetany. Roentgen therapy at least in therapeutic doses does not produce tetany.

Modified Biedle's technic:—The technic depends on whether the tumour in the parathyroid can be felt or not. If the tumour is not palpable, then with usual factors 200 K. V. 0.5 mm. copper filter plus 1 mm. aluminium, 30 to 40 cms. distance, 200 r. are given daily on

each side of the neck for 4 sittings or every other day thus giving a total dose of 800 r. on each side. If after 8 to 10 weeks, great improvement is noticed in the X ray appearance of diseased bones, no further treatment is given. If the improvement is but slight, a second series of 800 r. on each side may be applied. But if no improvement is noticed with the first 800 r. on either side, the second series will be useless and surgical intervention may have to be considered.

With palpable tumour:—Biedle's technic. 2 anterior and 2 posterior fields are given over the neck, same factors as above, with 250 r. to each field daily till 750 r. is given to each of the 4 fields. Allow an interval of 2 days between applications to each field. This dose will cause dryness of the mouth, temporary hoarseness, painful swallowing but no permanent ill effects. In 8 to 12 weeks after the first series it may be necessary to repeat 750 r. in fractional dosage over one large field on each side of the neck. If no results are observed, operation might still be tried in view of the fact that a cystic degeneration instead of an adenoma might be the cause.

Kaplan recommends low voltage X-rays to the parathyroid area of the neck. The factors used by him are 100 K. V. with 3 or 4 mms. aluminium filter, 30 cms. distance. 150 r. per treatment at semi-weekly or weekly intervals are given until 800 r. are given. This treatment he recommends to be repeated at monthly intervals until 3 series have been given.

Regarding radiation therapy of hyperparathyroidism, a case has been reported by Jacob, King and Bailey in 1939. They regard the actively hyperplastic tissue of parathyroids as radiosensitive. The case in question had no mass in the neck so localisation of the suspected parathyroid was tried with a selective therapeutic test of irradiation by giving 1600 r. (in air) in nine days, 200 r. daily, with 10 x 15 cms. field. The tests were made at intervals of 2 weeks on the right, then on the left side of the neck and over the upper anterior mediastinum. The average daily drop in blood calcium with rise in phosphorus content pointed to a lesion in the lower right parathyroid area or beneath the manubrium sterni. On operation no adenoma or enlarged parathyroid was found at operation. Two weeks later, another rise in blood calcium content indicated further irradiation, and 1000 r. given in 5 days through a 12 x 18 cms. field, over the lower part of the neck and upper part of the chest. Patient's bones began to show improvement, and 8 weeks later another 1000 r. in 5 days were given. Six months later patient had a fall and a fracture in the femur, another 1000 r. were given. Two months later another 600 r. were given in 3 days. The patient thus received a total of 9000 r. in 15 months. The blood chemistry showed that parathyroidism had not entirely disappeared. They came to the conclusion that there was a hyperfunctioning parathyroid without definite adenoma.

or hyperplasia, but they also say that an undiscovered adenoma may have existed or the roentgen treatment may have caused shrinkage of the tumour or hyperplastic glands so that they could not be found at operation.

The case in question proves that in some cases at least X-ray therapy produces satisfactory results. If there are contraindications to operation or if operation fails to produce a cure, roentgen irradiation may prove valuable.

The importance of blood calcium :—The blood calcium in the case quoted was 11.8 miligrammes. But the increased blood calcium cannot be regarded as the sole diagnostic criterion. Bloom found that in one case of adenomatous type of parathyroid tumour the blood calcium varied from 5 to 8.3 mgm.

(*Medical Bulletin*, Dec. 1943.)

THE LISTER TECHNIQUE

G. T. WRENCH, M.D. (LOND.),

Karachi.

Recently there has appeared in the medical press a number of pleas for the revival of the Lister technique to assist in the treatment of war wounds. The correspondents have been mostly senior surgeons and they have deplored the ignorance of the present generation of this technique in spite of the pre-eminence of its founder.

Lister in his day had to face a problem even greater than that of the terrible wounds that are inflicted by modern war. These wounds are purposely inflicted by other men with the object of causing death or mutilation. But the problem that Lister had to face was that the hospitals, which were provided for the help of those who were accidentally wounded or required operation, were themselves the cause of foul and agonising death. They more than failed in their purpose; they became its very opposite. If a man met with a compound fracture as the result of an accident, then, as John Bell, the distinguished surgeon, pronounced, it were better for him to be placed on a dunghill or in a stable than in a hospital provided for him by authority or charity.

In the year 1865 Lister, when thirty eight years of age, read Louis Pasteur's *Recherches sur la Putrefaction*. He read that Pasteur had put putrescible matter into glass flasks, boiled it and sealed the drawn-out mouths of the flasks while the liquid was still boiling. For however long these flasks were kept unopened, the matter in them did not putrefy. But, if drawn-out mouth were

broken so that air entered from outside and the mouth was again sealed, putrefaction invariably took place. If, on the other hand, flasks were opened and resealed on the glaciers and snows of lofty mountains, putrefaction very rarely occurred. Hence Pasteur concluded that putrefaction was due to the microbes in ordinary air.

The great work of Pasteur found an immediate convert in Lister, who, apart from his work as a practical surgeon in a large hospital, had given almost all his thought to the terrible problem of sepsis and had done much research work of a brilliant character on the nature of inflammation. "In the fields of observation" said Pasteur in an address at Lille, "chance only favours the mind that is prepared." Lister's was the mind prepared.

Lister at once set to work to apply Pasteur's work to practical surgery and sought for a chemical, which would kill the microbes that caused the putrefaction of wounds. The chemical of his choice was carbolic acid. The carbolic of that time was a dark fluid with tarry impurities and practically insoluble in water. So Lister was at first forced to use it at full strength. It might seem that this would poison the patient, but it did not do so. What it did do was to excite the exposed surfaces to bleeding, the blood mingled with the carbolic and formed a hard crust. This was the first form of Lister's famous antiseptic scab, which sheltered the wounded parts beneath it.

In Lister's hands this scab earned a partial success, but the crude carbolic burnt the surrounding skin. This started Lister's innumerable experiments from which the artificial scab emerged in the form of double cyanide gauze wrung out in a solution of 1:20 carbolic lotion applied direct to the wound; then a layer of dry gauze and over this dry cotton wool impregnated with carbolic acid. In the natural scab the under surface is wet yet clean, but the outer surface is dry. It should keep dry; an excess of wetness spoils the protective character of the scab. The scab is also pliant and does not break up with moderate movement of the injured part. Lister's scab followed these qualities; the inner surface was wet but not putrescent; the outer part was protective and dry, and lost its protective character when over-wetted; the dressing was pliant and its efficacy not broken by moderate movement of the injured part.

There was also antiseptic operative technique, the cleansing of the patient's skin, the hands of the operator and his assistants, the cleansing of the instruments, dishes and sponges or swabs, and, in the early years, of the air itself by means of a spray. For all these Lister relied on solutions of carbolic acid. This solution, Lister found, was blessed with a valuable peculiarity in that living organic substances, such as hair, skin, nails, fat and other tissues, selected carbolic from the water of its solution and became impregnated to the extent of 1:5 in place of 1:20. They also retained the carbolic well. Lister found that his hands, dipped into 1:20 carbolic lotion

for half a minute, were made non-infective for the time of the operation. This capacity of being held lightly by water and of ready transference to living organic matter, Lister always maintained was "a very great point" in his technique. Armed with it he built up a system of extraordinary simplicity and boldness, which he followed with complete confidence for thirty years of operative work. This system included the mastery of the complication of arterial hæmorrhage, which he established by several years of experiment, visits to factories of gut, experiments in twisting, scraping, drying, seasoning, etc., finally resulting in chromic gut.

We can now get a picture of Lister operating. The room, in which he operates, is an ordinary one, costing no more than any other room. The table on which the patient lies is an ordinary table, a plain wooden kitchen table sufficing in a private house. The patient is on the table and the skin in the area of the operation is washed over with 1:20 carbolic and covered with a towel or cloth wrung out in this solution.

Lister takes off his coat and puts an overall to protect his clothes. He turns up his sleeves, washes his hands in soap and water rinses them in freshwater and holds them in a basin of 1:20 carbolic for half a minute or more. He is then ready.

He does not use a nail-brush. He does not scrub his hands for several minutes. He does not put on boiled gloves, boiled robes, cap or boiled mask. He remains like an ordinary being in the eyes of a spectator, and is not attired like a mummer at a carnival, as is the aseptic surgeon, whose 'improvements' he never adopts for the reason that he has faith in carbolic acid used intelligently and conscientiously.

For his instruments there are dishes of the same lotion. After their previous use, they have been scrubbed in soap and water, dried and stored in a cupboard. They are now taken out of the cupboard, put straight into the dishes and covered with the solution. "For the instruments" taught Lister, "it is very much more convenient to be able to purify them by a solution like this than to boil them."

With this technique, operative wounds healed with the greatest regularity both in Lister's hands and in those of his followers. They did not have the failures which, however careful, the aseptic system occasionally exhibits. In the words of the greatest French surgeon of his day, Dr. Lucas Champonniere, himself a faithful follower and personal friend of Lister: aseptic surgeons "introduce new and incredible precautions incompatible with regular practice. And yet have they altered the results of surgery? Certainly they have caused it to lose its safety. That which Lister assured—the mathematical safety of surgical work done in accordance with the precautions indicated, applicable under all circumstances, in all places, with all

patients, and without lengthy preparation—that security has disappeared."

It has disappeared under the conditions of the present war. It cannot then be a surprise that those, who know Lister's technique and its safety and simplicity, have urged its revival in the treatment of war wounds and believe that it is the method of choice as "applicable under all circumstances in all places, with all patients, and without lengthy preparation," not that they deplore that to the majority of the younger generation of surgeons the practical application of the Lister technique is unknown.

This article will not be complete without a reference to the special war wound dressing, which Lister advocated in a short pamphlet in the year 1870, at the outbreak of the Franco-German War, and but three years after his initial trial of carbolic acid. The first step in the treatment was the excision of the dead matter in the wound. After this the injured tissues were cleansed with carbolic lotion and antiseptic ligatures tied on bleeding arteries. The cleansed tissues were then covered with a piece of oiled silk smeared with carbolic oil. This was the bland inner dressing or inner surface of the scab and was *not to be removed*. Layers of lint wrung out in oil were placed over this. As blood or pus soaked into these layers, the outer ones were removed and renewed. When oozing ceased, the outer layers were moistened with the oil every two days. *The wound was thus kept in a state of protected rest and its healing left to the healing power of nature* under the layer of irremovable oil silk. The closed plaster treatment, introduced by Dr. Trueta in the Spanish Civil War and widely adopted for war wounds in subsequent wars, is the Lister technique and principle in a later form.

(*Journal of the I. M. A. Dec. 1943.*)

THE MANAGEMENT OF GONORRHEA IN GENERAL PRACTICE PROCEDURES RECOMMENDED BY THE AMERICAN NEISSERIAN MEDICAL SOCIETY.

Gonorrhea in the United States is much too prevalent. Available data indicate that there are several million new cases every year. Although this disease occurs from three to seven times as often as syphilis, it should be controlled just as many other contagious diseases have been. If we are to succeed, each physician must (1) diagnose and treat the disease properly, (2) accept the responsibility of following up the contacts himself, or report them to the

health department which will take over this duty, and (3) hold the patient under observation until cure is established. The physician should inquire regarding all recent contacts in such a manner that the confidence of the patient will be gained. After the epidemiologic information is obtained, he should see to it that all alleged contacts are examined and treated.

Sulfonamide chemotherapy is a long step in advance of the older methods of treatment. Most cases of gonorrhea can be cured rapidly and easily by its proper use. There are three types of patients, however, who need special attention:

1. Those who stop treatment before there is good reason to believe that they are cured.
2. Those who do not respond to chemotherapy.
3. Those who appear to be symptomatically cured but whose infection remains latent.

Most of the first group consist of dispensary patients, among whom a 50-per cent lapse rate is common. More effort directed toward patient education and more personal interest in each patient will reduce delinquencies greatly. A good system of routine follow-up of lapsed patients will induce many more to continue treatment until they are discharged as cured. This follow-up service is frequently provided for physicians in private practice by local health departments.

PROPHYLAXIS

The value of Chemical as well as mechanical prophylactic measures in the male has been demonstrated. Other than continence, mechanical prophylaxis utilizing a condom assures the greatest measure of safety for both sexes. Inspection of condoms is now the responsibility of the Food and Drug Administration, Federal Security Agency, and it insures the availability to the public of satisfactory articles.

Men who use condoms should be instructed to grasp the sheath on either side by its open end and turn it inside out as it is removed. The hands and the external genitalia should then be washed with soap and warm water. The rather common habit of using a condom only at the end of intercourse should be condemned.

Chemical prophylaxis for those who have failed to make use of a condom is best carried out by a physician. However, the proper use of some of the chemical prophylactic procedures is practical for the average man who is sober.

The steps in carrying out chemical prophylaxis should be: (1) Thorough bathing with soap and warm water of the external genitalia, the pubic region, and the inside of the upper portion of the thighs. (2) The patient then should urinate, after which not more than 6 cc. of a nonirritating protein silver solution should be injected into the urethra and held there for 5 minutes by the clock. The

chemicals most commonly used for this purpose are mild protein silver, 10 per cent, or strong protein silver, 1 or 2 per cent. (3) When the protein silver solution has been allowed to escape from the urethra, the areas mentioned in (1) should be carefully anointed for 5 minutes with a 33 $\frac{1}{3}$ per cent calomel ointment as a prophylactic measure against syphilis; special care should be taken to rub the ointment well into the skin, particularly around the glans penis and the prepuce. (4) Toilet paper or other appropriate soft paper covering should be wrapped around the genitalia to protect the clothing, and the ointment allowed to remain for some hours.

The use of the condom by the man is the most efficient prophylaxis for the woman. While chemical prophylactic procedures have been recommended for women they have not been demonstrated to be effective and are so complicated that they must be carried out by a specially trained physician.

Inconclusive evidence is available to show that sulfathiazole administered orally before and after coitus may be a practical method for the prevention of gonorrhea.

DIAGNOSIS

The proper methods for the diagnosis of gonorrhea are the examination of smears by the Gram stain and the culture. A positive spread, utilizing the Gram method of staining is all that is needed when the preparation is made from a frankly purulent urethral or cervical discharge. Cultures have a most important place in the study of those patients with a microscopically negative discharge or no discharge and with a history of recent gonorrhea for which a sulfonamide drug has been employed.

The technic of proper staining and culture should be that recommended by the American Neisserian Medical Society. Any deviation from this method may lead to serious error in the diagnosis of gonorrhea.

Unfortunately, all physicians and dispensaries are not equipped for the laboratory diagnosis of gonorrhea. Under such circumstances, and in the presence of suggestive history and symptoms, it is probably wisest to make a provisional diagnosis of that disease, pending the time when the results of the laboratory examination are reported, and to proceed with sulfathiazole treatment as later outlined. This is necessary because too many patients with gonorrhea make only one visit, and the opportunity for cure otherwise may be lost. It is better to run the chance of treating a few persons who do not have gonorrhea than to allow those patients who have such an infection to remain untreated while the attending physician waits several days for a laboratory report.

When gonorrheal urethritis exists, frequency and "burning" on urination are often reported by men but less frequently by women. Leukorrhea is often found with gonococcal infections of the cervix.

However, leukorrhea is frequently due to other causes than gonorrheal infection in women who are not promiscuous.

Gonorrhea of the cervix does not present a characteristic appearance. This infection may be present in an apparently normal cervix showing slight discharge of mucus to one showing every evidence of violent inflammation with a profuse purulent discharge. A thick, tenacious ropy, mucopurulent cervical discharge is highly suggestive of gonorrheal infection. An everted, inflamed mucosa at the urethral orifice in the female, or tender and thickened Fallopian tubes, may give us further evidence of the character of infection in the patient with puzzling laboratory findings.

TREATMENT.

Chemotherapy.—Sulfathiazole given by mouth is the outstanding drug for the treatment of gonorrhoea. It should be given to every patient as soon as the diagnosis is made, and in some cases, as noted above, before a provisional diagnosis can be confirmed.

Dosage.—One gram (two 0.5-gm. or 7½ gr. tablets) of sulfathiazole should be administered orally to ambulant patients four times daily, after each meal and at bedtime, for 5 consecutive days. All patients under this treatment should drink at least 10 glasses of fluids daily (more if the weather is unduly warm.) Fluid intake above the normal is especially important for women during sulfathiazole treatment. This scheme of therapy has been found to be as efficient as schemes requiring larger doses and more efficient than those in which smaller doses are given over a longer period of time. When this plan is followed most patients show marked clinical improvement before the end of the 5 days of treatment. The determination of the blood concentration of the drug, routine blood counts and urinalyses are not necessary when the above dosage is used.

Patients should be warned to report at once to the attending physicians if nausea, fever, or a rash should develop. Occasionally a patient is seen who has an idiosyncrasy to one or all sulfonamides. In these cases the drug must be stopped and large amounts of water administered; such idiosyncrasies are rarely encountered.

The great majority of patients are cured by one course of sulfathiazole when the above plan is used. It is most important, however, to keep the patient under observation for a period of 3 months after all objective symptoms have disappeared in order to make certain that there is no recurrence.

Patients whose infection persists after they have finished one course of sulfathiazole, or in whom the disease relapses, are given another similar course of the drug after a rest period of 3 or 4 days.

Carriers.—In a few patients who have been treated with sulfathiazole, an apparent cure results but the infection persists in a dormant state; carriers are thus produced. *Even in the male, freedom*

from symptoms and the passage of a perfectly clear urine are not necessarily proof of a true cure. It is highly important then that the attending physician use all the laboratory methods available to determine whether the patient is cured.

Sulfonamide failures.—In some patients the sulfonamide drugs reduce the activity of the disease and prevent its extension but fail to banish completely the objective symptoms. In a small number of persons these drugs exercise no beneficial effect whatever at the time of administration. That this failure to react favorably to the drugs is sometimes a transient state is shown by the fact that many such patients are quickly rendered symptom-free and even cured by a repeated course which is given after a short rest from medication.

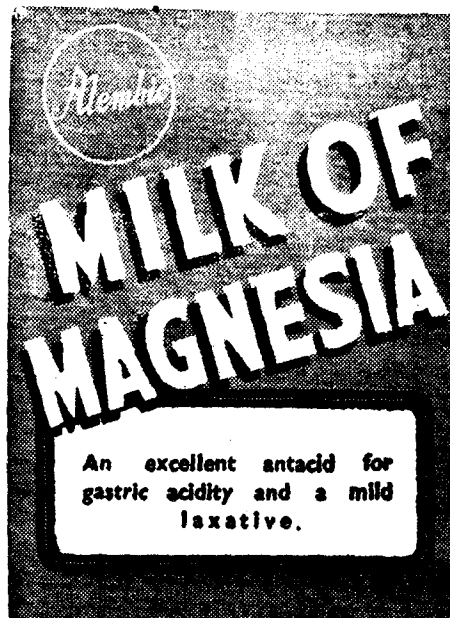
Those in whom sulfathiazole fails to exert any curative influence and for whom fever therapy is not available may often respond to older methods of local treatment.

Local treatment in the male.—The following method of treatment should be used in sulfonamide-resistant cases only. When the infection is confined to the anterior urethra, an anterior urethral injection once daily of not more than 6 cc. of a 5 per cent solution of mild protein silver or a 0.5 per cent solution of strong protein silver is advised. This solution should be retained in the anterior urethra for 5 minutes. The prolonged or too frequent use of chemicals tends to perpetuate the urethral discharge. This irritating effect may be recognised by the finding of many epithelial cells in the stained smear. All urethral injections should be administered by a physician. If this is not practical the physician should teach the patient how to self-administer properly an interior urethral injection.

All local treatment should be stopped if acute symptoms of posterior urithritis, such as urgency, painful or marked frequency of urination, or perineal or rectal pain develops. Treatment at this time should be limited solely to hot sitz baths. When acute symptoms have subsided, anterior urethral injections should be resumed and continued until prostatic stroking (massage) is begun.

Extremely gentle prostatic stroking (massage) should be tried when the second glass of urine has been clear, and the first glass nearly so, for 2 weeks. If gentle massage is painful or causes a recrudescence of other symptoms. It should not be repeated for 1 week, or until the symptoms have subsided. If it is not painful and if no recrudescence of symptoms occurs, the gland should be gently stroked at 3- or 4-day intervals, and smears of the prostatic secretion examined every 2 weeks. *When prostatic massage is instituted too soon or applied too vigorously it often induces complications and retards cure.*

No instruments of any type should be passed into the urethra while gonococci are present.



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Management of the female.—The recommended treatment with sulfathiazole is relatively so harmless that it is best to follow the maxim—"treat when in doubt." With the public health in mind it is far better to treat some women who are not infected, than to neglect to treat women whose infection is not obvious but who may serve as a source of infection to others. Any woman who has recently had intercourse with a man known to have gonorrhea should herself be given treatment regardless of clinical or laboratory findings. Women who are believed or know to practice indiscriminate sexual intercourse are usually infected and had best be treated if leukorrhea is present. Laboratory evidence in such cases is desirable but not essential for the institution of treatment by the foregoing scheme.

Ordinarily the administration of sulfathiazole gives such rapid symptomatic relief from leukorrhea and pain that no adjuvant local treatment is necessary or desirable. Vaginal douches or topical applications to the cervix are unnecessary and may be harmful. Cauterization of the cervix when gonococci are present is unwise, as an ascending tubal infection may result.

Adequate laboratory facilities are of enormous aid in the accurate determination of the presence or absence of gonococcal infection. Unfortunately, in many sections of this country such assistance is not available. Complete proof of gonococcal infection of women ordinarily depends on securing positive cultures. Culture material is obtained from the cervical canal after cleansing with a dry cotton sponge and from the clean urethral meatus after stroking the urethra outward until a drop of secretion appears. Positive cultures and positive gram stained spreads can usually be found in cases of acute gonococcal endocervicitis or urethritis. In most cases of chronic gonorrheal endocervicitis neither cultures nor spreads, even if repeatedly taken, will give positive evidence of the causative organism. Consequently one must always remember that a "negative" laboratory report, or series of such reports does not indicate that a chronic infection is not of gonococcal origin. Positive cultures are obtained more often than are positive spreads. Gram stained spreads in chronic cervical infections offer notoriously unreliable evidence of the presence or absence of gonococcal infection. Readings of identical spreads made by experienced bacteriologists disagree widely. In the case of chronic vaginitis of girls, only positive cultures should be accepted as evidence of gonococcal infection.

Patients with acute salpingitis with fever should be put to bed and given treatment with sulfathiazole exactly as described above (4 gm. each day for 5 days). Patients with pelvic abscesses should be sent to a hospital for surgical drainage through the vaginal vault. A pointing abscess of Bartholin's gland should be incised and drained;

5 days' subsequent treatment with sulfathiazole may result in cure. If a Bartholin's gland remains chronically infected it should be removed surgically in a hospital. Pregnancy does not contraindicate treatment with sulfathiazole.

The commonest error in treating men and women with gonorrhea is the failure to find and treat the infected sexual partner, and this is often the cause of reinfection.

GONORRHEAL VAGINITIS OF IMMATURE GIRLS.

In most instances, vaginitis of immature girls is not due to gonorrheal infection. An accurate diagnosis depends on securing positive cultures from discharge which is best obtained from the neighborhood of the cervix. A diagnosis which depends on an examination of spreads is not to be relied upon. Too many other Gram-negative organisms in the vaginae of children resemble gonococci. Ordinarily a gonorrheal infection is limited to the vaginal mucosa. Salpingitis occurs very rarely.

Girls with gonorrheal infections need be kept from school only while the discharge is profuse. If properly treated, this period should be a matter of only a few days. The spread of infections on toilet seats is not to be feared. The danger of institutional contacts has been grossly exaggerated. Ordinary isolation technic in well conducted hospitals is sufficient to prevent the transmission of infection to other patients. More intimate direct contacts in the family or with playmates constitute the most frequent modes of spread of the disease in immature girls.

Treatment.—Sulfathiazole given for 7 days in daily doses $\frac{1}{2}$ gr. per pound of body weight of the child, not exceeding 30 gr. a day for girls weighing less than 75 lbs. will speedily cure the great majority of these young patients. Local applications are useless or actually harmful.

UNTOWARD REACTIONS TO SULFATHIAZOLE.

It should be borne constantly in mind that there are a few patients who cannot tolerate sulfathiazole. For this reason, patients not only should be warned of the possibility of toxic reactions but should be seen by the physician three times a week, if practical, while under such medication. Should severe toxic effects (fever, rash, or vomiting) occur, the drug should be withdrawn immediately and the patient's fluid intake greatly increased. The following mild reactions may occasionally be noted but they do not necessitate the withdrawal of the drug: nausea, headache, vertigo, weakness, malaise, irritability, and insomnia. Blood studies need be performed only when there is evidence of a severe reaction. The danger of renal tubular deposits of sulfathiazole crystals is remote with the recommended plan of treatment. Before the plan of treatment recommended above is started, it is important to obtain history of previous treatment with sulfonamide and the patient's reaction, if any occurred, after prior treatment.

HIGHLY POTENT WHOLE LIVER EXTRACT

HG % RBC count

100	5
90	4.5
80	4
70	3.5
60	3
50	2.5
40	2
30	1.5
20	1
10	0.5
0	0



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PATIENT BEHAVIOR.

Patient behavior while under treatment is an important factor in determining the rapidity of cure. The physician or an assistant should take time to instruct the patient to avoid sexual excitement and the use of alcoholic beverages, to obtain plenty of rest, and to drink at least 10 glasses of fluid daily. Emphasis must also be placed upon the need for taking the prescribed medicine regularly. In the absence of cultural studies, the patient should return for clinical observation periodically for at least 3 months to be certain that the gonorrheal infection is cured.

FEVER THERAPY.

Fever therapy unfortunately is not available in many localities. It is definitely indicated in patients with severe complications and in those who are intractable to chemotherapy and local treatment.

WHEN IS THE PATIENT CURED?

A small percentage of both male and female patients harbor the gonococcus for some weeks after symptoms have disappeared. In the absence of cultural studies, all patients should be regarded as potentially infectious for a period of 3 months after all symptoms disappear. If such patients have sexual intercourse during this period, a condom should be used to protect the partner. Cultural studies are of great value in the recognition of carriers and offer the most dependable criteria of cure.

As scientific evidence of cure four consecutive negative cultures taken at intervals of 2 weeks may be accepted. In women one such culture should be taken immediately after menstruation. The first of these cultures should be taken a week after apparent clinical cure is affected. In addition to yielding negative cultures, the patient should show no clinical evidence of gonococcal infection before "cure" can be pronounced. Even after 3 months of such "established cures," recurrence may be found, but this is rare.

Practicing physicians interested in laboratory procedures for the diagnosis of gonorrhea and for the determination of cure should study the Report of the Referee on Gonorrhea and the Gonococcus for the Standard Methods Committee on Diagnostic Procedures and Reagents of the American Public Health Association.

The practice of physicians giving certificate of freedom from gonorrhea should be condemned and avoided except when required by premarital and similar laws.

CASE-HOLDING AND CASE-FINDING.

Very little attention has been given in the past to case-finding and case-holding in the control of gonorrhea. Each patient should be studied in relation to his environment. Because of the national campaign against gonorrhea and of its relationship to the war, every physician who treats gonorrhea must realize that he is just as much a protector of the public health as is the health officer. It is

the physician's duty to make every effort to get all contacts in for examination and treatment if infected. It is incumbent upon attending physicians to see that every infected patient is held under observation until cure is attained. In most large and many small communities, contact-tracing and case-holding services are available from the local health department. Such services should be extended and made more readily available.

Extract

THE CLAVICULAR SIGN IN CONGENITAL SYPHILIS

By K. D. LAHIRI, M.B.B.S.,

From the skin and Venereal Department,

Patna Medical College Hospital, Patna.

The enlargement of the sternal end of one or both clavicles in Congenital Syphilis is known as the 'Clavicular sign.' During the five years the author has been working in the Venereal Diseases Department and has seen this sign in only 8 per cent of cases of congenital syphilis. The age at which these cases came with the clavicular sign ranged between 8 and 12 years. In all the cases other stigmata of the disease were present; all the patients had a depressed bridge of the nose; the majority had keratitis; the rest had associated syphilitic osteomyelitis and chronic rhinitis.

Higoumenakis (1938) reported the presence of this sign in 20 cases of congenital syphilis, and has emphasized that this clavicular sign is superior in its diagnostic value to any other sign of congenital syphilis because of the regularity of its occurrence and the ease with which it may be detected.

Nair and Chetty (1943) reported 130 cases of congenital syphilis, and of these 130 cases, 103 cases showed the clavicular sign. The inner third of the clavicle was visibly thick and enlarged, and the enlargement was unilateral being on the right side in right handed persons and on the left side in the left handed.

Higoumenakis (1938) showed that the clavicular sign has a diagnostic value equal to other definite signs of congenital syphilis, that it occurs more frequently than other signs of congenital syphilis, and that consequently it is of greater diagnostic value. It is never encountered in persons with acquired syphilis or in healthy persons. The explanation of the enlargement is that the inner third of the clavicle arises from a secondary nucleus which appears between the 18th and 20th year, and the ossification of the bone

takes place directly from the connective tissue. The tissue is infected with spirochaetes in the syphilitic child. In early childhood the spirochaetes remain latent locally. The increased activity with the approach of puberty demands increased function of the clavicle. The movement of the arm not only reactivates the spirochaetes but also causes a constant friction of the medial extremity of the clavicle against the sternum, leading to hypertrophy of the sternal end of the clavicle.

(*Indian Medical Gazette.*)

NON-TUBERCULAR PULMONARY INFILTRATIONS.

By Major. J. R. OWEN R.A.M.C.,

O. I. C. Medical Division ; Bombay Military Hospital, Bombay.

1. Eosinophilic lung. The onset of the disease is insidious, with fever, lassitude and malaise, followed in a few days by the development of a troublesome and unproductive cough, which after a variable period becomes associated with bronchospasm and typical asthmatical attacks, usually nocturnal. The spleen now becomes enlarged to the extent of 2 or 3 finger breadths below the costal margin, and X-ray films show a fine mottling of broncho-pneumonic type in both lungs. A most striking and constant feature is the blood picture, which shows a leucocytosis consequent on an increase in the eosinophil cells.

The syndrome, described by Loeffler, of transient pulmonary infiltration with leucocytosis and eosinophilia is dissimilar in that no such constitutional disturbances or asthma is present.

Treatment. So striking is the administration of organic arsenical components that a therapeutic test is constituted. Two or three injections of neoarsphenamine, acetylarsan or meta-arsenobillon in doses slightly lower than those conventionally used in the treatment of syphilis are sufficient to abate the symptoms, and six injections to complete the cure. Organic arsenicals like stovarsol by mouth in a dosage of gr 8 daily are equally effective.

2. Pulmonary Amoebiasis. We are concerned with the so-called primary type of pulmonary amoebiasis. The cardinal symptoms are six in number:—

- (1) Cough (2) Sputum (3) Haemoptysis (4) Loss of weight.
- (5) Night sweats (6) Evening rise in temperature.

The sputum is of characteristic anchovy sauce appearance. Slight leucocytosis with eosinophilia up to 10 per cent is present and cyst forms of *E. histolytic* are present in the stools. X-rays

reveals a diffuse opacity, or as a mottling suggestive either of broncho-pneumonia or of tuberculosis.

Treatment. The usual remedies against amoebic dysentery are most effective, and, once more, may be regarded as a therapeutic test.

3. Epidemic Virus Pneumonia. The characteristics are:—

- (1) Abrupt onset of headache, fever and malaise without any marked catarrhal symptoms.
- (2) Transient and slight enlargement of lymphatic glands, most constantly the posterior cervical group.
- (3) The development after 2 to 8 days of a troublesome cough with scanty viscid mucopurulent sputum.
- (4) Variable fever up to 103° F with a relatively slow pulse, settling after five to fifteen days by lysis, sometimes showing a secondary rise.
- (5) Breath sounds may be either harsh or diminished with medium or coarse moist rales.
- (6) The persistence of these signs, in some cases for many days after the disappearance of pyrexia.
- (7) Enlargement of the spleen up to 3 fingers below the costal margin.
- (8) An absence of leucocytosis with a tendency to lymphocytosis in the differential count and sometimes leucopenia.
- (9) A variable radiological picture showing bronchopneumonic infiltration or diffuse opacity.
- (10) Complete lack of response to treatment by sulphonamides including sulfathiazole.

The severity of the condition is variable. So far no success has been achieved in growing the virus. The disease could be transmitted only to the mongoose by experimentation.

(*Indian Physician.*)

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"BLOOD AS THERAPEUTIC AGENT."

BY DR. S. N. CHAKRAVARTY, M.B.B.S.

HISTORICAL.

From time immemorial blood has been regarded as a vital fluid a symbol of life and strength—and it has been used as a valuable therapeutic agent to resuscitate and strengthen the weak. In primitive era it was used as a drink to restore health. Egyptian Pharaohs used to get poured on themselves the life blood of enemies and slaves for strength. Naam, the king of Syria, is said to have been cured of his illness by removal of blood from his body and replacement with blood from a healthy person. Pope Innocent the VIII in 1942 was probably the first to be transfused by his Jew physician by bleeding three boys to death.

Modern uses of blood.

- I. Secondary Shock.
- II. Acute hæmorrhage.
- III. Anaemias—(1) Primary & (2) Secondary.
- IV. Restoring plasma proteins.
- V. To restore immunity mechanism.
- VI. Chronic hæmorrhage.
- VII. Other diseases.

1. Secondary Shock may be:—

- (a) Wound Shock.
- (b) Post Operative Shock.
- (c) Burn Shock.

Pathology.

(a) *Wound Shock*:—Shock Syndioma results from disparity between the volume of the blood and volume capacity of vascular system. The area of open Capillary bed is increased immensely resulting in apparant albuminurea in the tissues, and very little blood volume for the heart to work on, is left for circulation. If all the capillaries open up there will be no blood left for circulation.

Capillary endothelium is changed in such a way in their permeability that it leads to serum exudation, out of the circulation. There is subsequently diminished blood volume, and Hæmoconcentration. Proteins are lost from circulation into the tissues. More the amount lost more prolonged and severe is the state of the shock and greater is the out-pouring of the fluid and plasma proteins from circulation.

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Haemo-concentration:—R. B. C. may go up from normal to about 10 millions per cmm. and Haemoglobin percentage to about 120 per cent. When R. B. C. is 8 million per cub. mm. the viscosity is increased four times which means circulation is quartered part from vasodilation and fall of blood pressure. The whole thing is more severe than haemorrhage. The actual plasma volume in body is still there but the effective volume is much less than is suitable for normal process of life. Dehydration increases the chances of severe shock. If shock is prolonged more than eight hours generalised capillary damage tends to occur and the patient dies.

Whipple has shown that the cells consist of two types of proteins: (a) Essential stable parts (b) Part that can leave the cell protoplasm. If the plasma protein is not adequately restored, immediately it is restored to normal value, slowly by synthesis of new proteins by liver. Infection slows down or stops the replacement of normal protein concentration in plasma. In cases of shock the osmotic pressure of blood is being lowered continuously and thus there is less chance of natural re-establishment of the normal blood volume. The primary requisite at this time is:—

- (1) To restore a circulatory volume.
- (2) To maintain the blood volume.
- (3) To reduce the viscosity of blood.

If we treat them with large amount of saline pulmonary oedema tends to occur. Lung tissue is, in fact, the first area in shocked cases, to give visible demonstration of exudation of the fluid in the tissues from the capillaries. Such being the Pathology, more than two pints of saline is not safe and the action is very transient. Neither you can make up the blood volume nor you can keep at for more than few minutes. To make up for this gum-saline was introduced and was a failure for it contained impurities and use of Isngloss (fish gelatine) is in experimental stage. Circulatory volume is temporarily raised by saline. Plasma proteins are diluted, much of the salt passes into the tissues and tends to increase the flow of the fluid out of the circulation to the tissue-spaces or is excreted out of the kidneys—Hypertonic saline has got also a transient effect. A combination of hypertonic intravenously and hypotonic subcutaneously has been suggested as a better replacement treatment by serum or plasma transfusion hitherto has been giving the most satisfactory result, for it is the same fluid that circulation has lost. It provides necessary osmotic pressure to keep the fluid in the vessels. Plasma protein reduces the tendency of fluid and crystalloids to escape from capillaries. Need of R. B. C. is not urgent unless haemorrhage is very severe. It is rare to lose more than three pints of blood for accompanying fall of blood pressure is so great that the

haemorrhage ceases while it leaves about 75 per cent of R. B. C. for carrying oxygen. If necessary amount of fluid can be introduced into the circulation and made to stay, the remaining R. B. C. should be entirely adequate to maintain life in a person who has been normal before. The use of whole blood will increase the Haemo-concentration and viscosity of blood and interfere in circulation. Once inside the body, plasma proteins can be used not only to raise the plasma protein concentration but also to assist haemoglobin formation and to provide proteins needs to replace normal tissue wastage.

PRINCIPLE OF TREATING SECONDARY SHOCK.

- (1) Arrest of haemorrhage.
- (2) To restore blood volume.
- (3) To combat the contributing factors, e. g. dehydration and exhaustion anaesthesia etc.

PREScribing HINTS:

(a) *Amount*. Aim should be to quantitatively restore the blood volume that has been lost, judged by immediate improvement of patient as indicated by colour, pulse, blood pressure, and increase of pain. For each pint there is a rise of 20 mm. of Hg. in the blood pressure.

(b) *Rate*. First pint in 10 minutes. }
2nd pint in 20 minutes, } Three pints in one hour,
3rd pint in 20 minutes. }

and is the maximal amount in the cases of quite severe degree of shock.

(c) Blood or serum should not be heated rapidly or over 100°F. Blood is to be warmed up at 40°C in the receptacle so that it may be at 31°C when it is entering the vein.

Contra Indications:—1. Primary shock.
2. Head injury.
3. Spinal injury.

(b) *Post Operative Shock* is of similar in nature but slower in onset. Treatment is same except that less amount of serum is required to resuscitate.

(c) In *burns*, in addition to exudition of fluid in tissues there is vesication with lot of fluid and toxins which are reabsorbed and add to the shock. In a treatment of shock plasma or serum is the ideal. Then comes the whole blood and saline.

II. Acute Haemorrhage. The whole blood unmodified is the nearest approach to a perfect tissue graft while plasma and serum are excellent substitutes for this condition and can be stored for longer period. The blood must be administered quickly to make amends for oxygen carrying power. Reactions are usually due to the use of citrate as anti coagulant and are rarely fatal.

III. Transfusion in Anaemias. Indications:—

- (1) Dangerously severe anaemia—Haemoglobin percentage less than 25 per cent.
- (2) Anaemias not so extreme but complicated by emergencies e. g. delivery, unavoidable operations, or radium treatment—to raise Haemoglobin to 80 per cent.
- (3) When other hæmopoietic remedies have been found ineffective.
- (4) Anaemias with septic and infective conditions.
- (5) Aplastic anaemia, Leukemias, Hodgkins, Splenic anaemia and multiple myeloma, when Haemoglobin falls below 60 per cent to maintain it at 70 per cent.

Action: It is mostly replacement therapy making blood capable of carrying adequate oxygen, and thus stimulate the bone marrow to normal activity, for all R. B. C. are destroyed in about thirty days. It might also substitute other constituents of blood and help to improve its general value. Some people advocate small repeated transfusions with the idea that they will not be endangering the life of the patient while it will stimulate the bone marrow. The only thing in blood which can stimulate the bone marrow is oxygen. The single transfusion of 100 c. c. of blood is too meagre to appreciably increase the oxygen carrying power of the blood and, clinically also, I have found that after about 400 to 500 c. c. of blood have been transfused there is clinical and cytological improvement. But danger of cardiac failure is diminished for heart has to manage a smaller addition to blood volume at a time.

THERAPEUTIC POINTS. AMOUNT.

(1) Fresh blood is the best. Stored blood can be used in emergencies. Haemoglobin is raised by 15 per cent after each pint of whole blood transfusion. In dangerous severe anaemias the haemoglobin percentage is to be raised from 25 per cent to 45 per cent—a safe level. Two pints are needed for this. If more than 3 pints are given, give two divided transfusions separated by two clear days. You can give concentrated R. B. C. in small amount of saline when there is basal congestion.

(2) **Rate:** Ordinary cases and internal bleedings—for 40 drops per minute or 2 c. c. per minute (for 120 lbs. weight). In cases with less than 35 per cent haemoglobin—20 drops per minute or 1 c. c. per minute (for 120 lbs. weight).

The blood should be given in slow continuous and uniform rate. It is inability to keep up the ideal that we find small transfusion so safe and advocated. Although it requires repeated transfusions to attain the same end as blood is in no way a hæmopoietic substance. If you give the transfusion rapidly the extra fluid cannot be thrown out of the circulation at the same rate uniformly. There is Oedema of the lungs and more strain on the right side of the heart which is

already flabby, fatty and dilated due to anaemic condition. There is grave danger of acute dilatation on the right heart and death.

(3) The reservoir should be shaken or blood periodically oxygenated and passed through veins.

(4) Clotting can be avoided by adjusting the screw every 10 minutes.

(5) Same donor should not be used more than once a month. His total red blood cell count and Haemoglobin percentage should be found out before taking his blood.

(6) **Anti-Coagulant.** Sodium citrate 3 per cent, 1 in 5 is used and the usual anti-coagulant, Heparin is coming in fashion. It is injected in the donor's blood and direct transfusion done by syringe.

Advantages of blood transfusion.

- (1) Extra burden on the heart is very slow.
- (2) Uniform extrusion of plasma means less increase in volume.
- (3) Heart benefits by increase of oxygen carrying power.
- (4) Rigor is less frequent and less severe.

Hazards of Transfusions.

1. **Incompatibility:** In spite of knowing the groups there must be direct matching of both serum and R. B. C. before transfusion. Disregarding of this precaution has caused many a death; once compatible may not always be compatible to the same person. Rh. positive individuals are potentially dangerous for multiple transfusion to Rh. negative recipient while other recipient may become hypersensitive to the same human serum.

PRECAUTIONS.

- (1) Determine the group.
- (2) Do direct matching of both R. B. C. serum.
- (3) While giving transfusion be slow for first few c. cs. of blood. Be on a look-out for any reaction. Have your assistant to count the pulse and shout it out every minute. Stop the transfusion if the pulse rate is going up as 100-110-120 to 130.

Symptoms. May take sometime to develop in the way of bursting headache. Severe back-ache with rigor and fever, flushes on face and collapse. Urine becomes brown in colour and there is jaundice. Death usually occurs due to anuria and uraemia. Donor's cells are agglutinated and then hæmolysed, haemoglobin is set free which reaches the tubule where normal Ph. is 4.6 to 5.4. So it becomes converted to met-haemoglobin which crystallises forming hæmatin which obstructs the tubules causing anuria and uraemia.

Treatment. Urine should be made alkaline. Alkalies should be given by mouth and intravenously 150 c. c. of 3 per cent Sodium Citrate to be run into the vein rapidly. Sodium Citrate 3ii Stat with tea every two hours and then T. D. S. by mouth.

Prognosis. Death usually does not occur when less than 300 c. c. of compatible blood is transfused, and death is sure when more than 540 c. c. of incompatible blood is given.

RIGORS.

Causes: (1) Too fast a rate is the commonest.

(2) Pyrogen bodies.

(3) In 10 per cent cause is found.

Reassure the patient for rigor rarely has any serious effect.

3. *Pyrexia.* 99 to 100°F is common due to dead pathogenic and non-pathogenic bacteria. It is not accompanied with lumbar pain.

4. *Air embolism:* When pressure is used to force in the blood quickly.

5. *Phlebitis:* Occurs 12 to 30 hours after transfusion and 2 to 5 days after saline. It is usually not due to infection but to some physicochemical phenomenon.

6. *Cardiac-Failure:* Is due to over loading of weak cardiac muscle.

7. Transferable Diseases.

(1) Syphilis.

(2) Malaria.

(3) Allergic conditions.

(4) Other diseases.

Advantages of serum and plasma.

(1) No grouping is needed.

(2) No malarial parasites can be transmitted.

(3) Easier to Store.

(4) No chance of transferring syphilis because there are no spirochaetes in the blood except in the secondary stage and they are easily filtered and killed in cold storage although some of the toxins may be left.

Disadvantages.

(1) It cannot be used to improve the oxygen carrying power of the blood.

IV. To restore Plasma Proteins.

It has been used with advantage in some cases with low serum protein as in the cases of hydræmic nephritis, war oedema and anaemia, but the clinical improvements have not been uniformly good.

V. Immunotherapy.

Cadham and Winnipeg have drawn particular attention towards the need of administration of fresh complement in cases of Streptococcal Septicemias. Still there is a great field of discovery and use in this direction. Patients acutely ill with low condition may be transfused with advantage. Saline infusion has proved to be of great help to a good many enteric cases of low general condition to

overcome the crisis. Serum may be a better substitute for that. While various antibodies and antitoxin can be had in greater concentration in human serum and can be safely administered intravenously.

VI. Chronic hæmorrhage.

Whole blood transfusion can be used in conditions associated with chronic hæmorrhage with advantage to improve the general condition.

VII. Other Diseases.

(1) Auto-hæmotherapy has been used to produce non-specific protein shocks in number of chronic cases with advantage.

(2) A. D. Lapp reports to have cured Hay fever and Asthma by subcutaneous injections of patients own serum.

(3) Carhav W. Haywar reports use of intravenous serum for chronic diseases with advantage. In cases of incipient and actual gangrene with marked improvement disappearance of rest pain, healing of ulcers separation of gangrene and has been also found to relieve intermittent claudication.

(4) While others have been used with advantage in cases of malignant diphtheria.

(5) It can be used with advantage to temporarily increase the coagulability in hæmorrhagic diseases e. g. Hæmophilia and Purpura.

(K. G. M. C. Clinical Society Journal.)

TACHYCARDIAS—THEIR NATURE AND TREATMENT

BY A. K. BOSE, M.Sc., M.B. (Cal.), M.R.C.S. (ENG.),

M.R.C.P. (LOND.)

PHYSIOLOGICAL.

The specific neuromuscular tissue of the heart is entirely different from its non-specific (that is the common muscle) fibres. Not only there are great differences functionally but also structurally and as regards their blood and nerve supply.

There are two collections of specific fibres. The sino-auricular system and the more elaborate auriculo-ventricular system. These collections can be distinguished macroscopically and more definitely microscopically. Not only the nodes but every specific fibre in these collections is capable of forming stimuli in themselves and by themselves when placed under suitable conditions.

Normally only one single specific fibre in the S-A node paces the heart while any other of the thousands of such specific fibres is equally able to start the impulse should necessity arise—a fact of great safety valve mechanism of the heart. Similarly the A-V node

and its system is capable of giving rise to stimulus formation in the very minutest of its parts.

The specific fibres nearest to the apex of the heart have the least degree of automatism, the A-V node having higher and the S-A node the highest degree of it. Therefore at any time, that centre or that part of this system controls the heart which forms stimuli at the highest rate, all other parts remaining, so to say, in a state of suspended animation. If for any reason this normal automaticity of the S-A node is depressed or of the lower node increased, the lower centre assumes control. It seems all the lower centres are always on the alert to fill up the gap in the pacemaker whenever this arises.

The specific tissue has a separate blood supply of its own as distinct from the common heart muscle. That is why in extensive coronary thrombosis or in cases of gross myocardial damage there may not be any defect either in the formation or in the conduction of the cardiac impulse.

Innervation of the specific tissue is very extensive, the fibres coming from vagus and sympathetic. Vagus fibres are found as far down as the A-V node but not below, whereas sympathetic fibres are found almost anywhere in the heart. Therefore as far as the ventricles are concerned, automatism is favoured by the absence of direct vagus control, again a fact advantageous to the organism.

Indirect reciprocity of pulse rate and blood pressure is maintained through the pressure-chemical changes in the carotid sinus reflexly acting on the vagus through the glossopharyngeal nerve. Similarly increase in the auricular pressure (as occurs in congestive cardiac failure) reflexly increases the normal sinus automatism.

So under different circumstances, the pacemaker of the heart may shift its position and the degree of its automaticity may vary, clinically giving rise to a variety of pictures.

There may be

- (1) a simple change in the normal pacemaker such as a sinus tachycardia or sinus bradycardia.
- (2) a new automatic centre or centres may appear such as an A-V rhythm, parasystole and interference dissociation
- or (3) an entirely abnormal type of stimulus formation may occur as an extrasystole, paroxysmal tachycardia, auricular flutter and auricular fibrillation.

CLINICAL.

Pulse rate of more than a hundred per minute is generally regarded as tachycardia. Clinically one is more concerned with sinus tachycardia, paroxysmal tachycardia, auricular flutter, auricular fibrillation and multiple extra-systoles.

Sinus tachycardia in which normal pacing is maintained, is found most commonly in fevers, in toxæmia, as a result of physical exertion, in shock, dehydration and thyrotoxicosis; also in cardiac

failure and neurosis and in profound anaemia. In all these the tachycardia to a great extent is a compensatory phenomenon, secondary to some primary factor, the ultimate nature of which varies as has been already mentioned in connection with the physiological consideration of the pace-maker.

Paroxysmal tachycardias on the otherhand are repeated extrasystoles arising away from the sinus node. Depending on which part it arises from, it is either called auricular paroxysmal tachycardia, ventricular paroxysmal tachycardia or nodal paroxysmal tachycardia.

Fibrillation and flutter are supposed to be due to forms of circus movement in the propagation of the auricular stimulus.

Multiple extrasystoles differ from paroxysmal tachycardia in being repeatedly interrupted by normal sinus beats.

"Nodal interference, as the name suggests, is a condition in which multiple pacemakers begin to work simultaneously and are coupled to each other.

Parasystole is a condition in which apart from the normal sinus node another deeper centre also works effectively and each completely uncontrolled by the other.

Though all these variation of tachycardias, in most instances, are very well determined with the help of E. C. G. the preliminary approach should always be clinical.

In sinus tachycardia, paroxysmal tachycardia particularly of the auricular variety, and auricular flutter, for all practical purposes the rhythm is regular, whereas it is irregular in auricular fibrillation, multiple extrasystoles, parasystole and nodal interference. The last two are detectable only by electrocardiographic studies and will not be discussed.

In sinus tachycardia cardiac rate usually varies between 100—120, but may rise to 150—180 (—200 very rarely). If the rate is 200 or above sinus tachycardia may be usually excluded. Instability of the pulse rate and its quick variation due to effort or excitement is very characteristic of sinus tachycardia. With slight exertion, say changing from sitting to standing posture, from a rate of 120 it may go up to 180 or so.

Paroxysmal tachycardias as their name implies come in paroxysms and are differentiated from sinus tachycardia by their sudden beginning and sudden end. They begin "as suddenly as light appears when the switch is put on" and stop as suddenly. Sinus tachycardias come less suddenly and always decline slowly.

Flutter and fibrillation may also be paroxysmal and be confused with paroxysmal tachycardia.

In paroxysmal tachycardias the heart rate varies from 120—300 beats per minute, usually keeping between 160 and 200.

If the heart rate is counted any number of times, in auricular paroxysmal tachycardia it will be found to be almost exactly the

same. Ventricular paroxysmal tachycardia unlike the auricular variety is invariably associated with organic heart disease, and careful auscultation for sometime may also reveal slight degree of irregularity.

In auricular flutter the rate of auricular contraction is between 250 to 350 per minute, but a block being invariably present, the heart rate does not usually exceed 175. Flutter tends to persist longer than paroxysmal tachycardia, sometimes occurring without break for months.

If a patient complains of sudden attacks of palpitation associated with irregular heart action (patients can as a rule detect this themselves), auricular fibrillation may be presumed from the history alone. Irregularity due to auricular fibrillation is increased and that due to extrasystoles is diminished by increasing the heart rate. Attacks of paroxysmal fibrillation are common in older patients with coronary sclerosis, but are also found in younger people with no detectable cardiac abnormality.

So sinus tachycardia is immediately excluded when a sudden beginning and a sudden end is recorded or observed. If the patient is first seen with a continuous tachycardia of regular rhythm, differentiation will have to be made between sinus tachycardia, paroxysmal tachycardia and flutter. It should be found out if slight exertion, such as sitting up and lying down in bed done several times, increases the pulse rate. As stated already this never fails in sinus tachycardia. If no acceleration appears after slight effort, then either flutter or paroxysmal tachycardia is present. Occasionally the pulse rate changes in some definite mathematical proportions proving the existence of flutter (due to change of the degree of block). Another clinical test that should be done is to put digital pressure on the carotid sinus. In sinus tachycardia this does not produce any appreciable slowing of the rate. If there is any slowing it is maintained only during the period pressure is exerted. Paroxysmal auricular tachycardia may stop with this procedure. There are many cases however of paroxysmal tachycardia and flutter which are not influenced by this. Sometimes even with the help of E.C.G. it may be difficult to differentiate flutter from paroxysmal tachycardia.

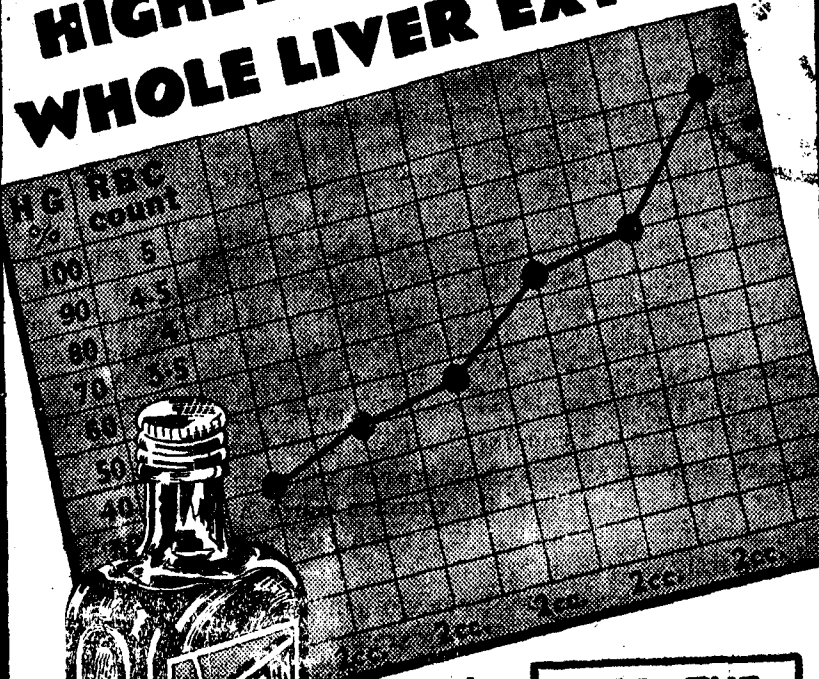
TREATMENT.

All tachycardias when of considerable degree and duration alter the haemodynamics in the same way. By shortening the diastole adequate filling of the heart is interfered with and a primary forward failure of the heart is established. Anginal pain is a frequent accompaniment of the condition due to diminution of minute-volume.

For sinus tachycardia there is no special treatment. Digitalis and quinidine are rarely useful and better not given at all. Treatment of the basic malady should be adopted, which naturally would

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vary from case to case depending on the etiology of the condition precipitating it.

Sinus tachycardia after infection vanishes after the basic malady is controlled. In thyrotoxic condition treatment of thyroid disease will cure the tachycardia. In cardiac neurosis attention should be directed towards the entire individual and not to the cardiac condition alone.

In mitral stenosis with failure but no fibrillation, in extreme tachycardia brought on by auricular reflexes, in myocardial injuries and in coronary sclerosis with sinus tachycardia the slowing effect of digitalis is not so well observed. Despite continuous digitalis therapy the pulse rate may not come down below hundred. Onset of fibrillation in such cases affords a better chance as then the rate is controllable by small doses of digitalis.

Another very common source of tachycardia is post operative conditions. Though auricular fibrillation, flutter and paroxysmal tachycardias occur as post operative complication, sinus tachycardia is by far the commonest and the common cause apart from infection, is dehydration. In such cases what can coramine, cardiazol etc. do when the body is crying for water? Bromide generally is helpful as a supplementary drug in many cases of sinus tachycardia.

Fibrillation and flutter, if they are paroxysmal and of very short duration and occur at long intervals no treatment may be indicated. If they recur frequently and last for sometime quinidine should be given prophylactically and the minimum dose worked out (gr. 1-3, 3-1, time a day).

When these attacks occur at long intervals only, it is better to treat the attacks rather than try to prevent it. For fibrillation quinidine should be used in the following way in a properly selected case.

Quinidine is not always an innocuous remedy and should be administered very cautiously. A test dose of gr. 3 is administered on the first day, two doses the next day and 3 doses the day after. If there are no ill effects such as nausea, vomiting diarrhoea, headache, vertigo, tinnitus, deafness, urticaria or other skin eruptions then the full dose is administered. The average dose is gr. 5 every two hours for 6 doses. If the rhythm and rate do not become normal similar doses may be administered for three consecutive days and then stopped for about 10 days to begin again in the same way. Three sets of such trials may be required but no more. As a rule however heart rate becomes normal on the first day in a large percentage of cases.

In flutter however digitalis is more effective. The drug is given as in comparable cases of failure with fibrillation. In a classical instance rhythm passes into fibrillation and when the drug is withheld normal sinus rhythm is restored. If digitalis is not successful quinidine may be tried in the same way as in fibrillation.

Paroxysmal tachycardias vary considerably in their manner of appearance. They may come once in a lifetime or may occur almost every day. Auricular tachycardias are much more common and are definitely of better prognosis. Though auricular tachycardias are commonly found in otherwise normal hearts, these and particularly the ventricular variety are found in association with some cardiac pathology. In some cases this may be the first and the only evidence of heart damage.

If a patient is seen during an attack it is better not to go on to drugs first. At first carotid sinus pressure should be tried, first on the right and if not successful then on the left side. A large percentage of the auricular variety will respond to this method and the attack will stop immediately. Pressure should be applied just above the level of the upper border of the thyroid cartilage anterior to the sternomastoid muscle. The degree of pressure necessary naturally varies from case to case. Sometimes it may be necessary to change the point of pressure because of abnormal situation of the carotid sinus. The patient should always be in the recumbent position as there may be a sudden stoppage of the heart for several seconds.

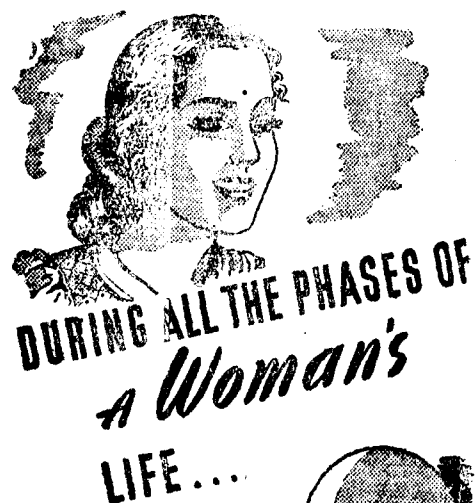
If the carotid sinus pressure fails other methods of reflexly stimulating the vagus may be adopted such as deep inspiration and then holding the breath as long as possible. In younger people bulber pressure is sometimes very effective—the patient looks downwards, closes the eyes and pressure is exerted with increasing force on both the eye-balls. Some patients learn to stop an attack by inducing vomiting by tickling the back of the throat.

Only when these reflex methods fail medicinal therapy should be started and quinidine is the drug of choice for the purpose and should be administered in the same way as already indicated.

Powerful stimulation of the vagus by acetyl-beta-methyl-cholin (mecholy) has been used to terminate supraventricular tachycardia and in some cases they are very effective. The dose is gr. $\frac{1}{2}$ — $\frac{3}{4}$ by subcutaneous injection. Sometimes carotid sinus pressure becomes effective after the injection of mecholy if it had not already produced the desired effect.

If quinidine fails in supraventricular tachycardia digitalis should be used. In view of the fact that digitalis may perpetuate the rhythm or even induce ventricular fibrillation it would appear that the drug is contraindicated in ventricular tachycardia. Digitalis would appear to be indicated in which cardiac dilatation and failure supervenes. In similar conditions stropanthin is also effective provided the patient did not have digitalis within the last seven days.

In the vast majority of cases extrasystoles are not associated with organic heart disease and need no treatment. However they occasionally presage development of fibrillation, flutter and paroxysmal tachycardias hence close observation of the patient is necessary. This is particularly so after an attack of coronary



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thrombosis when they may indicate the immediate possibility of ventricular fibrillation and ventricular tachycardia. Under such circumstances small doses of quinidine (1—3 gr. 3—4 times a day) should be administered to serve as a prophylactic against the more serious types of tachycardias.

(Medical College Magazine, Bengal.)

Extracts

SULPHAPYRIDINE ANURIA

By R. E. WATERSTON, MAJOR, R.A.M.C. AND
C. C. B. DOHERTY, CAPTAIN, R.A.M.C.

Agranulocytosis and anuria are the two most important complications which may occur in treatment with sulphapyridine, and there are numerous references to them in medical literature. While the onset of agranulocytosis can generally be anticipated by white blood cell counts, the onset of anuria is often dramatic in its suddenness and severity.

This report records five cases of haematuria followed by anuria which occurred in patients undergoing sulphapyridine therapy for gonorrhoea. In one of the five the anuria was relieved by the giving of intravenous saline alone, but in the remaining four, cystoscopy with ureteric catheterization was performed, and rapid recovery followed in all cases.

In view of the extensive use of sulphonamide drugs for so many infective conditions, it is considered that attention should be drawn to the possibility of the occurrence of renal complications, to the means of preventing their onset, and to a satisfactory line of treatment.

Discussion

The urinary complications of sulphapyridine treatment are due to the insolubility in water of its excreted products, mainly acetyl-sulphapyridine, which forms crystals in the urinary tract. The appearance of these is characteristic—thin, sharp-pointed, and arranged in bundles like sheaves of corn. Haematuria is caused by the mechanical action of the crystals, and anuria by ureteric obstruction due to calculus formation and reactionary inflammation. This finding has been recorded in a fatal case in which death, confirmed at autopsy, was due to blockage of the ureters with crystals of acetylsulphapyridine (Carson and Smith, 1942). There is no evidence that blockage of the renal tubules is a factor in producing anuria.

On this assumption the rational line of treatment is to remove the ureteric obstruction, and this can be done by ureteric catheterization through a cystoscope. The procedure in the cases described involved the breaking up of concretions impacted at the ureteric orifices and catheterization with lavage of the ureters. Removal of the concretions presented little difficulty as they were soft, and were easily broken up by the point of a ureteric catheter, but oedema prevented catheterization of one ureter in two cases. Intravenous pyelography at a later date, however, showed normal excretion from both kidneys in these two cases. Difficulty comes from the fact that visibility in the bladder is poor owing to the cloud of debris, pus from the urethra, and blood.

In one case the administration of intravenous saline produced diuresis sufficient to remove the obstruction, and this treatment alone may be successful in a mild case without anuria. It should nevertheless be employed in all cases as a preliminary to other measures; most of the cases had vomited, and all were suffering from varying degrees of dehydration.

Rogan and Cruickshank (1942) have described a case of sulphapyridine anuria which was successfully treated by 'Inductotherm' applied to the loins; however they agree that this treatment would have no effect if obstruction were in the ureters.

It will be observed that the dosage of sulphapyridine varies considerably in the series. This is accounted for by the fact that the intensive method of treatment adopted a short time before two cases were treated was later stopped, and as a routine the usual seven-day course of one gramme sulphapyridine four-hourly was substituted. Previously a series of 200 cases of gonorrhoea (fresh) had been treated by this course of smaller dosage and no complications had been observed. It appears that the risk of complications is greater with the intensive method of therapy, and notwithstanding the excellent results obtained by it, we do not consider that this justifies the risk.

As regards prevention, all cases were being given large amounts of fluids, and we emphasize, particularly in the tropics the extreme importance of a large fluid intake for all cases being treated with sulphapyridine. Four of the five cases were on alkaline mixtures four times daily, but it is doubtful if, by the oral administration of drugs, the urine can ever be made sufficiently alkaline to affect the solubility of acetylsulphapyridine.

(Indian Medical Gazette.)

VITAMINS IN DERMATOLOGY

BY MICHAEL. H. EBERT, M.D.

VITAMIN A

Follicular Hyperkeratosis. Disorders characterised by hyperkeratosis, such as keratoderma of the palms and soles, are benefited by the administration of vitamin A.

Pityriasis Rubra Pilaris. The disease also responds to vitamin A but very large doses, 1,50,000 units daily may be required. Local application of cod liver oil is also of value.

Darier's Disease. This is characterized by follicular keratotic papules which become covered by a greasy grayish or brownish crust. It usually begins in childhood and is slowly progressive. The administration of 2,00,000 units of vitamin A daily caused a gradual disappearance of the eruption in 3 of the 4 cases. Cod liver oil has been found to be antiseptic and an excellent stimulant to epidermis formation. It is useful in the treatment of burns and sluggish ulcers.

VITAMIN B COMPLEX

Thiamine. Madden found thiamine of value in the treatment of psoriasis.

Riboflavin. Seborrheic dermatitis of the nasolabial angles and ears respond to riboflavin. Riboflavin has proved efficient in the management of rosacea keratitis. The therapeutic dose is 15-25 mg. daily by mouth.

Nicotinic Acid. It is specific for dermatitis of pellagra. Lynch has suggested the administration of 106 mg. of nicotinic acid daily as a valuable treatment in acne vulgaris.

Kuhman advocated the administration of nicotinic acid for treatment of Lupus Erythematosus.

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VITAMIN D.

Psoriasis and Acne Vulgaris usually improve under treatment with high doses of vitamin D but treatment is to be used with caution.

(Medical Clinics of North America.)

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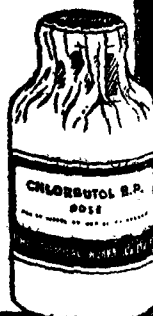
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(British Medical Journal.)

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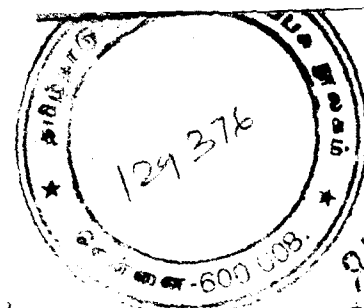
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TREATMENT OF CORONARY THROMBOSIS.*

BY **RUSTOM JAL VAKIL**, M.D., M.R.C.P., D.T.M. & H. (Lond.),
F.R.F.P.S.G., F.A.S.C., J.P.

K. E. M. Hospital, Bombay.

Though much has been written and said about the ætiology, pathology, diagnosis, prognosis and electro-cardiographic interpretation of coronary thrombosis, the question of treatment has been, comparatively speaking, rather sadly neglected by the medical profession. When confronted with anything out of the ordinary in a case of C.T., the attending physician turns from book to book in order to find a solution to his problem, and more often than not returns disappointed. A perusal of the literature on this subject leaves us unsatisfied; we are hampered by conflicting trends of opinion; our knowledge is vague, disseminated and controversial.

What impresses one, perhaps most, in private practice is the over-enthusiastic manner in which the average case of C.T. is treated by the medical practitioner.

The poor patient is subjected to several inhalations of amyl nitrite, he has been made to swallow several tablets of trinitrin in addition to sedatives, carminatives, stimulants, etc., and has also received injections of glucose, coramine, camphor, digitalis, adrenalin, veritol, etc., and all within the space of barely an hour. What surprises one in such cases is how the average patient manages to survive in spite of such drastic over-treatment. The tendency, at the present time, in the treatment of C.T. is unfortunately towards "over-treatment" rather than "under-treatment" and I honestly feel that in many a case it is the enthusiastic physician who is directly or indirectly responsible for the final breakdown of the patient's heart.

Mistakes in treatment are unfortunately much too common; they are mostly due to two factors: (1) mistakes in diagnosis; for example a case of angina proper may be mistaken for clot in the heart and treated as such and vice versa; also an acute thoracic or

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When ordering please mention *Medico-Surgical Suggestions*.

abdominal emergency may be mistaken for C.T. (2) The other factor responsible for wrong treatment is "lack of knowledge" on the part of the physician "of the underlying pathology of C.T." Unmindful or ignorant of these factors, the physician is likely to be guided by his enthusiasm into disastrous channels.

A word of warning before coming to the treatment proper. The doctor must realize that, thanks to American health magazines and the "lay press," the patient of to-day is unfortunately much too familiar with the word "coronary" and with all the danger it implies. It is therefore highly desirable, in the interest of the patient, to exclude any mention of the word "coronary" in conversations with the patient; such a slip on the part of the doctor is likely to turn the patient into a confirmed "neuropath" or "cardiopath" for life. Simple expressions like "clot in the heart" and "heart-muscle damage" are likely to convey much more information and much less dread to the patient than the designation "C.T."

The treatment of C.T. can be considered under 3 main headings, viz. (1) Treatment of the acute attack itself. (2) The treatment of complications and (3) After care of the coronary patient. Lack of time prevents me from considering each of these sections in detail.

Coming to the *attack* proper, let us consider "seriatim" some of the therapeutic measures which are in favour with the medical profession at the present time:

1. *Rest*: There is no doubt that of all the therapeutic measures used in the treatment of C.T., the most important and the most essential, by far, is *rest*. In order to be effective, however, such rest should be both complete and prolonged, both physical and mental. The deleterious effect of mental factors and emotional outbursts on the coronary patient are unfortunately not taken into account. Fussy but well-meaning relatives may actually impede the recovery of a patient and hence relatives and visitors alike, should be rigidly excluded from the sick-room for a period of at least 10 days from the attack.

Let us see, how this all-important therapeutic measure of "complete rest" helps our coronary case:—(a) It affords the "necrosed and soft" heart-muscle of C. infarction a chance to heal properly and form a firm and unyielding scar. (b) It serves to prevent the dreaded complication of "heart-rupture" which is said to occur in about 3 per cent of cases, according to Yaguda. (c) By forming a "firm scar" it prevents the delayed but incapacitating complication of "Aneurysmal dilatation." (d) By slowing the "tempo" or rate of the heart, rest increases the diastolic period, i.e., the "rest period" of the heart. (e) According to Crighton Bramwell, rest promotes an increase of "cardiac reserve" or the reserve-power of the heart.

Ideal posture: There are no hard and fast rules about the ideal posture of the coronary patient in bed. While perhaps the majority of patients prefer to lie flat in bed, there are others who find greater comfort or experience greater alleviation of their distress in the sitting-up posture or may be in the semi-sitting position or even in the lateral decubitus. The rule to observe in these cases is that the patient should be allowed to rest or be propped up in the position of "optimum comfort and minimum embarrassment."

Absolute rest: When we talk of absolute rest for the coronary patient, we mean absolute rest, the so-called "typhoid rest" where the patient is not allowed to make any form of movement on his own. He is not even allowed to turn in bed on his own. In this connection, I may mention that even "good" or so-called "ideal patients," who otherwise follow their doctor's instructions to the letter, often perform, unknowingly at times, movements like raising the shoulders at "feeding time" or "raising the hips for the bed-pan," movements likely to prove disastrous. Such movements should be carefully guarded against. There are, however, two kinds of movements which may be permitted at times especially in elderly subjects, viz. (1) passive turning from side to side in order to prevent the dreaded complication of hypostatic pneumonia and (2) passive movements of the lower extremities by the nurse with a view to preventing thrombotic complications.

Duration of bed-rest: The exact duration of bed-rest advisable in cases of C.T. has caused considerable controversy in medical circles. The majority of cardiologists and the majority of textbooks recommended a period of six weeks rest in bed; it is indeed unfortunate that such "dogmatic" views continue to be expressed for a condition like C.T. The rate of healing of a coronary or myocardial infarct is by no means constant; it is a factor highly variable and dependent on a host of factors, such as size of infarct, condition of the myocardium, the state of the coronary circulation, the age of the patient, etc. According to Mallory and others, small infarcts on an average take about five weeks and large infarcts about two months to heal. Since we have no method of gauging the size of the infarct during life, would it not be safer policy, in view of the pathological studies of Mallory and others, to err on the safe side and recommend a period of rest of two months or even longer? I am certainly in favour of extending the customary or classical "six weeks bed-rest" in cases of C.T. by a further two or three weeks. Such a measure, besides being sound theoretically, is likely to cause a firm "scar" formation and hence fewer complications in future.

2. *Diet*: Regarding the diet of the coronary patient, the majority of doctors are more or less agreed that for the first few days after an attack a "liquid diet" (comprising of small feeds of

diluted milk, orange juice, orangeade and kanjee) is highly desirable. Other items of diet may then be added very gradually from day to day so that by the end of the third week the patient is getting a fairly normal diet.

At this juncture, I may allude to certain trends of thought prevalent in the West at the present time. (1) Master, Jaffe and Dack advocate "low-calorie diets" (*i.e.*, 800 to 1,000 calories per day) in cases of C.T. for periods of as long as 3 to 4 weeks with corresponding limitation of fluid intake (*i.e.*, 1 litre per day); they report very encouraging results indeed.

(2) Some cardiologists recommend adoption of Karell's diet in C.T. for the first few days; my feeling is that patients in India are often intolerant of this diet besides finding it irksome and distasteful; they complain of abdominal discomfort, flatulence, etc., and are better off without this exclusively-milk diet. (3) Herrmann has recently stressed the importance of feeding the C. patient on "proteins of good biological character." I am afraid he is guided more by theoretical than by practical considerations.

3. *Morphia*: There is no doubt that of all the medical measures advocated in the treatment of C.T., the first in importance is morphia or one of its substitutes. Let us see how morphia helps the C. case: (a) It is a most effective antidote to pain. To the coronary patient, in the throes of an agonising pain *i.e.* literally "tearing his chest apart," it is nothing short of a charm. (b) It allays anxiety and lessens restlessness. In this connection, it may be noted that larger doses of morphia are needed to allay restlessness than are required for removing pain. Half-hearted doses of morphia may stop pain but fail to lessen the restlessness of the patient. (c) It induces a feeling of "euphoria" or optimism, according to Gold and such a mental attitude is highly desirable in C.T. There are other advantages also; for example, according to Eppinger and others it reduces the work of the heart; according to Manning and others, morphia may have a sort of "protective action" in cases of C.T. in virtue of its anæsthetic properties.

If we accept morphia as the drug of choice at the onset of an attack, let us consider for a moment, the question of *dosage*. A perusal of the literature on the subject reveals controversial views; there are some who advocate massive doses and others who find small doses just as satisfactory. According to Hymann and Parsonnet, to get the best results out of the drug, it should be used as early as possible and always in liberal doses; they regard "insufficient narcotization" in cases of C.T. as disastrous. My own habit is to give an initial dose of gr. $\frac{1}{4}$ morphia in mild cases and $\frac{1}{3}$ to $\frac{1}{2}$ in severe cases; the gr. $\frac{1}{4}$ dose is repeated two-hourly (or even hourly) until the patient finds relief. The next question to consider is: Should morphia be used in each and every case of C.T.? I

certainly do not think so. In cases of C.T., rare of course, where there is no pain, dyspnoea or restlessness, we have no justification for its use. Not only will morphia be useless in such a case but it may bring on its attendant evils and discomforts. For example, it may induce vomiting, it may cause abdominal distension, it may lead to constipation or urinary retention, skin irritation, mental excitement and a host of other undesirable symptoms in susceptible subjects. Of course, in the great majority of cases of C.T., there is either pain, restlessness or dyspnoea and here the advantages of morphia most certainly outweigh its disadvantages.

What about the much-applauded and much advertised *morphia-substitutes* like Eukodal, Omnopon, Codeine, Dilandid and Papaverine, which continue to flourish in the market. One can however say that they have not proved half as satisfactory as they have been made out to be by the medical press. Paullen, after a fair trial of these preparations, sums them up as "worthless" in one cryptic word.

Morphia-Resistant cases: In some cases of C.T., the pain is so intense that it proves refractory even to massive doses of morphia. What should be done in such cases to alleviate the suffering of the poor patient? I can merely enumerate some of the measures recommended and tried in such cases: (1) Intravenous use of morphia. (2) Local infiltration of the precordial skin with novocaine, (3) Intravenous use of Evipan Sodium. (4) The use of general anæsthesia, (5) Inhalation of Trichlorethylene, (6) Paravertebral or dorsal anæsthesia, (7) Injections intravenous of novalgin or cibalgine.

NITRITES.

More often than not the C.T. patient either subjects himself or is subjected by the doctor to nitrite administration. It is important to realize that "nitrites hold no place in the treatment of coronary thrombosis"; in fact, they are likely to endanger the life of the coronary patient; (1) by lowering further the already low blood-pressure of C.T. they tend to promote clotting or thrombosis, (2) by lowering the B.P. they cause impairment of blood-flow to the heart-muscle, (3) by dilating the peripheral blood-vessels they tend to increase the state of shock and (4) by acting on the cardiac nerves, they may precipitate ectopic rhythms.

There is only one rare type of coronary case where nitrites may be tried with benefit *i.e.* in the rare case of C.T. where there is an initial paradoxical rise of B.P. instead of a fall. In order to prevent such a rise from provoking chest-pain or some other complication, nitrites may be tried.

DIGITALIS GROUP OF DRUGS.

In the past, both English and American cardiologists were dead against using this group of drugs in cases of coronary thrombosis for the following reasons:—(1) The danger of "rupture" of the soft and

friable heart-muscle. (2) The danger of increasing the work of the heart. (3) The danger of inducing a coronary vaso-constriction. (4) The danger of precipitating dangerous ectopic rhythms.

On the other hand, continental physicians have for years been claiming excellent results in cases of C.T. with this group of drugs, especially with strophanthin (the "medication cardio-dynamique" of the French).

Present day American authors "steer a midway course"; their tendency is to restrict the use of these drugs to certain selected cases of C.T. only e.g., cases with cardiac failure or auricular fibrillation. According to Gold the objections usually levelled against digitalis are quite ill-founded.

Quinidine: In 1932, Levine suggested a routine administration of 3 gr. quinidine t.d.s. for the first 2 weeks in all cases of C.T. in order to prevent dangerous ectopic rhythms.

To my mind, such a procedure is unwarranted for (1) The dosage suggested by Levine, is totally inadequate and likely to do no good. (2) In sensitive individuals, the use of quinidine may be attended with alarming reactions. (3) After all, ventricular fibrillation is rare in cases of C.T.

A better plan perhaps is to restrict the use of quinidine to suitable cases only viz. cases with frequent ventricular extrasystoles or with ventricular tachycardia i.e. cases where ventricular fibrillation is likely to arise.

Glucose: For the past twenty-five years or so, glucose has been used very extensively (usually intravenously) in cases of C.T. both here and elsewhere. One meets almost daily with cases of C.T. where the attending physician religiously gives daily injections of glucose hoping for miracles. I have often wondered why glucose has gained such great favour with the medical profession and I have the following suggestions to offer for its popularity:—

(1) One reason perhaps is that a few of the senior doctors have found it satisfactory and the word is passed on from doctor to doctor and from generation. (2) It is a spectacular method of therapy which appeals to the layman and the doctor naturally likes to please his patient and the latter's relatives. (3) The manufacturers of glucose products have been particularly efficient at advertising their goods and have spared neither effort nor paper to that purpose. (4) Many different advantages and beneficial effects have been credited to glucose; for instance, it is said to be the "ideal food" for the heart muscle, an excellent diuretic in heart conditions, a synergist to the action of digitalis and a coronary dilator.

Though I am quite in agreement with the view that glucose is an excellent "food" for the heart-muscle and is often beneficial in cases attended by collapse or shock, I am not in favour of using it indiscriminately in every single case of coronary thrombosis. One

must remember that it has its disadvantages also and these may outweigh its advantages:—

(1) In high concentration e.g. 50 per cent glucose frequently induces thrombosis of the cubital veins; is it not therefore possible for it to actually predispose to or increase the condition of thrombosis in the coronary arteries? (2) It may give rise to pyrexial reactions with or without rigors and such reactions may prove fatal in coronary cases. (3) When administered in liberal quantities, glucose solutions may tax or belabour the already crippled or damaged heart of coronary thrombosis or induce a state of pulmonary oedema. (4) According to Gaston Levy, every time glucose is injected parenterally insulin is liberated from the pancreas and this may induce a dangerous hypoglycæmic reaction. (5) Having myself observed severe anginal pains, pallor, faintness, extreme perspiration and even death after glucose therapy, I am not in favour of using it in each and every case.

OXYGEN THERAPY.

Within recent years, it has been shown beyond any doubt that high-oxygen atmospheres are definitely beneficial in cases of impaired coronary circulation.

In 1929, Rezer and in 1940, Boland demonstrated the effectiveness of oxygen mixtures in cases of coronary thrombosis. They reported immediate and striking relief of pain as well as improvement in symptoms of shock. According to Levy and Barach, the indications for Oxygen therapy in cases of C.T. are (1) severe pain (2) signs of O_2 -want e.g. cyanosis (3) signs of failing circulation.

The oxygen probably acts beneficially by relieving the state of anoxæmia of the heart muscle.

O_2 may be administered in several ways. There is no doubt that the best method known to us at the present time is by the use of the Oxygen Tent; next best is perhaps the "forked-nasal" or the double-catheter of Marriott. The funnel method of administration is utterly useless.

XANTHINE DERIVATIVES OR DIURETICS.

These preparations have been the subject of much discussion in medical circles within recent years. They are perhaps the most extensively used drugs, at the present time, in coronary disorders.

The most popular of this series of drugs are Diuretin, Euphyllin, Theocin, Sodium Acetate, Theocalcin, Deriphyllin etc. but there are a dozen more.

According to some authors, they are indispensable; not only do they induce dilatation of the coronary arteries and an improvement in collateral circulation but also cause a diuresis. On the other hand, there are authors who having used the same clinical and experimental methods have come to the conclusion that the drugs are practically useless in cardiac cases.

Toxic symptoms e. g. nausea, vomiting, abdominal pains, headache and giddiness, may be observed during their administration.

At the present time, the fate of these preparations hangs in the balance.

Vitamin B₁: I have found the administration of Vitamin B₁ a useful therapeutic supplementary measure in cases of C.T. I have seen two or three cases of C.T. where the condition of the patient, considered critical, first showed signs of improvement after the parenteral administration of B₂.

Vitamin C: On the basis of certain clinical and experimental data, I have tried the routine parenteral administration of Vitamin C in cases of C.T. :—(1) Mallory has shown that the healing of myocardial infarcts depends upon the laying down of collagenous material. Since we know that Vitamin C promotes the deposition of collagenous material in the healing of surgical wounds and incisions, is it not fair to assume that Vitamin C may subserve a similar reparative function in the cases of C.T. ? (2) Its diuretic effects are well-known. (3) Tends to maintain the natural resistance of the body to infections.

The only risk of giving Vitamin C is that it may promote the tendency to thrombosis, either increasing the clotting in the coronary or producing a clot elsewhere. I have never seen any harm coming out of its use.

PHYSICAL FORMS OF TREATMENT.

Cold compresses are often useful in relieving the pain of C.T. and in alleviating the distress and tachycardia of the patient. Lian, however, believes that they may increase the degree of cardiac ischaemia.

Ultra short wave treatment: C. Lian has reported excellent results, even in acute attacks, with this form of treatment. After a fair trial of this form of treatment, I can only say that it is worth a trial. In some cases, it appears to do some good, sometimes for the relief of pain and at times for frequent extrasystoles.

In conclusion I may add that in a disease like Coronary Thrombosis with an uncertain prognosis and a variable course, it behoves us to keep an open mind when assessing the merits or demerits of any given therapeutic measure. Cases of C.T. make excellent recoveries in the absence of all treatment while cases treated with meticulous care and perfect judgment may prove fatal.

The future of a C. T. case is entirely "in the laps of the Gods"

(Medical Bulletin.)

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COMPLICATED BREECH PRESENTATION: MANAGEMENT OF EXTENDED ARMS.

DUNCAN MURDOCH, M.B.CH.B., F.R.C.S.E., MAJOR, I.M.S.,
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Nowadays there is general agreement that breech presentation is an abnormality which is serious for both mother and child. The importance and the frequency of this malpresentation has always drawn special study of its cause, its diagnosis and its treatment or management, and early references may be seen in the Hippocratic writings.

After centuries of observation and recorded thought it might be expected that on all leading points the rules for management would be standardised. It is pleasant to find that this is not the case, however, and in matters such as the conduct of the uncomplicated breech and the management of the cases of breech with extended legs interest is fresh today and discussion is often animated and agreeably stimulating and controversial.

My remarks this morning on a part of this subject concern cases of breech presentation in which no abnormality to cause the malpresentation is known to be present, and will be limited to a consideration of delay in the birth of the shoulders due to extended arms. This abnormality in the mechanism might, for example, come about during the vaginal delivery of a primigravida with a frank breech descending through a tight incompletely dilated birth canal so that the arms might become carried up into the extended position, or as another example when a leg has been brought down during version, the traction exerted to bring down the breech may promote extension of the foetus and so lead to extension of the aftercoming arms, however, much it might have been desired to avoid this complication of labour.

The situation will be recognised by noting immediately any delay in the birth of the shoulders and on passing a hand along the front of the foetus the absence of the arms from the normal folded position will confirm the diagnosis. Proceeding at once to the delivery of the posterior arm, the legs of the child are taken in one hand and traction is made first downward so that the axilla may come into view, and then the child's legs are held forward to enable the operator's other hand to be passed into the hollow of the sacrum and along the side of the child until the first and second fingers come to lie alongside the child's elbow when pressure must be given to cause the elbow to flex and the forearm to pass across the face and then the arm to be brought down by drawing the hand outside. The body of the child is now lowered and an attempt is made to deliver the

anterior arm with the same hand and in a similar manner. It is emphasised that during these manipulations the trunk must be drawn down sufficiently low for the lower angle of the scapula to be seen, if precise and prompt delivery of the arms is to be obtained, while at the same time the hold must be loose enough to permit the necessary manipulation.

In the event of delivery of the anterior arm not being possible it will be necessary to rotate the child so that this arm will become posterior and then by making use of the greater space in the hollow of the sacrum it should be possible to complete delivery of this arm fairly easily and quickly, provided that no new difficulty is encountered. It is, however, at this time that the serious difficulty of nuchal displacement is liable to arise and, therefore, the method of rotation is of great importance if this accident is to be avoided.

A case may be imagined where a primigravida with a half breech is received in labour and the legs have been brought down by Pinard's manoeuvre on account of delayed progress, and then one arm has been brought down but rotation is required for access to the arm. In such a case there will be concern as to the possible incomplete dilatation of the soft parts and perhaps some limitation of the capacity of the pelvis may be suspected so that the matter of prompt and gentle completion of the delivery is urgent and anxious. In these circumstances the occurrence of a nuchal displacement will be a most serious complication of the delivery likely to give dangerous delay and liable to lead to a broken humerus or clavicle or quite probably to the death of the child at a time when the greater part of its body has been born and is in the hands of the accoucheur. The thought of the humiliation and distress of such a situation may be a spur to further consideration of this matter.

The usual rule for rotation is that the body of the child which is slippery and greasy is grasped in a towel with two hands so that the anterior arm now becomes posterior. The movement of rotation should be made towards the side on which the back lies; if the child's posterior left arm has been brought down and the anterior right arm is extended the body should be rotated in an anti-clockwise direction towards the mother's right, and *vice versa*. This will avoid the risk of nuchal displacement and encourage folding of the forearm over the face where it will be more easily reached. During rotation traction should not be exerted lest the head be caught and twisted, but rather the rotation should be preceded by disengagement, and should proceed deliberately and gently but with precision to avoid delay.

This method is not universally taught and practised, and experience as an examiner has shown that the instructions concerning rotation as set out by Eden and Holland in their Manual of Obstetrics are widely followed. The influence and authority of this text

book are deservedly high and the authors in describing their method of rotation point to the advantage they claim of keeping the occiput forwards, and moreover they claim that the likelihood of such an occurrence as nuchal displacement is extremely remote. The method of rotation advised in that textbook ignores the risk of dorsal (nucha!) displacement of the arm by turning the child in a direction away from its own back, and this is the shortest movement to bring the required shoulder posterior while keeping the back of the head to the front (avoiding a posterior position of the head).

I venture to disapprove of this method and disagree that the risk is remote. If nuchal displacement occurs, at best it involves the risk of increased manipulations causing liability to injury or infection of the mother: if the child dies and the aftercoming head has to be perforated the operation will be more difficult because of the position of the arm which cannot always easily be brought down by the method of reversed rotation and manipulation.

With the aid of the manikin and doll I shall desire now to demonstrate the alternative methods of rotation for your consideration, and to indicate the method of correction of single or double dorsal (nuchal) displacement of the arms. It will be noted that in the recommended method of rotation the process of disengagement is emphasised in order to avoid excessive twisting of the neck of the child.

In endeavouring to avoid the complication of extended arms, traction should be applied to the foetus only when essential and to a minimal amount and along with the uterine contraction and may be supplemented by the judicious use of Kristeller pressure to augment the uterine power when necessary.

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Extracts.

GENERAL AND LOCAL ADMINISTRATION OF PENICILLIN.

BY M. E. FLOREY & H. W. FLOREY.

Methods of using penicillin for the cure of infections by both general and local administrations are discussed.

Of 15 cases of serious illness treated with penicillin by mouth or by intravenous or intramuscular injection, in 10 there was a staphylococcal infection, in 1 a sulphonamide resistant streptococcus meningitis, in 3 infection with actinomyces or streptothrix plus an anaerobic streptococcus and in 1 a subacute bacterial endocarditis due to strep-viridans. The staphylococcal cases comprised one of orbital infection, 4 of acute or subacute osteomyelitis, 3 of septiemia or pyemia, 1 of cavernous sinus thrombosis and 1 of chronic osteomyelitis; all recovered as also did the case of streptococcal meningitis. The 2 cases with actinomyces infections were not informative because the dosage was probably inadequate, in 1 case a streptothrix appeared to be eliminated. The subacute bacterial endocarditis improved during treatment but relapsed immediately it was stopped. It is clear from this series that a generalised staphylococcal infection can be cured by penicillin and that local lesions heal during parenteral administration. The healing of bony lesions is particularly striking. In 4 staphylococcal cases the sensitivity of the organism to penicillin was tested before and after treatment, in 1 there was evidence of increased resistance.

The most practicable method of administration of the drug is by the intramuscular route at 3 hourly intervals. An endeavour has been made so to regulate the dose that the blood at all times contains at least enough penicillin to inhibit the growth of the infecting organisms. The dose is about 15,000 Oxford units but it varies from case to case.

In assessing progress attention should not be too sharply focussed on the temperature chart, since other features, such as lessening of pain and improvement in appetite and sense of well-being are often more important. In staphylococcal osteomyelitis, X-ray examination shows increased rarefactions of the affected bones during treatment, although the infection is being overcome. The radiological appearances should be interpreted in the light of this knowledge.

No Toxic symptoms due to the drug have been met with. Local penicillin therapy has been used in 172 infections of the eye and mastoid process, chronic wound sinuses and miscellaneous septic local conditions. In most cases after adequate treatment staphylococci and streptococci were eliminated with subsequent healing.

—The Lancet.

**CHEMOTHERAPY IN CEREBROSPINAL FEVER : EXPERIENCE WITH
SULPHATHIAZOLE IN A RECENT EPIDEMIC OF THE DISEASE IN
OSMANABAD IN H. E. H. THE NIZAM'S DOMINIONS.**

BY S. RAGHAVENDER RAO, L.M.S. (Hyd.), D.T.M. (Beng.),
D.P.H., D.Sc. (Cal.).

H.E.H. The Nizam's Public Health Service, Hyderabad Deccan.

Cerebrospinal fever broke out in an epidemic form in Osmanabad town (population, 13,999) in the month of January, 1942. During this epidemic there were altogether 50 cases definitely diagnosed as cerebrospinal fever. Of these cases, 29 were treated as in-patients in the Infectious Diseases Ward of the Local Civil Hospital. Eleven cases were treated outside the hospital by isolating the patients, as far as possible, in their own houses. The remaining 10 cases either refused treatment of any kind or were treated by the local unqualified practitioners. Of this last group of 10 cases, 8 ended fatally, while out of 29 hospital cases only 2 died. All the 11 cases treated outside the hospital, but on the line adopted for the hospital cases, recovered.

In all the cases coming under observation during this epidemic, clinical symptoms were of the usual type. The onset was abrupt, though in some cases there was naso-pharyngeal catarrh, nausea and slight malaise for a day or two before the onset of the more cardinal signs and symptoms. Pain in the muscles of the neck and the back, disturbances of mental faculties, and persistent headache were the main symptoms in most of the cases. The headache was generally localized to the occipital region. Rigidity of the neck muscles with pain on the slightest attempt at movement, particularly flexion, was present in all these cases, and in the severer cases the pain and the stiffness extended to the muscles of the back also. Retraction of the head and opisthotonus were seen in more marked cases. Kernig's sign was always present and the deep reflexes were exaggerated. In only 2 cases were petechial rashes seen; one of these ended fatally. One constant feature noticed in this epidemic was that herpes febrilis was present in every case, though in some cases the fever was neither high nor very prolonged. This herpes is said to be due to a specific virus activated by the disease.

Treatment.

On admission, 1 gramme of the powdered drug was given suspended in 3 to 4 oz. of water. This was followed by another 1 gramme half an hour later. Afterwards for the first two days, or till the severity of the symptoms abated, 1 gramme of the drug four times during the day and twice during the night was administered in a similar manner. In the majority of cases, the intensive course was stopped after the first 48 hours, while in a few cases it was possible to reduce the dose even earlier. After the first intensive

course 0.5 gramme of the drug every 4th hour was continued for two or three days more. In children the dosage of the drug was reduced according to the age of the child and the severity or the mildness of the symptoms. In 75 per cent of the cases, the treatment was discontinued after the 4th day. In some cases, the drug caused severe nausea and vomiting, and a reduction in the dosage of the drug, and increase in fluids by mouth and an alkaline mixture were generally able to control these symptoms. In 1 case, anuria developed on the 3rd day. Immediate stoppage of the drug, plenty of barley water and an ordinary diuretic mixture helped to avert the danger. Constipation was the rule in all cases, and was treated by ordinary soap enemata. Diet during the period of the administration of the drug as well as during the acute stage of the disease consisted of milk alone or milk and sago. Barley water was given freely whenever the patient could take or relish it.

Results of the treatment.—As mentioned above, all cases, treated on the above lines but in their own houses recovered. Of the 29 cases treated in the hospital, 2 died and 27 recovered. These 2 fatal cases had been admitted into the hospital in a moribund condition, and died within few hours of the admission.

Summary and conclusion.—A study of recent literature on the treatment of cerebrospinal fever shows that by far the best results are obtained by chemotherapy. Serum alone or combined with chemotherapy does not show as good results as chemotherapy alone. The treatment so far has generally been carried out either with sulphapyridine (M. & B. 693) or sulphanilamide; the evidence is slightly in favour of sulphapyridine.

In the present series of cases, sulphathiazole alone has been used. Excluding the 2 fatal cases in which only a small quantity of the drug could be administered, the average quantity of sulphathiazole used in treatment was about 14 gramme. This is less than the quantity of M. & B. 693 recommended for a case.

The results of treatment with sulphathiazole are in every way comparable with those obtained either with sulphapyridine or sulphanilamide, and are definitely superior to those obtained with specific serum alone or in combination with other drugs.

Toxic symptoms arising from the use of sulphathiazole are few and can be controlled or treated by simple routine methods.

—*Indian Medical Gazette.*

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Medical Notes and Notes.
CLINICAL SOCIETY
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Medical Science Exhibition.

The above Exhibition—which is believed to be the first of its kind in India—was recently held at the K. G. Medical College, Lucknow, under the auspices of Clinical Society.

It has been always strongly felt that most of the diseases and ailments which present such a common site in our country are due to widespread ignorance, and that they can be easily wiped off if the masses are properly instructed—instructed in a manner which they can imbibe unconsciously. Attempts are being constantly made to teach the public to get rid off their self-inflicted sufferings by such bodies as Red Cross and Anti-T. B. League, etc., but they are far from being sufficient. This Exhibition was organised with an idea to meet that need, and further to dispell ignorance and superstition that exists in the layman's mind about the structure and working of human body, and in introducing public how modern science ensures health and longevity.

The Exhibition was divided under the following sections:—

(1) History of Medical Sciences—included an account of the Founders of Present day Medicine and Surgery; their progress through ages, and a series showing stages in evolution of Microscope, X-ray, Glasses and Blood Transfusion etc.

(2) Anatomy—(a) The unborn (b) Architecture (Skeleton bones, etc.), (c) The Internal Machinery, (d) The Plan of Unity (comparative anatomy), (e) and a journey through ages (the story of the races that ruled the earth thousands of years ago)

(3) Physiology—(a) The blood, its composition and circulation, (b) What happens to the food you take? The dictators of digestion and what they dictate (c) The special senses—showing how one sees, hears, speaks, taste and touches. (d) How the muscles work? (e) Urine—the abnormal constituents and what they indicate.

(4) Surgery—was illustrated with exhibits showing the diseases of various parts, artificial compliances and interesting surgical instruments.

(5) Ophthalmology Structure of the eye and its defects were illustrated by charts and specimens.

(6) Obstetrics and Gynaecology—included specimens of various monsters and abnormalities of foetus.

(7) Medical jurisprudence.

(8) Hygiene:—(a) A peep in the inside of man. (b) His food (c) His environment (d) Common diseases and their prevention (e) Personal and mental hygiene (f) Maternity and child welfare.

(9) Social diseases:—displayed the world's greatest Public Enemies No. 1 and 2 and the lesions caused by them.



(10) Pharmacology:—(a) Experimental section (b) Drug section (c) Endocrinology section.

(11) Pathology:—(a) What diseases we get by microbes (b) Parasites and their harmful activities (c) Alcohol—its effect on internal organs (d) Something about tumours (e) Diseases our parents give us (f) Freaks of Nature.

The exhibition was made more lively and easily understandable by the illustration of each item with numerous exhibits and illustrations which were explained by students demonstrators.

Judging from the public response the enthusiasm with which it was witnessed by people and its instructive value, we strongly urge the organisation of such exhibitions in the different medical institutions in their respective cities.

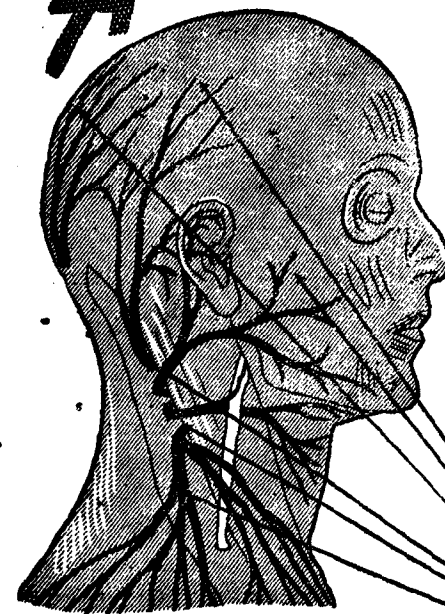
Any further information about it will be gladly furnished by the undersigned to any one who is interested.

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APRIL 1944.

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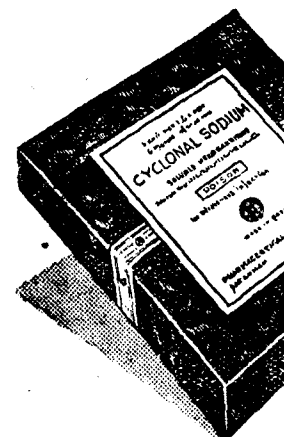
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APRIL 1944

NO. 4

MENSTRUATION

By DR. MISS H. BAHRY, M.B.B.S.

Prince of Wales Hospital, Amritsar

Definition:—The phenomenon is the periodic bloody discharge from the uterus recurring every 4 weeks during the normal reproductive period of the women (Menacoe Kisch) in the absence of pregnancy, associated with necrosis of the uterine mucosa.

According to Bartelmez Menstruation is a blood discharge associated with necrosis of the uterine mucosa, recurring in the absence of pregnancy, at the intervals of 3½-5 weeks in certain primates. Green-Armytage describes it as "the uterus weeping over the loss of a non-impregnated ovum."

Onset:—It begins at puberty usually at about 14 years of age, persisting for about 30 years. Age of onset may vary according to customs, racial and climatic conditions, environments, heredity and the type of person. It occurs earlier in warm than in cold climates. Girls in England menstruate at a later age than girls in India. Eskimos menstruate only in summer. Brunets and red haired girls menstruate early, blonds late (Kisch). A highly strung city girl has early periods, a country girl late. Girls, fond of luxury, who read novels, go to dances, etc., menstruate earlier than poor hard-working girls. If the mother menstruated early the daughter also does so. Cases of precocious menstruation are on record. (Certain new born babies are known to menstruate.)

Pseudomenstruation:—This is believed to be due to sudden withdrawal of oestrogen which the new born draws from the mother's blood.

PERIODICITY.

The menstrual cycle is usually of 4 weeks or 28 days measured by the time between the first day of one period and the first day of the next one. But it varies sometimes in different women. According to Allen and Fluhman menstruation is very irregular, the intervals being 17-42 days in different women at different times. In 90 per cent cases the cycle varies from 26-36 days—the commonest average being 26-31 days (Gunn). Usually 60 per cent cases are

regarded as having a normal rhythm of 28 days. Many a time there is a departure of 2-4 days from the normal 28 days rhythm, while in others the cycle is of 21 days or 35 days. In some women it is irregular being 3-6 weeks, with no sign of ill-health or ill-development of genitalia. A shorter interval is usually found in tropical climates. The cause of the normal rhythm is not yet known, but it may be regarded as a biological constant of adult women just as the pulse rate is a constant.

Now it is known that the rhythm is altered by disorders of ovaries or of those ductless glands which influence the ovaries by their internal secretion, as recent researches show that menstrual rhythm cannot be controlled by diseases of the uterus or fallopian tubes (This applies only to rhythm as the amount of blood lost and duration of hæmorrhage are effected by local changes in the uterus and the fallopian tubes.)

Duration of flow:—The usual duration is 3-7 days. But again this may vary in different individuals at different times. Variations occur from 1-8 days. Brunets bleed more than the blonds. At puberty the flow is moderate. It becomes more profuse and prolonged later on and especially after marriage due to sexual stimulation. It also increases in warmer climates.

The character and amount of flow:—This again is variable. The quantity varies from 2 ounces to 6-8 ounces.

Composition:—Varies from day to day, at first it is muco-serous, then mixed with blood and later it consists of almost pure blood which does not co-agulate either owing to the presence of a tryptic ferment (Anti-thrombin) secreted by the glands of the body of uterus which destroys the fibrinogen of the blood, (b) or due to withdrawal by the endometrium of the fibrin ferment. (c) Beckwith White-house is of the opinion that the blood coagulates as soon as it is shed in the uterine cavity. But the clot is soon liquified by the ferments secreted by the uterine endometrium. Majority regard the clot as pathological. The menstrual blood is alkaline in reaction consisting of dark altered blood, considerable mucus, many lymphocytes, epithelial cells and tissue fragments. It contains a large amount of oestrons.

Blair Bell, found that menstrual blood contains a larger percentage of calcium than the circulating blood and no fibrin ferment. Fibrinogen is normal in amount.

Mittelschmers Menstruation:—Some women have severe pelvic pain midway between two periods on about the 14th day of the cycle, frequently with increased vaginal discharge and in some cases with a little bleeding as well. This is attributed to rupture of Graafian follicle during ovulation. Pain is probably caused by tension at the time of ovulation either by a large ripening follicle or a Vascular proliferating corpus in the ovaries, which have sclerosed tunica

albuginea. This is frequently confused with some disorders of menstruation.

Endometrium in menstrual cycle:—The menstrual phenomenon in women is not quite analogous to the œstrus changes in the mammals in the respect that the human endometrium is almost constantly undergoing changes for the whole 28 days of the cycle. The endometrium is the surface lining of the body of the uterus lying above the level of internal os. It consists of surface epithelium, glands and stroma. In olden days curettings from the uterus taken at different phases of the menstrual cycle were considered to be pathological. In 1893 Ruge classified these cases into three main groups, regarding them pathological due to different forms of endometritis.

1. Interstitial.
2. Glandular.
3. Mixed.

This classification signifies the variations in the endometrium. Brennecke (1882) Schmal (1891) and Schauta were confused as to whether this glandular endometritis was due to infection. Next Hitschmann and Alder (1907) (Schauta's pupils) examined the endometrium at different stages of the menstrual cycle and showed that the structure was not constant and the variations at different stages were physiological. According to them Ruges interstitial cases alone were due to infection, the histological changes in these being comparable to similar infective changes in other parts of the body. They said that the glandular stage was the physiological premenstrual or secretory phase. After this discovery the whole idea about endometritis changed and the modern researches about sex-hormones etc. are all based on this. The endometrium has been investigated in greater detail by Schroder, Robert Mayer and Novak.

Hitschman and Adler classified the phases of menstrual cycle into four following groups:—

1. Post Menstrual.
2. Interval.
3. Premenstrual.
4. Menstrual.

Schroder's classification which is more exact and is usually followed as under:—

1. Proliferative of intermenstrual phase.
2. Premenstrual or secretory phase.
3. Menstrual or Destructive phase.
4. Post-menstrual or regenerative phase.

The endometrium is divided into two layers:—

1. Functional. Superficial layer of epithelium.
2. Basal or deeper layer. This lies next to the endometrium and consists of: (a) stroma cells which are packed together and are deeply stained.

(b) Capillaries.

(c) Lymph nodes.

(1) *Proliferative Phase*:—This phase begins about the fourth day after cessation of the menstrual flow when the regeneration of the endometrium is complete and lasts until the 15th day. These proliferative changes are concomittent with the secretion of oestrogenic or follicular hormones and Graffian follicle is under-going development and ruptures to discharge a mature ovum just before the end of the phase (14th day).

From this simple form proliferative changes take place under the effect of oestrone. The basal and functional layers are well defined, the former measuring 1 mm. in thickness and the latter commencing with an average of 2.5 mms. reaching to 3.5 mms. by the end of the phase i.e. 15th day. The glands of functional layers are tubules with regular epithelium. About the tenth day the gland increase in length, become more tortuous and their lining epithelium becomes more columnar with centrally placed nuclei. Many mitotic figures are seen in epithelium and stroma cells. The stroma becomes oedematous wide separation of individual cells and formation of intercellular lymph spaces.

Capillaries in superficial layer become dilated. In some cases this vascularisation is so intense that some blood oozes into the uterine cavity and is discharged from the vagina giving rise to intermenstrual bleeding.

(2) *Secretory Phase*:—Beginning on the 15th day of the cycle this phase lasts until the onset of menstruation. During this phase, a corpus luteum has been developing from the ruptured Graffian follicle of the preceding phase. The changes here are due to the combined action of the follicular hormone and the corpus luteal hormone the progesterone both of which are controlled by the gonadotropic hormones of the ant-lobe of the pituitary gland. Two days before the end of this phase, the corpus luteum begins to degenerate and both the corpus luteal and the follicular hormones cease to be formed.

The functional layer continues to hypertrophy until at the end of the phase it is 3.5-4 mm. thick-going upto 8 mm. thickness in some cases. Most marked signs are seen in the glands. Mitotic figures are not seen. The epithelial cells develop spherical translucent areas between their nuclei and the basement membrane which contains the precursors of the glandular secretion and which persists about the 21st day of the cycle. Later the nuclei sink towards the base of the cells as the globule of secretion moves forwards the free surface. The adjacent glands lie more closely together, the inner border of the epithelial cells irregular through discharge of secretion into the gland lumen. Hence just before menstruation glands are full of secretion and stain deeply with eosin. The gland becomes crenated and gives the characteristic dentate or cork screw shaped appearance.

Where the glands are most distended the stroma is consequently condensed giving a spongy appearance.

The stroma cells become swollen and after 21st day they tend to be collected just under the surface epithelium, surrounding the ducts of the glands. Nuclei stain less deeply.

The endometrium continues to be vascularised. Large thin walled blood sinuses form and blood from these escapes into the stroma forming small haematomata which raise up the epithelium from the stroma. Lymphocytes from lymph nodes move towards the surface and by the end there is a lymphocytic infiltration of the endometrium but no haemorrhage.

Here the endometrium appears like one of early pregnancy with identification of all three layers.

1. *Basal layer*:—Bases of glands adjacent to muscle layer.

2. *The stratum spongiosum*:—This contains widely dilated glandular portions.

3. *Stratum compactum* containing the large stroma cells which form the decidua cells if fertilisation occurs.

Another analogous thing to pregnancy is that glycogen accumulates in the endometrium in this and the next phase.

4. *Destructive phase*:—This occurs due to sudden withdrawal of the follicular and the corpus luteum hormone occurring at the end of the previous stage. The corpus luteum begins to degenerate, the cells show hyaline changes with vaculation, deposition of lutein takes place which gives them the yellow colouration. These changes explain the withdrawal of corpus luteal hormone. But the withdrawal of follicular hormone cannot be explained.

The first signs of degeneration are noted in the course of capillaries of the compact layer. Small haemorrhages occur into the stroma as the result of breaking down of capillary endothelium. Superficial part of epithelium breaks down and is shed into the uterine cavity with R. B.Cs. leucocytes, stroma cells and gland tissues. Later the degenerative changes establish themselves in the spongy layer, and a large portion of it is shed. By the second day of this phase the compact layer and superficial part of the spongy layer have all degenerated and by the third day the endometrium is raw and thus the glands of deeper portion of spongy layer open directly into the uterine cavity. After this the bleeding is due to the oozing from the capillaries of this denuded stroma.

It is said that recurrent and painless contractions of the uterine muscles occurring at 1-2 intervals help the discharge to escape, thus the flow being intermittent and not continuous.

It is found out that in cases of abnormal uterine bleeding these degenerative changes are localised only to a portion of the endometrium. By the third day even before the bleeding has stopped

the reparative changes begin by the epithelium going over from the lining of the glands to cover the raw stroma.

4. *Regenerative Phase*:—Repair of endometrium already starts in the latter part of the preceding phase and is complete 48 hours after the cessation of menstruation. During this time in the ovaries the corpus luteum continues to degenerate, while in another part a new Graffian follicle begins to mature in order to control the next menstrual cycle.

New epithelial lining of the endometrium is formed by the proliferation of the glands, the glandular epithelium growing over. At first a large number of lymphocytes are seen in the stroma, but these decrease as the glands resume their own tubular form and the stroma is readjusted as in the beginning of the proliferative stage.

THE MECHANISM OF MENSTRUATION

This has ever been a subject of great controversy.

(i) At first it was thought that this menstrual bleeding was due to the activity of uterine muscle which drove the blood into the uterine endometrium where fatty degeneration was caused due to increased pressure resulting in disintegration of capillary walls. Endothelium was this thought to be shed, and regenerated from basal tissue.

(ii) Pfleger later thought this to be a nerve reflex which was set up by changes in the size of Graffian Follicle of the ovary via the ovarian nerve, producing by response the dilatation of blood vessels of uterine wall.

(iii) But now it is being proved that these functions are independent of the central nervous system. For the last 25 years researches have shown that the menstrual changes in the uterus are controlled by hormones secreted by the ovaries which in turn are controlled by the gonadotropic hormones secreted by the anterior lobe of the pituitary gland.

Green Armytage (1925) summarises the whole phenomenon as follows:—

"Menstruation may be looked upon as the uterus weeping over the loss of an ovum, and it depends on ovarian hormone which is sensitized by calcium. This hormone cooperates with other hormones from the endocrine glands, and it will perhaps make it clearer for you to understand this, if you will imagine that tear is a form of executive board in the human female body for its common welfare. Some members of the board are inhibitors while others are accelerators of menstruation and both these parties have calcium as their bond of union.

The proof of the above is determined by the following clinical findings.

- I. (a) If thyroid is over-working (As in exophthalmic goitre) we get menorrhagia.

- (b) If it is deficient (As in myxoedema, delayed puberty, or cretinism) we get amenorrhoea.
2. (a) If the anterior pituitary gland secretion is excess.
- (b) If it is deficient we get amenorrhoea and non-development of the genitals, and such conditions as infantile or coehleate uterus.
3. (a) If the supra-renal gland secretion is in excess we get amenorrhoea with atrophy of ovaries.
- (b) If it is deficient we get precocious menstruation of children with hypertrophy of genital organs.
4. When the thymus gland atrophies menstruation and ovarian function begin.

If the thymus persists, puberty is delayed.

5. The endometrium controls the excretion of calcium. The proof of this fact is that menstrual blood contains far more calcium than the premenstrual circulating blood.

What happens is that calcium content of the blood rises gradually to a certain height. This calcium sensitizes especially the thyroid and the anterior pituitary glands which sends a hormone to the endometrium, which in turn fires the trigger of menstruation. When the thyroid, endometrium and the ovaries have opened their energy, the inhibitors function and the process of building up next menstrual period begins."

Ovulation:—Its relationship to menstruation.

Definition:—Ovulation is the act by which the ripe Graafian follicle of the ovary ruptures and the ovum is discharged from its cavity into the peritoneal cavity, when the intra-follicular pressure is high enough to allow it to burst.

CHANGES IN THE OVARY DURING OVULATION

Just before the rupture takes place, the ripening follicle comes to lie near the surface of the ovary with the discus Oophrens directed towards the peritoneal cavity. The process of ovulation is properly studied in animals like rabbit and ferret where ovulation occurs at a certain fixed time after coitus. Dilated capillaries and a plug of coagulated plasma is seen in the intima layer and this raises up the intra-follicular pressure. Stigma or the aperture through which the ovum is discharged is closed by a plasma plug soon after ovulation. In spite of the sudden release in the intra-follicular pressure due to expulsion of the ovum there is no hæmorrhage into the follicular cavity as the membrana limitans externa separates the hæmorrhagic theca interna layer from the cavity and the granulosa layer is avascular. The follicle collapses and the opposing surfaces come together with small convolutions.

RELATIONSHIP OF OVULATION WITH MENSTRUATION

Ovulation is the essential factor in normal menstrual cycle. They both appear and disappear about the same stage of human life

and are closely associated during the sexual life. American Gynaecologists think that the two processes are not essential to each other as (1) anovular bleeding occurs in certain women in whom the endometrium does not show the secretory hypertrophy produced by corpus luteum and is associated with sterility. (2) Pregnancy where menstruation has not been established e.g. during lactation, before puberty and during amenorrhoea of tuberculosis and anaemia.

Usually only a single ovum is discharged but some-times two are discharged and if both of these are fertilised twin pregnancy results.

Time of ovulation:—In a normal 28 days cycle ovulation occurs about 14 days from the onset of the preceding period. This time is determined by the following methods:—

(i) Ovaries removed at operations have been examined histologically by Robert Meyer, Schroder, Novak and others and the stage of development of Graafian Follicle or early corpus luteum indentified with the menstrual history. Early corpus luteum is a greyish structure which may be easily missed where the menstrual cycle is abnormal the date of ovulation is arrived at by calculating 14 days back from the onset of the next period. Gynaecologists believe that this period is fixed.

(ii) By Washing through the fallopian tubes at operations. Allen has recovered human ova and showed that ovulation is restricted to the 14th day.

(iii) An indirect but a very reliable method is by studying the changes of endometrium during the secretory phase which can be produced by the action of hormones of corpus luteum and is found to begin from the 14th day.

(iv) Onset of Mittelschmerz:—Some women develop pelvic pain midway between two periods and this is thought to be due to tension within the ovaries by the ripe follicle which is to rupture. This is unreliable.

(V) Recently Pillay (1940, 41, 42) has determined the day of Ovulation by vitamin test, which is done by the estimation of Vitamin C secreted in the urine.

Schroder believes that the range of variation is never more than 2 days from the 14th day. Corner and Robert Meyer and Grosser believe in a wider range.

CHANGES IN THE OVARIES.

Ovaries are two almond shaped, egg producing, densely fibrous organs lying in the pelvis on the posterior surface of the broad ligament in the ovarian fossa. Each measures 1½"-2½" the right being larger than the left. At birth ovary is relatively large and upto puberty enlargement is due to enlargement of primordial follicles and formation of connective tissue and blood vessels. After

the commencement of menstruation the surface becomes roughened and puckered with repeated rupturing of follicles. After the menopause the ovaries shrink, to small fibrous organs. An ovary is divided into 3 regions:

(i) **Hilum:**—This adjoins the mesovarium and ovarian vessels, lymphatics and nerve enter here. It contains some tubules, connective tissue and unstriated muscle.

(ii) **Medulla:**—Similar in structure to the hilum it subtends the hilum as a semilunar area enclosed by the cortex.

(iii) **Cortex:**—This forms the main mass of the ovary and is the specialised functioning part consisting of:—

(a) connective tissue stroma for vessels and Graafian follicles.

(b) Epithelial structures in which is

(i) the germinal epithelium which is one layer deep covering the free surface of the ovary upto the hilum.

(ii) Interstitial glands of the ovary. There are epithelial cells scattered throughout the ovary.

(iii) Graafian Follicles which are formed round the ova.

Graafian Follicle:—Described by Regnier de Graaf (1672).

This can be studied in various stages.

The formation of ova begins in early foetal life and the ovary of a new born child contains also 1000,000-3000,000 oocytes and by puberty this number decreases to 30,000

(i) **Primordial Follicle:** is the stage in the new born baby and throughout life. Some follicles in this stage can be seen. It is the ovum a large clear, central spherical cell surrounded by a layer of flat cells. These young follicles are collected towards the surface of the ovary.

(ii) **Ripening follicle.** usually one near the hilum begins to ripen and sinks towards the centre of the ovary, at or just before puberty. The ovum becomes larger and the cells surrounding it proliferate. At first there is a single layer proliferating several layers of cells and then it is called *Membrana Granulosa cells*.

Fluid:—Liquor folliculi appears in the cell mass pushing the ovum into an eccentric position. Liquor folliculi is clear, viscid, alkaline albuminoid, fluid containing a few oil globules and granules, coagulates after formaline fixation and contains oestrin. A small clump of cells of stratum granulosa is seen at the periphery of the follicle, containing the ovum and this is called *discus proligerous* or *cumulus oophorus*. The nucleus stains deeply and occupies the major portion of the cell. The deepest layer of membrana granulosa rests upon a basement membrane and has a regular arrangement.

(iii) A **mature follicle** is seen as a rounded swelling on the surface of the ovary measuring on an average between 12-16 mms. or 1/3" in diameter after puberty. The ovum is about 1/120 inch in diameter and is enclosed by a cell membrane around which there is

a clear space-the perivitteline space which in turn is surrounded by another clear space-the *zona pellucida* which is traversed by a series of fine fibrils. The granulosa cells surrounding the *zona pellucida* have a radial arrangement and are known as *Corona radiata*. Along with these changes, changes also occur in the surrounding stroma. The basement membrane of the granulosa layer is known as the *membrana limitans externa*. Among this, there are no capillaries and hence the granulosa layer is non-vascular. There are small spherical globules-bodies of cell and exner-scattered amongst the granulosa cells, especially in the vicinity of discus proligerus.

The *tunica interna* or the layer of stroma cells next to the follicle is differentiated by *membrana limitans externa*. *Tunica interna* cells are derived from the stroma cells of the ovarian cortex, are variable in size and are larger than granulosa cells just before ovulation.

Ova of all stages of ripening are in the ovary at the same time. Some of the follicles never complete the process of follicularisation. In them the ovum dies and the follicle shrinks forming the corpora fibrosa. *Atresic follicle* is the one which retrogresses at any stage of development.

As the follicle increases in size it rises towards the surface of the ovary where it is seen as small bulge of congestion. During this process there is the rotation of the discus proligerus, so that when complete follicularisation has taken place the ovum becomes the most superficial part and the *membrana granulosa* layer is thinned too especially at its superficial portion where it ruptures at a point called *stigma* which closes with a plasma plug soon after. When the ovum escapes it carries some of the granulosa cells with it.

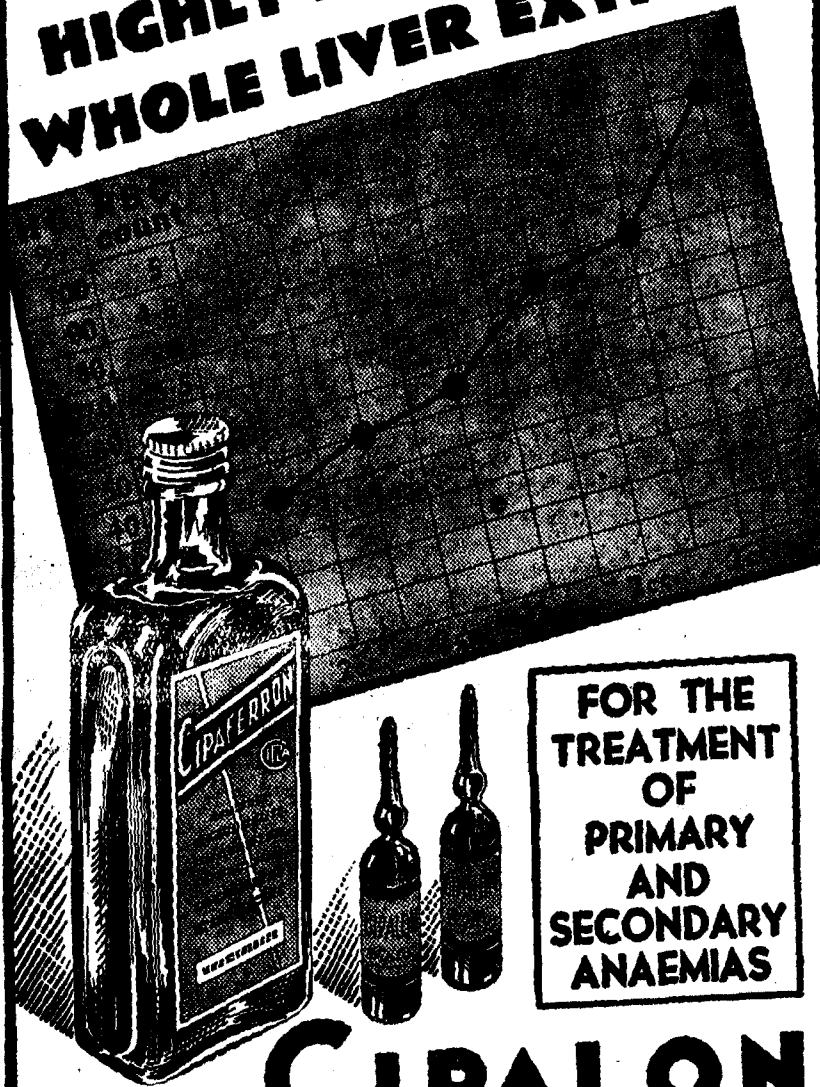
The function of the interstitial cells is not known as yet but many people believe that the secretions from these cells determine the secondary sexual characters.

The cause of the Graafian follicle suddenly becoming active is not understood yet. Some-thing either nervous or endocrine acts on the pituitary gland to elaborate a hormone to stimulate follicularisation, ovulation and later the formation of the corpus luteum.

(iv) *Corpus Luteum*. After ovulation has taken place the follicle collapse. Some time ago it was believed that the stratum granulosum disappears and the lutein cells develop from theca interna cells. Recently Novak & Sabotta (Lower animal) Walford Shaw and Mayer human beings) and Biscoff have shown that lutein cells are modified cells from stratum granulosum. Some believe that theca interna cells retrogress while others think that they play a part in the formation of corpus luteum.

Soon after ovulation the granulosa cells proliferate showing mitotic figures, so that 8-10 layers are seen. The theca interna cells

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also show some proliferation and are sometimes known as *paralutein cells* and the lutein cells from granulosa cells are known as the granulosa lutein cells. Yellow refracting pigment, Lutein (Escher thought it to be corotin) appears in the cells. With the proliferation convolutions appear in the yellow cell layer and the cavity is narrowed to thin space. This proliferation continues until the 22nd day of the menstrual cycle and remains stationary till the end of the cycle (28 days).

A fully formed corpus luteum is about $\frac{1}{2}$, $\frac{2}{3}$ inch in diameter and consists of large closely packed polyhedral cells containing a large clear nucleus and a lipoid substance called lutein.

Small capillaries from the surrounding hyperaemic ovarian stroma pass into the corpus luteum. This vascular supply is like that of ductless glands and it is from this point that the analogy of the corpus luteum to endocrine glands was thought of.

Retrogression of corpus luteum. If the ovum is not fertilised the corpus luteum begins to regress after the menstruation. The cells degenerate by fatty infiltration and hyaline degeneration. Hyaline tissue increases in size as the cells degenerate till at the end of 9 months (Ruhl) it is transformed into a complete mass of hyaline tissue termed *corpus albicans*.

(To be continued.)

THE INCIDENCE AND RESULTS OF TREATMENT OF SUBCLINICAL AMEBIASIS.

FRANK H. CONNELL, PH.D. AND HARRY T. FRENCH, M.D.
Haver, N. H.

During the last twenty-five years, sizable segments of practically every population group in this country and abroad have been examined for intestinal parasites. As Faust and his colleagues have pointed out, "it is practically impossible to compare data on the parasite rates based on different population groups utilizing different techniques of diagnosis, and evaluating results according to individual idiosyncrasies." Nevertheless, because of such survey it is now known that *Endamoeba histolytica* can be demonstrated wherever man is found without regard for race, latitude or social position. Furthermore, though accurate comparisons are impossible, it has been established beyond question that variation in incidence occurs among geographic, age and economic groups.

Craig, on the basis of such surveys, has estimated that between 5 and 10 per cent of the population of this country as a whole harbors *Endamoeba histolytica*. If it is important for medical men to appreciate the seriousness of the picture for the country as a whole, it is equally important that they know with some degree of accuracy the incidence of amebiasis in their own locality. If surveys have served a useful purpose in the past, there still remains for the future a real need for accurate local investigations of the civilian non-institutional population. Without an accurate idea of the amount of amebiasis occurring in his practice a physician may, and often does, fail to consider the possibility of an amebic infection if he lives in a region in which the incidence is low. On the other hand, it leads to distrust if a clinical laboratory in such a locality is forced to report a long series of negative examinations to a man who expects an incidence of 10 per cent.

Until the Craig complement fixation test becomes more generally available or new tests are devised it is unfortunate that contact between the patients and the clinical laboratory, which in the last analysis must make the diagnosis, should be so distinctly second hand. Dobell in 1917 wrote: "The errors committed by an examiner of little or no previous experience are such as I could not have believed possible if I had not actually encountered them and in cases where the health of a patient is at stake, it is I believe, almost better that no examination at all should be made than that it should be made by an incompetent and inexperienced person." A little more than a year ago, Kellogg and Scott reported that in California the laboratory diagnosis of amebiasis was in a unsatisfactory state because of universal lack of trained personnel for work of this type and that this together with an equally widespread lack of understanding and appreciation of the situation on the part of everybody concerned, is productive of such a high percentage of unreliable reports, and their blind acceptance that the situation is worse by far than if no laboratory tests and all were made in many, perhaps most cases." What Dobell said over twenty years ago is still true today. What is true of Europe and California is equally true of New Hampshire and it would be strange indeed if other points could not be found between the Atlantic and the Pacific where similar conditions exist.

The whole fault does not lie, however, with the training of our technicians. No technician can demonstrate amebas which have disintegrated by the time the specimen reaches the laboratory. Not only should a thoroughly trained and experienced person conduct the search for amebas but such a person should supervise the collection and subsequent handling of all specimens. How many patients, student nurses or physicians, for that matter, are familiar enough with the biologic peculiarities of *Endamoeba histolytica* to collect a

specimen intelligently? It is a well known-pedagogic principle that students will do just about as much as is required of them. By wider application is it not likely that if it were realized how much more one ought to require by way of training for technicians there would be no problem?

It may appear that we have been merely restating old truths, but that lack of confidence in the diagnosis of amebiasis is widespread may be illustrated by the fact that in our annual examination of Dartmouth freshman for amebiasis it has been found expedient to make, before treating a student, two permanent slides in order that we may have proof of his infection.

There exist, in and around Hanover, a stable rural, nonindustrial population living alongside a college population whose members are drawn not only from all corners of the country but very largely from that stratum of the population which economically possesses a surplus over and above the demands of daily existence.

A selection of all the known local rural population from our records reveals that 205 of them have been referred to our laboratory during the past six years on the basis of gastrointestinal symptoms and not one has been found positive for *Endamoeba histolytica*; this in spite of the fact that examination of a single specimen has been the exception rather than the rule and that the method or methods used were adapted to the nature of the specimen.

During the same period five faculty members returning from foreign travels and three other residents of the state, all suffering from diarrhea or dysentery, have been found positive. One of the latter returned from the Spanish-American War with severe attacks of diarrhea and dysentery which persisted at frequent but irregular intervals down to the time of treatment for acute amebic dysentery in October 1936.

Fecal examination of the entering class at Dartmouth was undertaken by one of us (Connell) five years ago and has been retained as a part of the routine physical examination administered at matriculation. Five years ago, on the heels of the Chicago epidemic, the role of the food handler in the transmission of amebiasis was not as well understood as at present. In fact, as McCoy put it there was little choice, from the point of view of society, between a carrier *Endamoeba histolytica* and a leper. With nearly 100 freshmen working as food handlers it seemed a worthy project, especially since on the basis of the current surveys, one might expect an incidence of better than 5 per cent. The early finding of two carriers waiting on the same table in college commons did nothing to lessen this impression. Furthermore, since Hanover seems to lie in the midst of a parasitologic desert with minimum opportunity for reinfection and since all patients treated might be expected to be available for reexamination for four years, it was felt that valuable information

could be gathered on the efficacy of treatment in a disease prone, according to all records, to relapse.

The results of our examination are as follows. In 1934 and 1936, when comparable methods of diagnosis were used, i.e. two specimens per man were obtained and a smear stained with Heidenhain's iron hematoxylin made from each, a total of 1,351 men were examined and twenty-four found positive for *Endamoeba histolytica* an incidence of almost 1.8 per cent.

In 1935 lack of trained assistants made the satisfactory completion of a survey impossible. Recently, however forty-five members of this class, taking our course in parasitology, were examined by a variety of methods, including culture and the zinc sulfate centrifugal flotation method devised by Faust and his colleagues at Tulane University of Louisiana School of Medicine. Of this group 10 were found positive for one or more species of amebas and three of these, or nearly 7 per cent, were infected with *Endamoeba histolytica*.

These samplings have been a voluntary spare time undertaking; therefore, as the burden of college duties has varied, so have the methods used and the number of specimens examined per man been varied.

In 1937, with less time available, a slide, was prepared as before but only one specimen was collected. In a class of 684 men five positive specimens were found. This year, 1,638 a single specimen was again collected and the De Rivas concentration technic was used. The eighty four men found positive for some species of ameba were later reexamined by the zinc sulfate method and five men in a class of 670 were shown to be positive for *Endamoeba histolytica*.

How to explain the drop in incidence from approximately 11 per cent for the years 1934 and 1936 to around 0.7 per cent for the years 1937 and 1938? While it might seem to confirm the observation of Spector, who noted that in Chicago the incidence of *Endamoeba histolytica* among clinic patients fell from a high of 42 per cent for May 1934 to 2.4 per cent for February 1937, the drop in incidence among our students is unquestionably more apparent than real and due to variation in method.

Even though we do not believe that our examinations, even in 1934 and 1936, revealed more than half the infections actually present, they did at least point out again what everyone seems prone to forget—that no part of the country is free from amebiasis. With positives from such widely separated points as Phoenix, Ariz., and Boston, Montreal and New Orleans, with fifteen states represented including all the North Atlantic states except Delaware, Rhode Island and Maine, no one can afford to ignore the possibility of amebiasis for patients with gastrointestinal symptoms.

Granted that comparisons are dangerous, it nevertheless seems obvious, when one views the records for our rural and student groups alongside those of Andrews and Paulson for Baltimore clinic patients and those of Melaney and his colleagues for rural Tennessee that, in the temperate parts of our country at least, the probability of acquiring an amebic infection depends more on how one lives than on where one lives.

With nearly all workers in this field agreed that no one carry *Endamoeba histolytica* without harm, we are impressed by the casual way in which many physicians refer to carriers as "just cyst passers." Several workers have reported extensive lesions including liver abscess found at autopsy in persons who were known to have been without recognizable symptoms of amebic infection. The carrier state is, therefore, as Craig makes clear, dangerous not only to society but to the individual. Not only may be at any time come down with amebic diarrhea or dysentery but lacking such spectacular manifestations of the disease, may go on for years in a state of lowered efficiency without suspecting that there is anything wrong.

Only eight of the thirty-seven students found infected had ever felt bad enough to seek medical attention, and only three of these for diarrhea or dysentery. It did them little good however, for none were ever examined for amebas and among the previous diagnoses which may be noted in their histories are chronic appendicitis, ulcerative colitis and low grade peritonitis. One man with a history of frequent and sometimes severe attacks of diarrhea and dysentery over a period of four years had been treated by a diet consisting of boiled milk and rice!

While most of the twenty-nine infected students who had never sought medical attention for relief of symptoms readily admitted to one or more symptoms suggestive of the carrier state it is significant that not one of these men thought he had anything really wrong with him. Two men even professed to believe that diarrhea once or twice a week was perfectly normal.

These same men, within a few months after treatment, almost invariably insisted that they felt better, had more energy engaged in more extra curricular activities and were able to prepare for their classes more easily. If such statements are founded in fact rather than wishful thinking, some reflection of such changes might be expected to appear in a man's scholastic record. While many marked reversals of form have occurred, we must conclude that a course of carbarsone is not the answer for every poor student in college.

Several papers have been published fairly recently which report the results of treatment for such large numbers of persons with amebiasis that it would seem hardly worth while to report so small

a group as ours if it were not for the fact that none of the thirty-seven persons treated have had a relapse, even though the minimum post-treatment examination procedure has consisted of examination of no less than three consecutive stools at the termination of treatment and a twice yearly check up of two or more specimens for as long as the patient remains available. For the group reported, twenty have already remained negative for more than three years.

Carbarsone has been used in conjunction with emetine ever since it became available, and but one of our earliest cases received any other form of medication. The procedure has, of course been varied to a certain extent according to the severity of the symptoms, but both carriers and those suffering from the more acute manifestations of the disease have received identical treatment, for the first five days; i.e., emetine hydrochloride, one-half grain (0.03 Gm) intramuscularly twice a day for five days and, simultaneously carbarsone, 0.25 Gm. orally twice a day for the same period. For most patients, including all those treated by French, carbarsone has then been continued for five additional days at the same rate. In a few cases, after the first five days of treatment, a rest period of five days was observed, after which the initial treatment was repeated. In all cases, including three persons suffering from acute dysentery, it has been impossible to demonstrate amebas in the stool after the third day of treatment. All men have been kept under close observation during the period when they were receiving both emetine and carbarsone. Those with diarrhea or dysentery have been kept in bed. No toxic symptoms have been noted.

While apparent relapses within forty days are reported by Craig in 81 per cent of 130 persons treated with emetine alone and while apparent relapses following the use of carbarsone alone are not uncommon (Hakansson) it seems unlikely to us that the perfect results achieved in our small series should be ascribed entirely to either chance or the procedure followed but to a considerable degree it should be credited to lack of opportunity for reinfection.

Furthermore, though Craig warns specifically against the use of emetine, except for control of severe diarrhea or dysentery, we feel that the marked degenerative changes noted by James in *Endamoeba histolytica* in vivo following very small doses of emetine (from 1/6 to 4 grains [0.01 to 0.26 Gm.]) should not be ignored and that emetine in small doses may well be retained in the treatment of carriers in conjunction with other drugs, as reported for those patients treated by French.

SUMMARY.

1. In this study 2,750 male college students were examined for amebiasis.
2. All Atlantic states north of Virginia (except Maine, Rhode Island and Delaware) are represented in the group found positive for

Endamoeba histolytica, and no section of the country is without representation.

3. Carbarsone in conjunction with emetine has been used in treatment with no toxic symptoms or relapses noted. Twenty of the men treated have remained negative for more than three-years.

Extracts.

A CLINICAL STUDY OF FIFTY CASES OF MENINGOVASCULAR SYPHILIS

By B. K. RAMAKRISHNA RAO, B.Sc., M.B.B.S.,

M.R.C.S. (Eng.), M.R.C.P. (Lond.)

Incidence of Neurosyphilis. This is said to vary from about 10 per cent (Brain, 1940) to about 25 per cent (Grinker, 1936).

Kinds of Neurosyphilis. It is divided into two kinds:—

- (1) Interstitial, meningovascular or cerebrospinal syphilis.
- (2) Parenchymatous, parasyphilis or meta syphilis includes tabes and general paralysis. This form is very rare in India.

The nervous manifestations may occur long after the initial infection and everything may have been forgotten about it. Primary lesions have been inconspicuous or entirely absent in some cases. History of secondary stage, such as sore throat, dermal eruptions and arthralgia can rarely be elicited from patients suffering neurosyphilis.

The latent interval. All the author's cases with a history of primary sore came under his observation within 3 years of infection: The average interval was about 15—18 months. Cases in which vascular catasyllisms occur seem to have a much shorter latent interval. The acute forms of myelitis also seem to have a very short latent interval.

Age incidence. Majority of the cases were between 25—35 years of age.

CEREBRAL SYPHILIS (34 CASES)

Clinical features. The symptoms of cerebral syphilis are by no means pathognomonic, since identical pictures may be produced by other lesions. The study of the particular combination of symptoms is very useful. The main lesions of the disease may be vascular or meningeal; the lesions may be diffuse or localized in any portion of the brain, or cranial nerves may be involved either singly or in any combination; therefore a combination of symptoms is usual. In

many cases it is the multiplicity of symptoms, their presence in unusual combinations and the changes in their intensity and distribution from time to time that give the clue to a correct diagnosis.

Prodromal Symptoms. Commonest are headache, insomnia, fatigue, and mild changes in the temperament. Headache is the commonest. It was present in more than half of the author's cases. These prodromal symptoms seem to be more common in meningeal types.

Intracranial Symptoms.

- (1) Cranial Nerve palsies. The commonest nerve to be affected is the 3rd nerve, and next to it the 6th. Next in order is the affection of the 7th nerve. The other cerebral nerves also may be involved, and it is not uncommon to get them affected in combination.

Of the author's 34 cases of cerebral syphilis, six came under his observation for cranial nerve palsies. It is sometimes very difficult to distinguish a 7th nerve paralysis due to syphilis from Bell's palsy. In syphilitic cases there is often a prodromal period of headache and the onset of facial paralysis is more insidious than in Bell's palsy. A paralysis which takes more than 24—48 hours to develop is not Bell's palsy.

One case had involvement of the 5th nerve and was referred to the author as a case of trigeminal neuralgia. The patient complained of severe attacks of pain over the whole of the left side of the face. A simultaneous affection of all the three branches of the 5th nerve is practically unknown in trigeminal neuralgia. The motor division of the 5th nerve was also affected as revealed by loss of power in the left masseter and temporalis, which of course cannot occur in trigeminal neuralgia.

- (2) Fits. Fits may be general or local. Three of the author's cases came for generalized convulsions. Two of the cases showed signs of optic neuritis on ophthalmoscopic examination. It is worthwhile to remember that idiopathic epilepsy rarely commences after the teens. One came for local fits.

- (3) Vascular manifestations. Vascular thrombosis may occur with or without prodromal symptoms. These cases are usually more acute rather than chronic. These vascular accidents tend to occur within about 18 months of infection. Syphilitic hemiplegias may not differ essentially from hemiplegias due to other causes; but in syphilitic cases it is more common for 'Warnings' to be present, and often consciousness is not lost. In the author's series of fifty cases, eighteen came for arterial thrombosis.

Latent Meningovascular syphilis. It may happen that patients who come for other complaints are discovered to have some

neurological signs due to syphilis. The common signs observed are slight blurring of the edges of the disc, pupillary abnormalities, loss of light reflex, unequal tendon jerks and a positive Babinski's sign.

Ocular manifestations. Inequality and irregularity in the outline of the pupil, loss of light reflex, Argyll-Robertson pupil are seen rarely in India. Meningeal cases show slight swelling of the disc congestion and blurring of the edges on ophthalmoscopic examination.

Prognosis. It is bad in extensive arterial lesions. Cases of acute meningo-encephalitis also do not do well. The cranial nerve palsies almost always recover with antisyphilitic treatment.

SPINAL SYPHILIS SIXTEEN CASES.

Spinal syphilis may be said to give rise to various syndromes. Of the author's sixteen cases, 5 cases belonged to acute transverse myelitis, 6 cases belonged to chronic meningo-myelitis 1 case to spinal arterial thrombosis, 3 cases to Radiculitis, and, 1 to cervical pachymeningitis.

Acute transverse myelitis. Flaccid paraplegia in flexion develops. Some Warning signs are present. The prognosis is always bad.

Chronic meningo-myelitis. The patient usually come for difficulty in waking. He complains of pain in the back, often radiating down the limbs. History of disturbance of bladder function and diminished libido is present. Spastic paraplegia is found and some sensory loss is common. The signs are usually bilateral and often asymmetrical. Mild sphincter disturbance is the rule.

Spinal arterial thrombosis. It is rare.

Spinal radiculitis. Both the anterior and posterior roots may be involved, but the sensory symptoms always precede the motor symptoms and so they come for root pains.

Cervical pachymeningitis. It is very rare.

Diagnosis. The most useful laboratory test for diagnosis is the Wasserman reaction in the blood and cerebrospinal fluid.

Treatment. The usual drugs used are mercury, bismuth, arsenic and iodides. Iodide is undoubtedly useful. It should be given in fairly large doses. But the specific treatment should be prolonged. Pyrotherapy is indicated in cases resistant to the specific treatment.

(Indian Medical Gazette).

HEAT IN THE TREATMENT OF SHOCK

BY ANDREW W. KAY, M.B., F.R.C.S.

The application of heat has become fully established as a cardinal principle in the treatment of traumatic shock. It has been believed to exert a favourable influence, mainly by relieving the cutaneous vasoconstriction and thus augmenting the venous return. The possibility that the cutaneous vasoconstriction is a compensatory mechanism and that heat may be harmful has only recently been entertained.

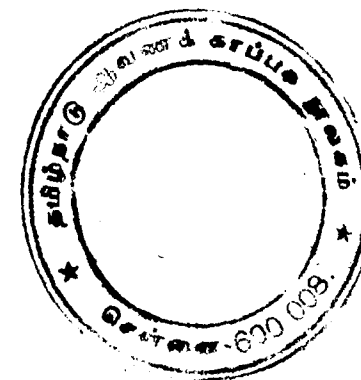
To assess the value of heat in clinical cases of shock, experiments were conducted on normal subjects to investigate the effects of heat.

Fifteen normal subjects were exposed for one hour to the hot-air cradle the temperature varying between 38°—40° C. observations made were: (1) arterial blood pressure (2) venous blood pressure (3) pulse rate, (4) oral temperature, and (5) the patients' clinical condition.

Certain constant changes were observed: (1) a progressive fall in arterial blood pressure; (2) a rise in venous blood pressure; (3) a rising pulse rate; and (4) a rise in oral temperature. In three cases headache, nausea and exhaustion were prominent symptoms. In 9 cases symptoms of dehydration were present in varying degree viz, dry tongue, weakness and thirst. In all cases general perspiration was noted. In 6 cases nausea was present, and vomiting occurred in two of these. Other symptoms were abdominal discomfort, Muscular pains, and exhaustion. These subjective effects were not prevented or lessened by concomitant intravenous administration of saline or plasma.

The result of this study shakes the confidence which has for so long been placed in heat therapy for patients suffering from traumatic shock. Definite dehydration occurred after exposure despite concurrent administration of intravenous fluid. This is not consistent with the aims of treatment for patients already suffering from the effects of fluid loss.

(British Medical Journal.)



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