

MEDICO-SURGICAL SUGGESTIONS

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No. 5.

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XV

MAY 1946

NO. 5

PENICILLIN: AN ABSTRACT REVIEW

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Calcutta

INTRODUCTION

The discovery of the drug, penicillin, was first announced in 1929 by Fleming and its astonishing properties were revealed in 1940 and 1941, when the Oxford workers, Florey, Abraham, Chain, Fletcher, Gardner, Heatley, Jennings, Orr-Ewing, and Sanders, succeeded in producing a stable extract of the active principle, and demonstrated by animal experiment and clinical use that penicillin belongs to that rare class of drugs—the true chemotherapeutic agent. "It is a remarkable tribute to the original laboratory workers", writes Jeffrey, "that long before the drug was first used on any human patient, almost all the essential facts as regards the type of infections likely to benefit and the dosage and technique of administration which we now apply, had been worked out in the laboratory."

Penicillin is an acid, but it rapidly loses its activity in acid form and is, therefore, supplied for clinical use in the form of its sodium or calcium salt. The salts are equally efficacious, but calcium penicillin is less hygroscopic and is, therefore, easier to handle and less liable to deterioration. Even in the form of its salts penicillin is more liable to loss of activity than other drugs commonly handled in clinical use. It is destroyed by acid and alkali, by the heavy metals, by alcohols, and by oxidizing agents. Since most of the common antiseptics fall into one of these categories, penicillin must be used alone, or if any preliminary cleansing of a wound is necessary it should be done by soap and water, saline, or Cetavlon. It loses activity when heated above body temperature and should be stored in the cold. Penicillin is also destroyed by 'penicillinase', an enzyme found in many common airborne bacteria such as members of the coliform and subtilis-mesentericus group.

MODE OF ACTION

The action of penicillin is bacteriostatic and not bactericidal. Penicillin, without killing the bacteria, interrupts cell division. As soon as the influence of the drug is removed, the remaining bacteria are able to resume multiplication. Penicillin must, therefore, be kept continuously in contact with all infected tissues until the natural body defences have had time to deal with the infection. As the drug is rapidly excreted from the body repeated and continuous

administration is necessary. Its action is not appreciably impaired by serum, blood, pus, or tissue autolysates, and this ability to act in the presence of pus is one of its great advantage over the sulfonamides.

SENSITIVE AND RESISTANT BACTERIA

In general, the Gram-positive organisms and Gram-negative cocci are sensitive, and the Gram-negative bacilli insensitive. Naturally resistant staphylococci are occasionally encountered, but no naturally resistant strains of *St. pyogenes* have yet been reported. Resistance can be built *in vitro* or *in vivo* in animals, by dose which are not large enough to prevent growth completely, but in clinical practice this is not common. The mechanisms of resistance to penicillin and to sulfonamides are different, since sulfonamide-resistant strains are sensitive to penicillin, and the reverse has been shown.

The following organisms are sensitive to penicillin:—*N. gonorrhoeae*; *N. meningitidis*; *Staph. albus* and *aureus* (occasional insensitive strain); *Str. pyogenes*; *Str. viridans* (most of the pathogenic strains are sensitive); *Str. pneumoniae*; *Cl. welchi*; *Cl. oedematiens*; *Cl. Septique*; *B. anthracis*; *C. diphtheriae*; *Trep. pallidum*; *Trep. recurrentis*; *Leptospira icterohaemorrhagiae* (probably sensitive though variation); Virus of ornithosis and psittacosis; Virus of Lymphogranuloma inguinale.

The following organisms are moderately sensitive to penicillin:—*Vibrio El Tor*; *S. Goertneri*.

The following organisms are insensitive to penicillin:—*Ps. pyocyanea*; *proteus*; *B. Coli*; *B. typhosus* and *paratyphosus*; *Str. faecalis* and some other strains of *Str. viridans*; Occasional strains of staphylococcus; *Listeria*.

ABSORPTION AND EXCRETION

Penicillin is destroyed by acid in the stomach. It cannot, therefore, be given satisfactorily by mouth. For systemic administration the intramuscular route is the method of choice. Little is gained by intravenous injection, as after intramuscular injection maximum concentration is reached in the blood within fifteen minutes. Excretion in the urine begins as soon as the penicillin reaches the blood stream. In the fourth hour after a dose of 15,000 units a bacteriostatic concentration as a rule no longer exists in the blood, so that the dose should be repeated three-hourly. Excretion is so rapid that possibly no advantage is to be gained by increasing the single dose above 15,000 units.

Systemic administration is the method of choice for most conditions, for thereby the drug will reach all parts of the body. The meninges, the pleura, and serous membranes of joints are relatively impermeable to penicillin, so that injections of these sites are best treated by local application.

ADMINISTRATION AND DOSAGE

(A) *Systemic Treatment*:—Repeated three-hourly intramuscular injections (120,000 units a day when the dose is 15,000 units) must be continued unremitting for several days. The individual dose is readily dissolved in 2 c.c. pyrogen-free normal saline or distilled water. The constant injections can be trying to the patients, and the impurities in the preparation may cause transient pain at the site of the injection, and rarely an urticarial reaction. Continuous intravenous drip (100,000 units in four pints saline in twenty-four hours) is comfortable for the patient, but thrombophlebitis usually occurs at the site of injection after forty-eight hours. Probably the most convenient method of administration is by continuous intramuscular drip (100,000 units a day in 100 c.c. saline). Apart from the above mentioned ill-effects, no toxic reactions have occurred in penicillin therapy.

In the systemic treatment of early or localizing infections, a course lasting three to five days may suffice. For a general or severe local infection treatment should be continued for at least two to five days after the infecting organism can no longer be found by bacteriological methods. In a condition such as staphylococcal septicaemia the total period of treatment is seldom less than ten days, and may be much more. The only condition which appears to be cured by treatment lasting twenty-four hours is gonorrhoea.

(B) *Local Treatment*:—The same general principles hold good for local as for systemic use, i.e., a continuous concentration of the drug must be maintained in contact with all infected tissues until the infection has been dealt with by the cellular and humoral defences. Every infected portion of tissue must be removed completely, as they will harbour organisms out of reach of the drug.

PREPARATIONS FOR LOCAL USE

(1) *Powder*:—Dry penicillin (preferably calcium penicillin) is diluted with one of the sulfonamide powders to give a concentration of from 1,000 to 5,000 units per gramme. Dilution is necessary in order to spread the minute amount of penicillin required over a large area, and because pure penicillin powder locally applied can be necrotoxic. The sulfonamides are suitable as vehicles because they are less injurious to the tissues than other powders. The powder can be blown with an insufflator on to raw surfaces to form a thick hoar-frost. The application should be repeated every twenty-four hours, and is only of real use on relatively dry surfaces, as blood or exudate rapidly washes it away. Calcium penicillin powder retains its potency for many months, even at room temperature.

(2) *Cream*:—Penicillin can be incorporated in a cream of thirty per cent lanette wax in water, at a strength of 250 units or more per gramme. Or it can be dispensed as follows:—

Arachis oil	...	125 c.c.
Lanette wax SX	...	60 g.
Water	...	275 c.c.

[Heat sterilized oil to 70°C. Add wax. Heat water to 60-65°C. Add water to wax and oil with gentle stirring. Maintain at 65°C. for two hours to sterilize. Store in 100-g. pots in refrigerator till needed. *Before use* add, mixing well, 2.5 c.c. of penicillin solution of 10,000 units per c.c., in closed room, or better, under cover of glass cage. This gives a cream of 250 units per gramme.]

These creams make good dressings for surface infections or deeper wounds, and need not be renewed more often than twenty-four hours, or sometimes every forty-eight hours. A disadvantage is that lanette wax, which is ideal as a base for the penicillin, is an inert substance that requires mechanical removal from the tissues. Penicillin cream should be stored at a temperature of about 5°C., and will probably deteriorate within a fortnight.

(3) *Solutions*:—These can be made up in distilled water or saline at 250 units per c.c. for instilling twelve-hourly through fine rubber tubes into wounds which have been closed; for injecting into abscess cavities; and as a spray for skin and mucous membrane infections. Solutions of a strength of 1,000 to 2,000 units per c.c. are suitable for injecting into the cerebrospinal, pleural, and joint cavities, and for two-hourly drops for the eye. Penicillin in solution rapidly deteriorates. If kept at room temperature the solution should be made up fresh daily. At 5°C. solutions will keep for two to three days.

CLINICAL APPLICATION

Because of the shortage of supply of penicillin the drug has been reserved for use in the more serious clinical conditions, so that many lesser complaints for which the drug is probably eminently suitable have not yet been widely investigated. As the drug has been reserved largely for service cases, most of the reports from Britain refer to war casualties. Large-scale investigations of civilian conditions have, however, been reported from America. There is agreement in both countries about the indications of the drug, *viz.*, in infections due to susceptible organisms. But there is no universal agreement regarding the dosage, the best method of administration, and the duration of treatment.

In infections by the most susceptible organisms, the gonococcus, and the meningococcus, the results have been brilliant. In infections by pyogenic organisms such as staphylococcus and streptococcus the results are better than was ever achieved before. Nevertheless, although these organisms are susceptible, it has not

proved possible to avoid many of their ill effects. Pus still requires drainage. Gram-negative infection appears to flourish when the Gram-positive organisms are brought under control by penicillin, and such organisms as pyocyanus, proteus, and coliforms are proving obstinate opponents. Many of the results in bone infections have been disappointing. The treatment of bacterial endocarditis by penicillin has so far been a history of failure. In venereal disease, however, the picture is very different. Here for the first time we have a drug that appears effective against both gonorrhoea and syphilis.

GONORRHOEA

The gonococcus is the most sensitive of all organisms to penicillin, and in no other disease have the results been so consistently excellent as in gonorrhoea. Penicillin is the most effective agent we have for treating the disease, the cure rate being usually about 95 per cent. It should, however, be remembered that one hundred thousand units will not cure all cases, and recurrences are possible. In cases not responding to two courses of penicillin a careful study of the genito-urinary tract should be made. Treatment for gonorrhoea rarely lasts longer than twenty-four hours, and can be given to ambulant and out-patients.

Robinson reports the results of treatment of one thousand cases of sulfanamide-resistant gonorrhoea. Of these, 94.5 per cent were free from gonorrhoea after one course of 100,000 units of penicillin, given intramuscularly in 10,000 unit doses every hour, or in 20,000 units every three hours; 5.3 per cent of this series required a second course of penicillin varying from 100,000 to 150,000 units; 7 per cent of the 1,000 cases had developed complications other than posterior urethritis, and penicillin therapy hastened recovery in this group. Another group of one hundred cases of acute gonorrhoea, previously untreated, responded satisfactorily to penicillin therapy—97 per cent were free with one course of 100,000 units (20,000 units intramuscularly every two or three hours) of penicillin.

Anwyll-Davies concludes that this chemotherapeutic agent causes the prompt disappearance of inflammatory reaction simultaneously with the death of the gonococcus, and may be used alone or in combination with the sulfonamides. Ferguson and Buchholtz report a large series of seamen treated with penicillin, with four per cent failures. Mahoney, Ferguson and Buchholtz found excellent results in another series which received 10,000 units intramuscularly every three hours, night and day for forty-five hours. Van Slyke, Arnold and Buchholtz consider that one optimal course demands 120,000 units over a fifteen-hour period. Sternberg and Turner report that no case of gonorrhoea in their series (in fifteen US Army hospitals) was penicillin-resistant or intolerant, but that

the development of early syphilis was delayed or masked in several cases.

Miller, Scott and Moeller studied the action of penicillin, and came to the conclusion that penicillin is brought to the infected (urethral) mucosa by the blood stream rather than from the lumen of the urethra. The interval between the onset of treatment and the first negative culture varied from one to six hours, and symptoms disappeared within two to five hours. The prompt disappearance of inflammatory re-action, which occurred almost simultaneously with the death of the infecting micro-organism and not after an appreciable time-lag, was particularly remarkable. The authors also found that the ambulatory cases progressed as satisfactorily as those who were hospitalized. Although previous reports have advised spreading the injections over twenty-four to forty-eight hours, the authors believe such prolonged treatment unnecessary, either in acute or chronic gonorrhoea, with or without complications.

Dawson and Hobby report a case of arthritis of the wrist with early destruction of the joint (which failed to respond to sulfonamide and other measures), in which the response to penicillin was unequivocal within forty-eight hours and the final outcome was a normally functioning joint. Another case of arthritis was treated locally by the injection of 10,000 units daily for three days into the knee-joint. The patient was discharged on the fifth day, when all signs of infection had subsided.

Van Slyke and Steinberg report a series in which 93 patients received four intramuscular injections of 16,000 units between 9 a.m. and 4:30 p.m., and a fifth injection at 9 a.m. the next day, a total of 80,000 units—the cure-rate was 87 per cent. In another series in which 43 patients were given 25,000 units intramuscularly at 9 a.m., 11-30 a.m. and 50,000 units at 4-30 p.m., a total of 125,000 units within seven and a half hours—the cure rate was 84 per cent.

Cohn, Studdiford and Grunstein treated forty-four women with gonorrhoea which were resistant to sulfonamides. Dosage varied from 50,000 units in two doses, to 100,000 units in five doses, at three-hourly intervals; forty-three became bacteriologically negative during the follow-up period, the remaining patient relapsed, but responded to an additional 100,000 units in four doses. Individuals vary in susceptibility to penicillin. A minimum total dosage of 75,000 units in six hours appeared satisfactory. The concurrent trichomonas vaginalis infection in eleven patients remained entirely unaffected. A child aged 5 years, with sulfonamide resistant gonococcal vaginitis, was given four single doses of 10,000 units at three-hour intervals; she promptly became negative and remained so during twenty-five days' observation. The course of pregnancy in four women was unaffected by penicillin. Greenblatt

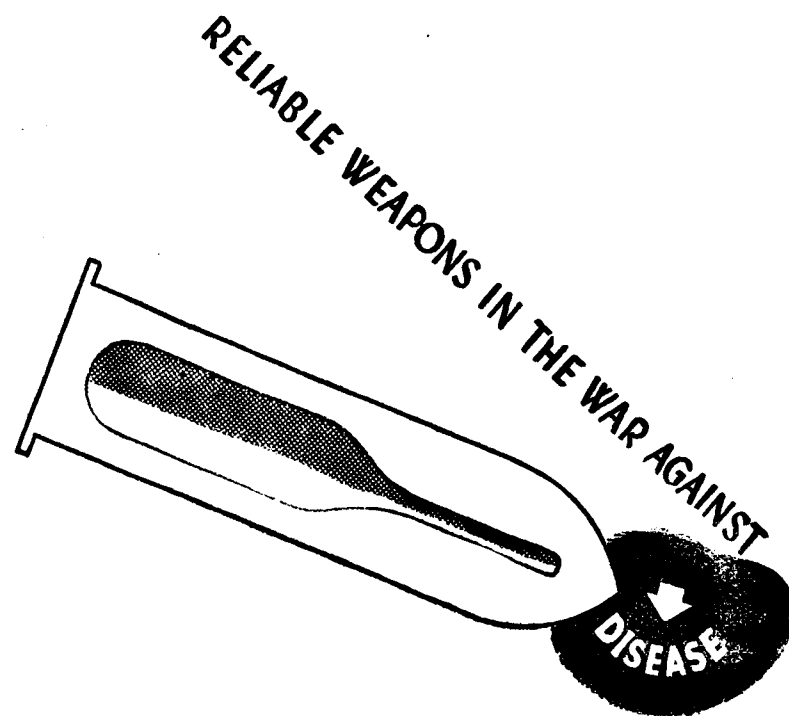
and Street recommend 150,000 units, and found chronic pelvic inflammatory disease with salpingitis and peritonitis frequently abate within twenty-four to forty-eight hours.

Oard, Jordan, Nimaroff and Phelan have found that sulfonamides enhance the effectiveness of penicillin. A combination of sulfathiazole, 12 g. in two days, and 50,000 units of penicillin—10,000 every three hours over fifteen hours on the second day—was given to 232 patients, with only 4.31 per cent failures. Patients were cured promptly, and failure to cure was obvious in three or four days. When failures occurred, the patients were immediately given 100,000 units of penicillin alone. All were promptly cured.

Keyes found penicillin useful in both local and systemic treatment of gonococcal infections, and parenteral treatment of eye diseases should, therefore, supplement local instillations in gonorrhoeal ophthalmia in infants and adults. The practice is to instil two to three drops of penicillin solution, 1,000 units per c.c. as frequently as every hour (or half-hour in severe cases). Intravenous and intramuscular dosages range from 5,000 to 15,000 units, administered every two or three hours, with a total maximum dosage of 120,000 units in twenty-four hours.

SYPHILIS

Mahoney, Arnold and Harris were the first to report the rapid spirochaetocidal effect of penicillin in man, the prompt regression of early lesions of syphilis, and the absence of significant reactions to treatment. They treated four patients, each of whom had a single penile chancre, by intramuscular injections of 25,000 units of penicillin at intervals of four hours until a total of 1,200,000 units had been given (forty-eight injections in eight days). Spirochetes were present in the lesions in all four patients before treatment, but were not demonstrable after sixteen hours of treatment. Before treatment was begun all of them had positive serologic tests for syphilis. The Kahn tests in the four patients became negative in 30, 36, 37 and 51 days respectively, and the ulcers all healed in a few days. One of them became seropositive again after nine months and developed a lip chancre, probably through a fresh infection. The authors warn that no extravagant claims should be made, for several years may have to elapse before it can be said for certain that the patients have been cured. Relapses do occur after penicillin therapy as at present conducted, though a cure seems likely if treatment is begun early. Within nine months, eleven out of twenty-two patients with secondary syphilis relapsed, but of thirty patients with primary syphilis only three relapsed. In tertiary syphilis there have been no reliable reports of cures, but there has been noticed regression of the gummatous lesions, and improvement of the cerebrospinal fluid findings.



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Wise and Pillsbury hold that in *early syphilis* penicillin offers great possibilities. They gave 20,000 units intramuscularly every four hours, night and day, until a total of 500,000 to 1,000,000 units had been injected. Moore, Mahoney, Schwartz, Sternberg and Wood reported a series of 1,148 cases of early syphilis from twenty-three clinics. They found that penicillin has a profound immediate effect in terms of disappearance of surface organisms, healing of lesions, and a trend towards serological reversal. These results are brought about by 1,200,000 units—20,000 units intramuscularly every three hours, day and night, to a total of sixty injections in seven and a half days. The relapse is in inverse ratio to the dosage employed in the seven and a half day course. Relapse is more frequent after intravenous than after intramuscular penicillin. Penicillin has a favourable effect in asymptomatic neurosyphilis, acute syphilitic meningitis, early syphilis resistant to arsenic and bismuth, and infantile congenital syphilis. The minimum dose, especially in secondary syphilis, should be not less than 1,200,000 units. To reduce the relapse rate, they state, the dose has now been doubled to 2,400,000 units in seven and a half days.

Studying the effect of penicillin in *late syphilis*. Stokes, Sternberg, Schwartz, Mahoney, Moore, and Wood found that it has distinctly beneficial effects on neurosyphilis. Its action on gummata of skin, mucosa and bones is striking. In ocular syphilis, simple inflammatory process respond; more complicated lesions such as optic neuritis and interstitial keratitis recover, relapse, and are resistant according to the damage already done. This is probably also true of visceral syphilis and of eight-nerve involvement. Herxheimer reactions may be serious in late syphilis, and should be guarded against by reducing dosage during the first twenty-four to forty-eight hours.

PNEUMOCOCCAL MENINGITIS

Chairs, Duthie, Lewin and Smith believe that since only minute amounts of penicillin pass through the barrier of the meninges after large doses systematically, the penicillin must be injected directly into the cerebrospinal fluid. If there is no blockage of the cerebrospinal pathways by fibrino-purulent material, daily injections by the lumbar route will often suffice and the penicillin will diffuse into the ventricles and cerebral subarachnoid space. If there are signs of spinal block due to adhesions it is necessary to supplement with injections into the lateral ventricles through burr-holes. (Occasionally severe reactions followed injection into the lateral ventricles, with pleocytosis and short-lived meningitis. These are probably due to impurities in the preparation, and are an indication against massive dosage). The dose of 10,000 units daily for four to seven days is recommended. The penicillin is injected as a solution containing 1,000 units per c.c.; it is prepared at twice this strength and diluted with an equal amount of the patient's cerebrospinal fluid before injection. The authors recommend simultaneous use of sulfonamides in the form of sulfadiazine or sulfamethazine. [N.B.—In all injections of penicillin solution into the cerebrospinal pathways or brain tracks the solution should be passed through a Seitz filter, and full aseptic precautions must be taken to avoid contamination with penicillin-resistant gram-negative organisms. Fatal cases of pyocyanus meningitis have been reported.]

CEREBROSPINAL FEVER

Rosenberg and Arling obtained striking results from the use of penicillin. The following method was followed:

(a) After complete drainage of the spinal canal 10,000 units in 10 c.c. isotonic sodium chloride was injected. Thereafter, 10,000 units was injected at twenty-four hours intervals until a sterile fluid was reported. When the patient was judged severely ill on a clinical basis intrathecal injections were continued until the cerebrospinal fluid was bacteria-free for three successive lumbar punctures.

(b) Parenteral therapy was begun by continuous intravenous drip, 5,000 units per hour being given for the first eight hours. [The infusion fluid was 5 per cent dextrose containing 40 units penicillin per c.c.]. Thereafter, divided intramuscular injections (15,000 units three-hourly) completed parenteral treatment in a few very ill patients the initial intravenous therapy was stopped up to 10,000 units per hour for the first four hours.

PNEUMONIA

The pneumococcus is very sensitive to penicillin, though there are strain variations. The results of treatment of lobar pneumonia are at least equal to, and probably better than, treatment with sulfapyridine, particularly in sulfonamide-resistant pneumonia. 'Atypical pneumonia' does not appear to respond to penicillin. Dawson and Hobby noted dramatic response of pneumococcal pneumonia to quite small doses of penicillin (10,000 units every four hours for one and a half to two days).

SOFT-TISSUE WOUNDS

The topical application of penicillin to soft-tissue wounds has resulted in a quicker healing of wounds than has hitherto been possible. Bentley's technique of penicillin application is given below:

(a) *For Superficial Wounds, if clean*:—A single insufflation of penicillin-sulfathiazole powder (5,000 units per gramme) and suture.

(b) *For Superficial Wounds, if dirty*:—Preliminary insufflation once daily, for two to three days, then suture over a further frosting.

(c) *For Deep Wounds* where the powder could not reach all crevices:—Suture and instillation through fine indwelling rubber tubes, 3 c.c. down each tube twice daily for four days, of penicillin solution, 250 units per c.c.

COMPOUND FRACTURES

Penicillin has a place in the management of compound fractures, since they are usually infected at an early stage with staphylococcus and clostridia. In Furlong and Clark's series, the course of systemic penicillin lasted five to fourteen days (average 800,000 units in eight days). The patient was 'penicillinized' for twenty-four hours before definite treatment was carried out. This consisted of surgical revision of the wounds and partial suture, and immobilization by skeletal traction and Thomas's splint. They found a reduction in serious infection in the penicillin group.

Although major sepsis and its effects were minimized, there was persistent minor infection, as evidenced by a sinus down to bone after three months, in about one-third of the penicillin series, which is similar to the infection rate of the control series (with

sulfanomides). A routine penicillin course and partial wound suture should be part of the treatment of most compound fractures. In performing wound suture it is important to leave adequate drainage for the autolytic products and gram-negative pus; anterior wounds can be safely sutured, but posterior and main drainage wounds should only be sutured in any part well away from the main drainage channel.

GAS GANGRENE

While penicillin has a definite place in the treatment of gas gangrene, radical surgery remains the keystone. While the drug can deal with the clostridia at the advancing edge, it cannot gain access to gangrenous tissue which no longer has a blood supply, so that radical surgery is necessary to remove the gangrenous muscle, and antiserum to counteract the toxemia. With full treatment it is possible to arrest the progressive myositis, though late ill effects must be anticipated, notably uremia through damage to the kidney from retained dead-muscle products.

The prophylactic value of penicillin in the onset of gas gangrene is open to question. As the drug cannot penetrate into devitalized tissue, it is probable that gangrene can develop in muscle deprived of blood supply, but should remain localized to that area.

INTRAPLEURAL INFECTIONS

Intrapleural instillation is the method of choice in the treatment of empyema. d'Abreu, Litchfield and Thompson hold that the pleural cavity can retain instilled penicillin for as long as three days. Their treatment of established infection was to aspirate the chest and instill penicillin in solution at forty-eight hour intervals. For average cavities holding from ten to twenty ounces of fluid, 60,000 units was the dose given (10,000 units per c.c. saline); 120,000 units was given for total empyema, and 30,000 units for small pockets. Three or four aspirations and instillations usually sufficed. Patients with much air in the pleural cavity were postured for three hours on each side so as to distribute the penicillin widely. In cases where rib resection and surgical drainage was performed, penicillin was instilled along the tube which was then occluded by a spigot for several hours. The authors also obtained good results in closing with local penicillin of large septic chest-wall wounds.

HEAD WOUNDS

Cairns is of opinion that penicillin is useful in gunshot wounds of the head, only when it has followed surgical excision of dirt, hair, bone chips, pulped brain, blood-clot and accessible missiles. His methods are given below:—

(1) In recent brain wounds (up to seventy-two hours) penicillin is applied as a powder (5,000 units per gramme one of the sulfanomides) followed by primary closure.

(2) In older brain wounds where pus is already present, penicillin is applied as follows. (a) After excision and primary closure of the wound deitz-filtered penicillin solution (250 to 1,000 units per c.c.) can be instilled through tubes twice daily for three to five days. (b) The wound can be cleaned surgically and left open for two or three days with daily application of penicillin powder; secondary suture can then be performed. (c) If the scalp is grossly infected, the wound is excised, the scalp is partially closed, and a three-day course of systemic penicillin given.

(3) In ventricular wounds, following surgical toilet of the wound, penicillin solution (1,000 units per c.c.) is injected into the ventricle or lumbar theca in amounts of 4,000 to 8,000 units once daily for as long as there is a suspicion of ventricular infection.

(4) Abscesses arising in a brain wound within the first few weeks of injury should be treated by open drainage, and twice daily instillations of penicillin solution through an indwelling tube.

(5) Closure of non-penetrating wounds of the head after excision (including removal of bare bone) and insufflation of penicillin powder is followed by primary healing in 95 per cent of cases. Careful hemostasis is required before closure to prevent the powder being washed away by the blood.

SEPTICEMIA

Keefer and co workers reported on *Staph. aureus* septicemia. Without penicillin or sulfonamide therapy the fatality-rate of septicemias about 85 per cent, the patient usually dying in ten to fourteen days. In the penicillin series, the most favourable outlook was in patients under forty years of age who had an infection localized in an area that could be drained surgically, and who were not suffering from debilitating disease. These septicemias require long and full systemic course of treatment. The best results were obtained when treatment was continued for at least seven days after the temperature became normal. The fatal cases occurred in those with deep-seated abscesses, in the elderly patients with other debilitating disease, and in every case where there were signs of bacterial endocarditis at the beginning of treatment.

ENDOCARDITIS

The results of treatment of subacute bacterial endocarditis with penicillin have been disappointing. Priest, however, mentions less disappointing, if not encouraging results with large doses (200,000 to 300,000 units a day for three weeks). Certainly the scale of penicillin dosage that appears adequate in other infections in the body is useless in subacute bacterial endocarditis.

OSTEOMYELITIS

The combination of adequate surgery and systemic penicillin seems likely to be the standard future treatment of osteomyelitis. In acute osteomyelitis a satisfactory result can be expected, though orthodox surgery for the local lesion is usually necessary. In chronic osteomyelitis the results can be disappointing unless one is prepared to go on with penicillin for a long period. The treatment of choice seems to be pre-operative penicillin for several days in order to prepare the field for intervention; then careful excision of all infected soft tissue and bone; followed by further systemic therapy for at least two weeks.

SKIN DISEASES

Penicillin may help some skin infections, applied either as a cream or as an hourly spray of penicillin solution (250 units per c.c.) Roxburg, Christie and Roxburgh found it of obvious value when the infection was mainly staphylococcal and in clearing up secondary infection.

(Calcutta Medical Journal, March 1946).

Medical News & Notes.

MEDICAL COUNCIL OF INDIA.

THE MEDICAL COUNCIL OF INDIA met for its twenty-fourth Session at New Delhi on the 23rd March, 1946. The President, Dr. Abraham S. Erulkar, M.D. was in the chair.

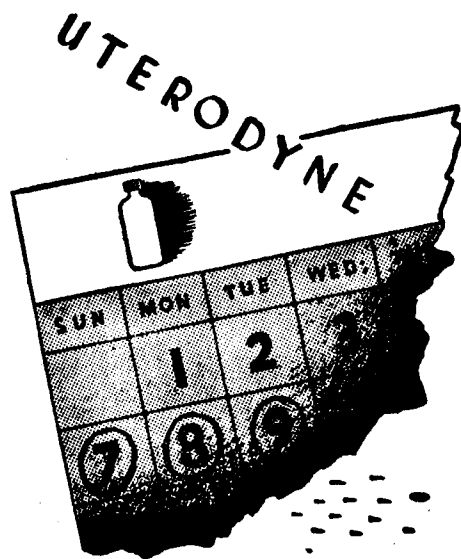
The Council elected Dr. K. S. Ray as its Vice-President, Rai Bahadur Dr. B. N. Vyas, General Hay and Colonel Bharucha were elected to be members of the Executive Committee.

Amongst the several important matters discussed by the Council, the question of the establishment of an All-India Medical Registrar which has been agitating the Indian Medical world for a considerable time was one of the most important. The Council had discussed this question at several of its previous sessions and had made certain recommendations which have been considered by the Provincial Governments as well as by the Provincial Medical Councils. During this Session, the Council gave further consideration to the various points raised by these authorities. As the result of these deliberations, the Council has made certain additions to their previous recommendations, and the All-India Register will now include all persons holding qualifications on the Schedules of the Indian Medical Council Act and those practising modern system of scientific medicine in British India and possess qualifications granted by Licensing Bodies in British India together with those Indian Nationals who hold foreign qualifications not recognised by the Indian Medical Council but recognised and registered by Provincial Medical Councils. These will be divided into three groups and this distinction will remain till such date when there is one minimum standard of medical qualifications established throughout the country. The Council were of the considered view that this was not only a decided advance on the previous position but under the limitations of the existing conditions had the merit of meeting all the various points of view in the country.

The Council also deliberated on the question of the recognition of the medical degree granted by the Agra University. Their Inspector had already reported on the courses of Instruction as well as the various examinations held by the University. The University authorities' observations on the reports of these Inspectors were before the Council. The Council has now appointed two of its members to act as Visitors and to report to the Council as to how far the recommendations by their Inspectors have been carried out.

The question of the consideration of the Bhore Committee Report has been referred to the Executive Committee, a special session of which is being held shortly for the purpose.

The next meeting of the Council has been fixed for the 19th of October, 1946.



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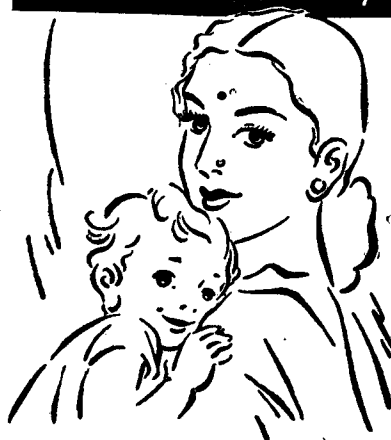
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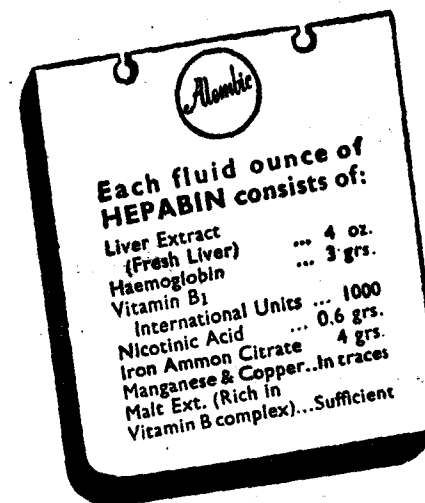
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JUNE 1946.

No. 6

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XV

JUNE 1946

NO. 6

MEDICO-LEGAL ASPECTS OF ARTIFICIAL HUMAN INSEMINATION*

BY DR. H. S. MEHTA

Mr. President, Ladies and Gentlemen,

When I was first invited to read a paper before this conference I was not sure whether to select a purely medical problem for my subject, or one of a forensic character. I ultimately decided to speak of the Medico-legal aspects of artificial Human Insemination as this is a subject of current interest.

So far we in India have very slight first-hand experience of Artificial Human Insemination, either of its technique or of its legal consequences; but, bearing in mind the importance, not to say the sacred duty, of having male issue to succeed to one's estate it will be readily recognised that the subject will sooner or later be studied very closely and thoroughly in this country.

At the outset, therefore, I should make it plain to you, ladies and gentlemen, that the substance of my paper is not based on original research but is drawn up largely from various Medical journals and the reports of meetings and discussions which have taken place elsewhere particularly in England and America.

As we all know the prayer of the barren woman for the gift of a child has echoed through the ages and here in India as well as in Europe and America the adoption of children has become a well recognised custom. With the development of science, however, has grown the desire to have a child born as far as possible of the flesh in preference to a little stranger taken in adoption. This has led to the investigation of the possibilities of Artificial Human Insemination.

From what I have read it appears that the medical profession as a whole has not readily accepted Artificial Human Insemination as a remedy for the alleviation of certain conditions. Possibly this is due as much to the consequential legal difficulties of this line of treatment as to the impact against the moral susceptibilities of many people.

* Lecture delivered at the Third Bombay Medical Congress, held at Bai Sunderbai Hall, Bombay, on 25th August 1945.

Historical review; Origin and Evolution

Artificial Insemination of human being is one of those medical achievements which cannot be traced back to antiquity. In fact the human application was made only 150 years ago. In 1790 John Hunter succeeded in effecting by Artificial Insemination, the impregnation of the wife of a Linen Draper in London. The husband suffered from Hypospadias and the Semen introduced by Hunter was taken from the husband and resulted in normal pregnancy. In America, Marien Siems in 1866 successfully effected an Artificial Insemination, but strangely enough he denounced it later on as being an immoral form of medical practice.

The idea of Artificial Human Insemination was probably evolved from the Artificial Insemination of Animals. Of recent years, the Russians have done considerable research work in this field for the improvement of their cattle. Thereby they have not only increased their numbers but have also improved their stock. Due perhaps to social conventions and human frailty, the doctors who have ministered to the human race have not kept pace with such rapid advances.

Population problem.

Many observers are convinced, however, that the time has come when these conventions and platitudes must give way before the vital needs of the day. Europe emerges from the chaos of the Second World War with gross disparity between the female and male populations and with the flower of her manhood gone and with her cities in ruins. Above everything else man-power will be needed for the prodigious work of future all round reconstruction and this serious problem of man-power must now be tackled without delay. It is against such a background that one must gauge the value of Artificial Insemination.

In this connection it must be borne in mind that although a specimen of semen cannot be used for more than a few hours after it is obtained, it can during that period be utilised for at least twenty Inseminations and some research workers in England have reported that even a single Insemination with 0.01 cc of semen may suffice to procure pregnancy.

Although official statistics are not available one writer has stated that Artificial Insemination of human beings produces a slightly larger number of male children than females.

I now pass on to some cardinal questions regarding Artificial Human Insemination.

When, (if at all) should artificial Insemination be used in human subjects?

(A) Selected patients.

(i) Artificial Insemination may be employed in those cases where married people find it impossible by reason of mechanical

factors to effect intravaginal coitus, e.g., Impotence, Hypospadias, Vaginitis tumours or excessive obesity.

(ii) There is also a group of cases where the married partners are unproductive owing to absence of, or an error in the structure of spermatozoa of male.

(iii) Still more rarely a Biological antagonism of the Endocervical secretions for the spermatozoa may exist.

However, the cases suitable for Artificial Insemination must be chosen with great care and only after thorough medical examination of both the parties.

(B) Choice of Semen.

If the practitioner is dealing with a fertile husband and a fertile wife, semen of the husband would naturally be the semen of choice. These are called "Homologous cases." In this type of cases the practitioner endeavours to ensure that the husband's sperm reaches its appointed termination and accomplishes its physiological objective and in doing so, the practitioner does not violate the moral, religious or Biological basis of married life.

If he deals with a sterile husband and a fertile wife the semen has to be obtained from an alien source which complicates the matter. In such a case he must resort to a donor, semen bank or bureau. These are called "Heterologous cases". In these cases the doctor has to determine what qualifications the donor should have before his semen can be used for Insemination.

Qualifications of a Donor.

(i) He should not be a relative of either spouse in order to maintain secrecy and to prevent any emotional disturbances involving the husband and the wife.

(ii) The mental and physical history, both personal and familiar and the general health of a donor must be satisfactory as established by investigation and thus should include such tests as Wasserman and Kahn Tests, Rh. factor, grouping and a complete blood count together with elimination of Tuberculosis, Diabetes, Epilepsy, Endocrine dysfunctions and Psychosis. The donor must be fertile and should have children of his own. The donor's blood group must be identical with that of one parent if it is desirable to minimise the possibility of bastardisation. For this reason the parents usually desire the donors of the same race or community; though as we are well aware some of the results of crossbreeding are full of promise and develop into geniuses.

(iii) He must preferably be under 30 years. In Europe and America this age-limit is higher, but the average expectation of life in India being much lower than in those countries, I suggest 30 years as the maximum age.

(iv) The characteristics and the race of the donor should harmonise as far as practicable and desirable, with those of the husband.

(v) As far as possible temperamental and emotional make-up of a donor should resemble those of the husband. The fecundity of the donor must be fairly high.

(vi) As regards the semen itself it must have a volume of at least 1 ccm, it must liquefy and rapidly become Homogenous; the sperm count must exceed 30 millions per ccm and there must not be spontaneous agglutination.

It has been suggested by some writers that the use of subfecund semen may lead to dysgenic conception. Though we have no detailed figures on this subject, we know that the exposure of the father to certain poisons has been stated to affect the off-spring. Again in normal sexual intercourse it has been noticed that a high rate of miscarriage is often associated with subfecund semen; as a matter of fact threatened miscarriage occurs in more than 35 per cent of women conceiving from sub-fecund semen.

In this connection it must be borne in mind that in artificial insemination the cervix receives many abnormal spermatozoa which could not normally reach there under their own power. Much more experience will be required before we can properly assess the standard of the progeny of subfecund parents.

Semen Banks or Bureau.

In order to provide facilities for those in need of a donor, there are in the U S A. certain organisations which maintain a list of donors whose fertility and physical conditions are known and whose semen and its physical and chemical characteristics have been fully investigated. It may be argued that by resorting to a "Bank" the practitioner delegates his responsibility to an Organisation. It is, therefore, desirable that in such cases the practitioner should satisfy himself regarding the professional standing and the method employed by the Organisation concerned to ensure the suitability in all respects of semen preferred for use. Taking all these difficulties into consideration the best thing is for the doctor himself to select the donor.

II. We now pass on to some of the legal obligations and the social potentialities of artificial Insemination of a Human subject.

The insemination of a woman with the semen obtained from her own husband is less likely to be associated with the subsequent medico-legal trouble than the insemination of the same patient with the semen from a donor or Bank. In the latter case the matter becomes complicated from a Clinical and medico-legal point of view. In short all methods of using the Heterologous semen gives rise to several medico-legal problems and may bring about devastating repercussions on the wife, the husband, the donor, the sponsors of the semen Bank, the relatives, the Physician and the child.

We must bear in mind that the law is not interested in the exact process preceding the institution of fecundation provided that

the husband of the woman concerned is the biological father of the child. Therefore, in a successful Homologous case the child would probably have the same legal status as a child conceived and born after normal sexual intercourse between the husband and wife.

In a Heterologous case however the resultant child may be declared illegitimate and the donor if known could be named as a co-respondent in divorce proceedings.

There are three important pitfalls to be avoided by the practitioner treating a patient by artificial Insemination. They are,

- (i) An allegation of negligence.
- (ii) An allegation of adultery.
- (iii) An allegation of conspiracy.

Negligence.

Just as in any other surgical or medical act undertaken by a medical practitioner, so in artificial Insemination it will be expected of him that he will exercise that degree of reasonable care and skill which he is supposed to possess in the prosecution of his professional work.

The following may be considered acts of negligence:

- (1) Failure to use properly appraised semen.
- (2) Occurrence of Salpingitis or some other condition due to faulty technique at the time of introduction of semen.
- (3) Physical damage to the genitals.

These may be treated as grounds for action by an aggrieved patient or husband against the attending Doctor.

Adultery.

One may expect that at the time of artificial insemination, the husband and wife are both agreed about the procedure. If disputes arise later on, the husband may ask for divorce on the ground of misconduct, as fecundation *ab extra* is deemed to be adultery. The Doctor should therefore see to it that his patient and the donor of the semen are not dragged into the Divorce Court, and to achieve this end both spouses should be made to understand clearly what is being done and that the insemination is carried out at their request. The practitioner should if possible also secure the consent of the donor's wife, so that she may raise no trouble later on.

Conspiracy.

Generally speaking the Law of succession provides that Estates and titles shall be inherited by heirs of the body, and in default they pass to others. It is therefore possible that some interested parties may proceed against the doctor, the spouse, and the donor for conspiring by means of artificial insemination to defeat the claims of the person who might have inherited in default of the husband and wife having any legal issue.

Registration of Births—

Some difficulty may arise when registering the birth of a child by artificial insemination in Heterologous cases. It would be a false declaration if the husband of the child's mother were named as the father; on the other hand if the donor's name is revealed, it would be a breach of secrecy, and serious results might follow later on. Perhaps it would be in the interest of all concerned merely to state that such and such a woman gave birth to a male or female child on such and such a date, (This form of registration prevails in the Bombay Municipality in case of illegitimate children)

In view of these difficulties the following safeguards have been suggested:

A practitioner undertaking artificial Insemination might take the following precautions:—

Firstly,

The practitioner should obtain a signed document from the patient and her husband, setting forth the desires of both the parties, the reasons actuating those desires and the declared consent of each to the act of artificial insemination.

Secondly,

The practitioner should make and keep a full clinical record of the details of the procedure followed, indicating the source of semen together with essential dates and the material data that usually appears on medical records.

Thirdly,

The practitioner should take in writing an assurance from the husband and wife that the birth of the child by the wife would not defeat claims of any person who would benefit in default of issue.

Fourthly,

A nurse should be present when a patient is inseminated and she should add her signature to a document indicating knowledge of what has transpired.

Fifthly,

The practitioner should explain to the parties in the presence of an impartial third person (possibly the Nurse) the reasons for the legal documents involved and the signature of the third party should be obtained as a witness.

Just as the practitioner has to be protected in cases of artificial insemination, the donor must also be safeguarded.

(1) The donor should furnish the practitioner with a signed statement signifying his knowledge and his consent to the procedure of using his semen for the artificial insemination of a patient.

(2) If the donor is married a similar statement should be obtained from his wife to obviate a subsequent accusation of adultery.

(3) The name of the donor should not be disclosed to the husband or the wife and equally so, the name of the married couple should not be given to the donor.

It may be argued that a doctor who has acted in good faith and with a clear conscience need not bother about getting such written evidence, but unfortunately the law is no respecter of persons, and a good deal of needless trouble and vexation may therefore be spared if the medical practitioner takes these precautions. If he has obtained such documents it is highly improbable that any of the parties would be successful in prosecuting the doctor for conspiracy to defeat an inheritance, for adultery and misconduct. However no document can protect a practitioner against negligence due to an accident or an error or omission.

Summary of conclusions:

The status of artificial insemination as a means to overcome sterility in a barren couple, wherein the male is principally at fault, is a medical procedure valuable only as a final answer in certain selected cases.

Artificial Insemination may have its place in the medical Armamentarium for the relief of sterility although modern research in the Physiology of human reproduction indicates that resort to it will become less and less necessary. The need for artificial Insemination will diminish in direct proportion to our increasing knowledge about the male sex cells and the Ovulatory mechanism in the female. As the years go by and as more experience is gained by medical practitioners it is obvious that more suitable measures will be suggested both for carrying out the procedure of insemination, and for protecting completely all the parties concerned including the doctor himself.

Nevertheless as the matters stand at present the foregoing suggestions if adequately carried out are probably sufficient to enable the practitioners to avoid the snares that may lie in their path.

"The artificial insemination never is and can never be an assembly line kind of medical treatment. The artificial insemination should be kept out of mercenary column and be viewed as a personal medical service the contribution of an Aesculapian to the happiness of some miserable unfortunate but worthy sterile couple."

DISCUSSION

Dr. J. N. Karande,

One had come with the expectation to hear about technique of artificial insemination and number of cases dealt with by the lecturer. I had one case in which the semen of the father was used for the purpose.



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Reply by Dr. Mehta.

From the very outset it was made clear by me that I was going to speak on medico-legal aspect only being a Medical Jurist. If Dr. Karande desires I might acquaint him theoretically from whatever I have studied. Much stress is laid today by Sexologists on abnormal Spermatozoa as regards non-fertility.

Mr. Keshwani.

Will the Lecturer kindly state about any method or substance known by which a male or female child could be produced according to the desire of the patients, since he has stated that artificial insemination produces slightly larger number of male than female children?

Reply by Dr. Mehta.

No chemical substance or method known by which a child could be produced according to the desire of the parents.

I have stated what I read in sexology literature. The original reference of it was in German language which I do not know.

(*Medical Bulletin, Foh. 1946.*)

Extracts.

PENICILLIN BY MOUTH.

Little and Lumb opine that they were satisfied that penicillin could be given by mouth to patients with wide ranges of gastric pH and that a satisfactory bacteriostatic level would result in the blood. According to Garrod (1944) "a concentration giving complete inhibition in pure serum is probably adequate for full therapeutic effect."

The treatment was tried first on patient who would not suffer if it proved ineffective. The method of administration is as follows:—A level tea-spoonful of sodium bicarbonate, or of magnesium trisilicate, was swallowed with a quarter-pint of milk, and after an interval of 10 minutes the dose of penicillin was given, dissolved in 1 or 2 c. cm. saline and mixed with a raw egg. If this mixture was not thought palatable, it was further mixed with milk and sugar. Results in cases of tonsillitis appeared satisfactory, and the method is now being tried in pneumonia, gonorrhoea and surgical sepsis.

Experiments show that penicillin undergoes a "stabilising" change during passage through the body. It becomes more resistant to heat and to alterations of pH.

Admixture of penicillin with raw egg makes it more resistant to heat and alterations of pH. The change produced by mixing penicillin with egg may not be the same as the change produced by its passage through the body, but the resulting resistance is of the same kind. When volunteers were given a dose of alkali followed by penicillin in egg, the bacteriostatic activity of their blood rose to satisfactory levels. Similar results were obtained in a volunteer with hyperchlorhydria and a patient with achlorhydria.

Lancet (1945) Feb. 17, p. 203.

THE TREATMENT OF SULFONAMIDE RESISTANT GONORRHOEA WITH PENICILLIN SODIUM.

A total of 1,686 patients resistant to at least two courses of a sulfonamide were treated with total dosages varying from 40,000 to 160,000 Oxford Units per case, the individual dose being 10,000 or 20,000 units intramuscularly every 3 hours.

It is concluded from these observation that penicillin is remarkably effective drug in the treatment of gonorrhoea, usually causing disappearance of symptoms and reversal of bacteriologic

findings within forty-eight hours. One course of treatment with a dosage of 160,000 units per case effected cures in 98 per cent; 80,000 to 120,000 units in 96 per cent and 50,000 units in 86 per cent. No significant differences in the final results were noted when a given total dose was administered in individual injections of either 10,000 or 20,000 units, although it is suggested larger initial dose followed by smaller doses at an interval of two hours would be more effective. Those who did not respond to this were retreated with 100,000 unit dose and 99 per cent were cured. No case proved to be penicillin-resistant. Complications of gonorrhoea responded well to penicillin although the more serious forms of complications required prolonged treatment with higher dosage.

Finally, it should be recognised that the treatment of gonorrhoea has been completely revolutionised in the past few years, first by the introduction of the sulfonamides and more recently by the development of penicillin.

Because of the known effects of penicillin on *Treponema pallidum*, the possibility of masking or delaying the development of early syphilis must be considered.

Sternberg & Turner: *J.A.M.A.* (1944) Sept. 16, p. 157.

COMPARATIVE EFFECT OF SULPHONAMIDE AND PENICILLIN IN PNEUMONIA.

ANDERSON AND FERGUSON (*Lancet*, 2:805, 1945) write that a series of 126 patients over the age of 35 years suffering from pneumonia was divided by random selection into two groups, one of which was given sulphathiazole, the other penicillin. All patients received the same symptomatic treatment and general clinical control.

The distribution of factors known to influence the course of the disease was the same in the two groups.

Each method achieved fairly similar results. In 3 patients, however, it was thought that penicillin had produced an unexpected recovery.

There is no reason for abandoning properly controlled sulphonamide treatment for the average case; and it is suggested that penicillin should be used for selected patients, usually in combination with a sulphonamide. Indications for the use of penicillin are tentatively suggested. The cause of delayed resolution is discussed.

Some tentative guides for the efficient use of penicillin may be formulated. In the first place, in severe cases, an adequate dose of

a sulphonamide should be given during the first twenty-four hours. The authors believe that results with sulphathiazole, are satisfactory for unselected patients in this age group, and that pneumonia in the person over 40 years should be regarded as a medical emergency. In the second place, a preliminary blood-culture (before administering sulphonamides) becomes of increasing importance; for a positive result, especially if the infection is heavy, should suggest the need for starting penicillin. Thirdly, a routine white-cell count, when treatment is begun, will be of value in picking up the leucopenic patient (not uncommon in this age-group) who may respond unsatisfactorily to sulphonamides. Lastly, but not least important, the clinical assessment of the patient should be taken into account. They are satisfied that a poor cardiovascular system remains the most important prognostic factor in pneumonia, and should constitute an indication for combined therapy. Extensive pulmonary involvement, severe cyanosis, and dyspnoea are other indications which may call for the support of chemotherapy by penicillin. The fact that we now have two effective methods of attack makes it more than ever important that the closest co-operation should be established between the laboratory and the clinician if the best results are to be obtained in the management of pneumonia.

PENICILLIN IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS.

FLIPPIN AND OTHERS (*J.A.M.A.* 129: 841, 1945) give in the following lines the summary of their observations:—

Twenty cases of subacute bacterial endocarditis were treated over one year with penicillin. Since there have recently appeared several excellent papers in which the salient features of this disease have been discussed, we will limit ourselves to several factors concerned with the management of these cases.

Results of Penicillin Therapy—Of the 20 patients with subacute bacterial endocarditis, 16 had definite subsidence of their infection, 12 are still alive and with 1 exception are all well. Of the 8 who did not survive 4 were completely free of active infection and died as a result of heart disease. Three patients in this group failed to respond to therapy, and the eighth died soon after treatment was completed as a result of an acute pulmonary embolus.

Establishment of Diagnosis by Positive Blood Cultures before starting Penicillin—Not infrequently a patient suffering with this disease is started on relatively small doses of penicillin before a positive blood culture is obtained. The dangers from this practice are threefold: 1. The organism may lose its sensitivity to penicillin. 2. The chances of obtaining a positive blood culture are lessened,

despite the addition of penicillinase to the culture material. 3. The cardiac lesion itself undoubtedly progresses. Therefore it would seem best to withhold penicillin until a positive culture is obtained or, if the clinical diagnosis warrants, to administer adequate amounts of penicillin for the disease. In several cases not included in this series, in which routine blood cultures were negative, we obtained positive results by employing anaerobic and arterial cultures.

Adequate Penicillin Dosage—At this writing we are unable to make any conclusive statement regarding the amount or route of administration of penicillin for the treatment of this disease. As indicated, we employed 300,000 units a day for fourteen days as the initial course. This appeared adequate in 14 of the 20 cases. However, in view of subsequent experience with 16 additional cases of the disease, not included in this report, we believe that all patients with subacute bacterial endocarditis should receive at least 500,000 units a day for at least five weeks.

We have used a continuous intravenous infusion of penicillin where possible, but we have no reason to believe that this method is any better than the intermittent intramuscular route. Sternal infusion of penicillin is practical for limited periods of time.

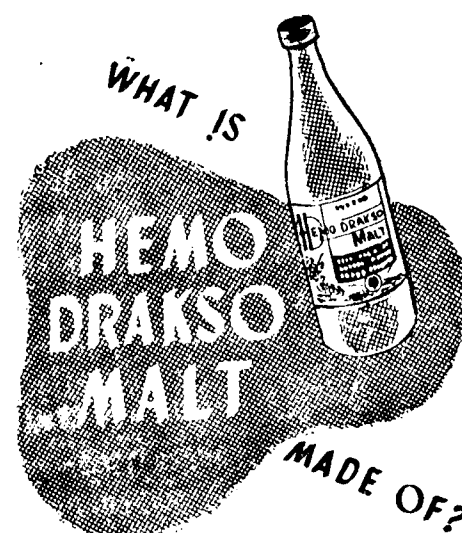
Eradication of Possible Foci of Infection—As a precaution against reinfection, a careful search for possible foci of infection, such as infected teeth and tonsils, should be made; and, if surgical procedure is warranted, the patients are given full doses of sulphonamides or, preferably, penicillin before and after operation.

Penicillin X—In a case in which the infecting organism had become highly resistant to penicillin, we employed penicillin X with apparent success.

Medical Notes & News.

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COMPOSITION: Each fluid drachm represents:

Liq. Arsenicalis	1/4 Min.
Tinct. Lobelia	
Aether	1 1/4 Min.
Tinct. Belladonna	5/8 Min.
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Tinct. Ephedra	
Vulgaris	20 Mins.
Syrup Vasaka	30 Mins.
Liq. Ext. Kush	8 Mins.
Potash Bromide	1 1/2 Gr.
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RELY ON **Alembic** ALWAYS

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INDICATIONS: As an antacid in gastric acidity, it is preferred to bicarbonates, because it does not produce carbon-dioxide or increase secretion of hydrochloric acid inside the stomach.

Being tasteless and odourless it makes an excellent laxative for constipation.

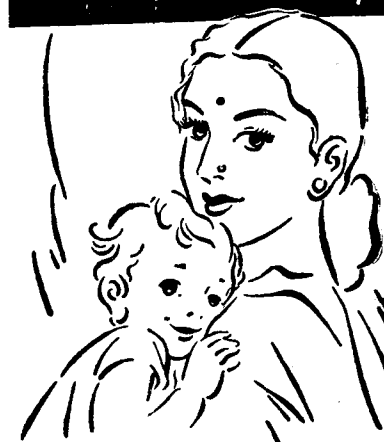
It is also useful as a mouth wash to neutralise the acids arising from the fermentation around the teeth.

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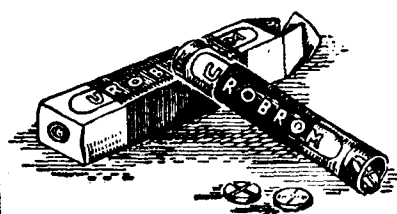
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DOSAGE:—Adults: 1 to 2 tablets as required. Children: Proportionately less.

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JULY 1946.

No. 7.

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MEDICO-SURGICAL SUGGESTIONS

(Established 1932.)

VOL. XV

JULY 1946

NO. 7

LOBECTOMY FOR BRONCHIECTASIS

BY B. R. BILLIMORIA, F.R.C.S.

(Harefield E. M. S. Thoracic Surgical Unit.)

The surgical treatment of bronchiectasis is now readily accepted by all workers in the field of pulmonary diseases. Apart from minor variations the general principles of the operative technique are established. Only part of the subject will be surveyed here as the vast minutiae of the preliminary investigations and post-operative management cannot be covered in this brief paper.

Indications.

(a) Symptoms:

- Large quantities of foul sputum.
- Progressive general toxæmia obviously attributable to bronchiectasis
- Recurrent attacks of hæmoptysis.
- Recurrent attacks of pneumonia in the affected segment of the lung.
- Symptomless bronchiectasis in young children needs careful consideration as regards surgery.

It should be remembered that very few patients with established bronchiectasis travel the normal span of life without eventually developing pulmonary complications. As a broad principle, therefore, in otherwise surgically suitable cases, lobectomy should definitely be considered in symptomless cases of bronchiectasis in children.

(b) Age:

There is no lower age limit to the performance of the operation. Lobectomy should be avoided after the age of 40.

(c) Extent of the disease:

The ideal cases for surgery are those in which the disease is confined to one lobe on one side. This, however, is the exception rather than the rule and most patients with lower lobe bronchiectasis have ectasia of the bronchi in either the middle lobe or the lingula. In these cases the entire diseased area must be removed i.e., right lower lobectomy plus a middle lobectomy or, on the left side, left lower lobectomy plus lingulectomy of the left upper lobe.

In suitable cases one can undertake a bilateral lower lobectomy together with middle lobectomy and lingulectomy. Such cases are rare and most patients with extensive bilateral disease are unsuitable for surgery.

(d) Associated disease:

Gross cardiac renal, etc., lesions exclude surgery unless it can be shown that the bronchiectasis is acting as a toxic focus, e.g., causing nephritis.

Anaesthesia.

A very large part of the success of thoracic surgery is due to advances in anaesthesia. A thoracic surgeon is helpless without the aid of a trained chest anaesthetist. It is impossible to enter into the details here of this highly specialised subject. We have long since abandoned local or spinal anaesthesia for thoracotomy. General anaesthesia, using Cyclopropane under pressure, with continuous or assisted respiration, is used. In very "wet" case the affected bronchus can be blocked off with a balloon by a bronchoscopy before induction; alternatively the normal bronchus is intubated and blocked off with an inflatable balloon and a one lung anaesthesia maintained through the operation.

*Operative technique.**Preliminary Pleurodesis:*

There is considerable controversy as to the value of inducing a preliminary pleurodesis. We induce an artificial pleurodesis of the upper lobe in all cases where a pneumothorax shows the upper lobe to be free; we perform this by powdering the upper lobe, through a thoracoscope, with iodised talc. The subsequent pleural effusion is aspirated as frequently as is necessary. The pleura is usually dry at the end of about 10 days. Lobectomy is undertaken three weeks after the chest is dry.

Technique:

The standard position on the table is the lateral one. More recently we have started using the head down prone position. The details of the latter will be published in the near future. A drip blood transfusion is started in the leg and the patient usually needs two to three pints of blood.

The standard approach is a postero-lateral thoracotomy through the bed of the 7th rib. In the head down position, resection of the 6th rib gives a better approach to the hilum.

The tourniquet technique of lobectomy has now been abandoned in favour of the individual dissection and ligation of the elements of the hilum. A tourniquet should, however, be kept at hand in case it is necessary to terminate the operation in a hurry.

Dissection starts with freeing of the lobe from its parietal adhesions. The pulmonary ligament is divided and ligated. It should be remembered that the inferior end of the ligament may contain an aberrant vessel. If this vessel is divided accidentally in a right lower lobectomy, the cut end will retract into the left side of the chest behind the pericardium and may become inaccessible.

The next move is to define and free the interlobar fissure. This dissection may prove extremely difficult owing to the presence of dense vascular adhesions. Injury to the upper lobe during this stage must be carefully avoided. As the fissure is opened, the lower artery will be seen in the floor of the fissure.

Owing to the situation of the pectoral and lingular lobe arteries the lower lobe artery has to be tied after it has given its branch to the apex of the lower lobe. The pulmonary artery has very thin walls and dissection is frequently complicated by the presence of surrounding glands. Occasionally the vessel is closely adherent to the bronchus and it may be damaged at this point. Needless to say, every care must be taken to avoid injury to the pulmonary artery as the chest is immediately flooded with blood and the bleeding ends are very difficult to secure and tie.

After the artery has been ligated and divided, attention is turned to the inferior pulmonary vein which must next be dissected free. The vein should be ligated and divided close to the heart but the pericardium should not be opened. The vein must be treated with the utmost respect: it may reach the thickness of a thumb and if it is accidentally divided or if the ligature slips, haemorrhage is torrential. Furthermore, the bleeding end is almost impossible to clamp as it retracts into the pericardium.

Apart from the dangers of haemorrhage from the accidental injury of the vein, there is the real danger of an immediate fatal air embolism. I have had the misfortune, when assisting a highly skilled thoracic surgeon, to be present at the deaths on the table of two patients from massive air-embolus along the pulmonary vein.

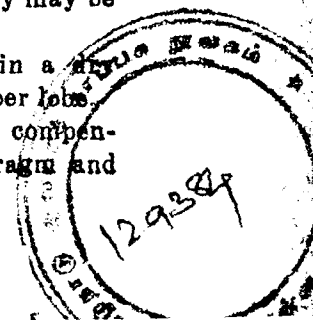
After the vein and artery have been secured, the main lower lobe bronchus is identified and freed. Innumerable methods have been devised for closure of the bronchial stump extending from simple encircling ligatures to the formation of intricate muscle grafts. The main principle of the various modern methods is to make certain that the bronchial stump is buried and not left dangling free in the pleura.

If lingulectomy is required, the lingular vessels and bronchus are ligated individually and the lingula stripped off the upper lobe.

The chest is closed without drainage over a leak tube. In children, or if there has been any soiling of the pleura, a 48 hour under-water intercostal tube is inserted. We employ local and systemic Penicillin as a routine. An immediate postoperative bronchoscopy may be required to clear the bronchial tree of secretions.

The aim of the postoperative treatment is to maintain a dry pleural space and achieve complete re-expansion of the upper lobe.

The space left behind after lobectomy is obliterated by compensatory emphysema of the residual lobe, a rise of the diaphragm and a shift of the mediastinum.



Complications.

Apart from the usual surgical complications, such as shock and haemorrhage, the four complications peculiar to lobectomy are :—

- i. Postoperative collapse of the residual upper lobe.
- ii. Fistula formation.
- iii. Empyema.
- iv. Fulminating spill-over broncho-pneumonia.

Conclusions.

It is now established beyond doubt that surgery has a definite place in the treatment of bronchiectasis. Selection of the cases and their pre-and postoperative management call for considerable practical experience and the co-ordinated team work of surgeon, physician, radiologist, physio-therapist and the nursing staff.

The operation is now standardised to the dissection technique but it should be remembered that in the presence of dense adhesions, dissection of the hilum may prove more difficult and dangerous than any other in the field of surgery. However, the postoperative complications of a tourniquet lobectomy are so serious that there is no justification for its use except in an emergency.

I wish to thank Mr. T. Holmes Sellors and Mr. Vernon C. Thompson for their permission to publish this paper. I also wish to express my appreciation to Dr. Parry Brown for his patience and his skill in maintaining a perfect anaesthesia with a stable mediastinum through the tedious stages of hilar dissection, as without this I would never have been able to achieve successful results in the following cases operated on by me

*Case Reports.***CASE I:**

Miss A. P., Aged 12: Recurrent colds since scarlet fever at age of 2. Branch-pneumonia in 1941. In January 1943 course of inoculation injections for colds: no improvement. July 1944 right antrum puncture, after which she felt better and had less nasal discharge. General condition continued to be poor.

Bronchogram showed bronchiectasis of the left lower lobe.

Operation: Left lower lobectomy following left poudrage. Anaesthetist: Dr. Parry Brown. Face and head down position. Upper lobe well stuck. Interlobar fissure poorly defined posteriorly and apex of the lower lobe was stuck to the mediastinum and paravertebral gutter. Dissection lobectomy performed. Main lower lobe artery tied in 2 parts (a branch to main lower lobe and a branch to dorsal lobe). Main lower lobe and bronchus dorsal lobe bronchus divided and closed separately. Thread ligature to bronchus reinforced by interrupted mattress. Hilum stump oversewn with adjacent pleura. Penicillin/sulphonamide powder to wound. 48 hour intercostal drain.

There was a great deal of pus in the respiratory tract throughout the operation, at the conclusion of which bronchoscopy was

performed. Bronchial tree was sucked dry of a large quantity of very viscid mucopus.

Progress: Immediate postoperative recovery good. 48 hours after operation she developed collapse of the residual upper lobe which re-expanded following immediate bronchoscopy. Subsequent recovery was uneventful and she was discharged one month after operation.

CASE II:

R. W. S., male, Aged 28. *History:* Measles as a child; chicken pox. Cough with sputum as long as he can remember, gradually becoming worse in last two years.

Bronchogram showed bronchiectasis of the right lower lobe.

Operation: Right lower lobectomy following right poudrage. Anaesthetist: Dr. Parry Brown. Head and face down position. Lower lobe densely stuck to diaphragm and the lower fissure was poorly defined at the apex of the lower lobe. Fissure between right lower and middle was also poorly defined. Dissection right lower lobectomy performed. Artery taken first with separate ligature on branch to dorsal lobe. Inferior pulmonary vein tied in two parts. Bronchus clamped at level of first dorsal, $\frac{1}{2}$ cm. below middle. Closed with interrupted and continuous thread. Oversewn with adjacent pleura. Penicillin/sulphonamide powder to stump and pleura. Chest closed over leak tube.

Progress: Immediate postoperative recovery good but two weeks later he developed slight staining of the sputum. He had no evidence of a fistula and it was presumably due to separation of a bronchial suture. Bronchogram after lobectomy showed no evidence of a fistula or residual pocket.

Progress since discharge was satisfactory.

CASE III:

D. S., girl, aged 12: *History:* 1935, mumps; 1937, scarlet fever. Aged 5 she developed cough with progressive increase in quantity of sputum which on admission varied between 2 to 3 ounces a day.

Bronchogram showed bronchiectasis of the right middle and right lower lobes.

Operation: Right Middle and Right Lower Lobectomy following Right Poudrage.

Anaesthetist: Dr. Parry Brown. Head down position, posterolateral thoracotomy via 6th rib. Upper lobe well stuck. Fissure between middle and upper lobes shallow. Inferior vein in three tributaries which were ligated individually. Right middle and lower arterial branches taken separately. Bronchus ligated with encircling thread and reinforced with interrupted thread and oversewn with pleura. Penicillin/sulphanilamide to wound. Chest closed over 48 hour leak tube.

Progress: Postoperatively showed signs of small pulmonary leak presumably from site of separation of pulmonary fissures which healed spontaneously in a week. Otherwise, uneventful convalescence.

CASE IV:

Miss A. P. aged 24: *History:* March 1939 pneumonia and bronchitis, right side; subsequent chronic cough with increasing quantities of sputum.

Bronchogram showed bronchiectasis of the right middle and right lower lobes.

Operation: Right middle and right lower lobectomy following right poudrage. Anaesthetist: Dr. Parry Brown. General anaesthetic and bronchial blocker Lateral position. Postero-lateral thoractomy via rib 6. Upper lobe well stuck. Lower and middle lobes collapsed and densely adherent to diaphragm and paravertebral gutter with vascular adhesions. Fissures between upper lobe and middle and lower lobes defined by division over clamps. Artery tied above origin of middle lobe artery. Inferior vein ligated. Middle lobe vein ligated at origin from superior vein. Bronchus divided at level of origin of middle lobe bronchus. Closed with mattress and continuous thread, oversewn with pleura. Chest closed over leak tube.

Progress: Uneventful recovery.

CASE V:

Miss M. W., Aged 21. *History:* Aged 15 months severe attack of pneumonia, persistent cough as long as she can remember, cough and sputum worse in Winter.

May 1945 symptoms increasing rapidly.

Bronchograms showed right lung: bronchial dilatation in the anterior branches of the right lower lobe.

Bronchogram of left lung: bronchiectasis on the left lower lobe and lingula.

Left A. P. induced, showed upper lobe was well adherent.

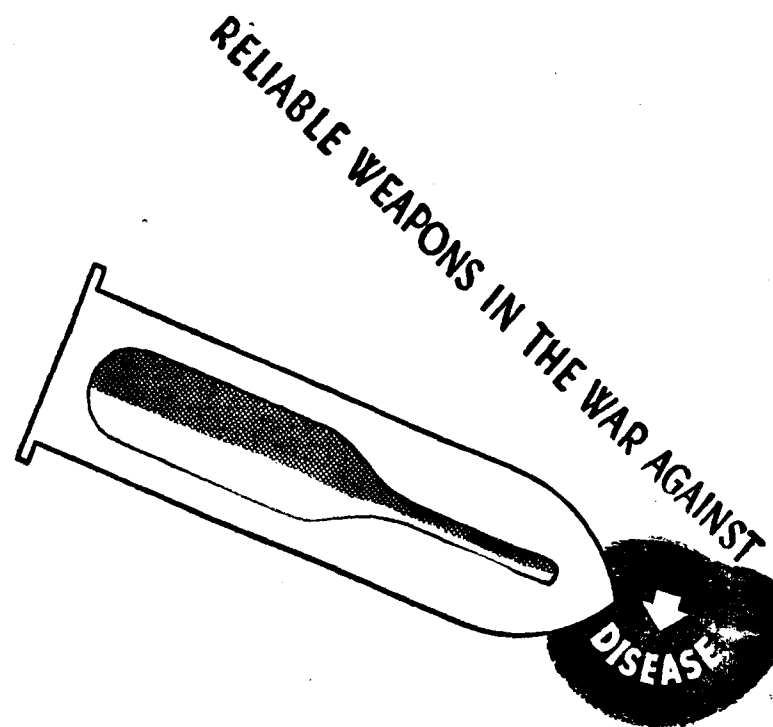
Operation: Left lower lobectomy and Lingulectomy. Anaesthetist: Dr. Parry Brown. Face down position. Postero-lateral thoractomy via 8th rib. Straight forward dissection lobectomy and lingulectomy. Bronchus closed with interrupted mattress and continuous thread, and oversewn with pleura. Pencillin/sulphonamide powder into wound. Chest closed over leak tube.

Progress: Uneventful recovery. Discharged from hospital 3½ weeks after operation.

CASE VI:

Miss E. K., aged 25 *History:* Aged 17, pleurisy with pneumonia, 1939: severe cold accompanied by another dry attack of pleurisy.

1940: Another attack pleurisy. During Winter of 1940 cough with increasingly productive sputum up to ½ cupful per day, slight haemoptysis on one occasion.



Alembic Injections have never been challenged for purity and uniform quality. Rigid scientific control and strict accuracy of ingredients are our guarantees for the safe action of all *Alembic* Injections. The latest of these Injections include:



SYLOMIN: Each 5 cc. ampoule contains 30 grs. Hexamine, 12 grs. sodium salicylate and 3 grs. Caffeine Sodio-salicylate. Indicated in pyelitis, pyelonephritis, cystitis, urinary infections, catarrhal jaundice, encephalitis.

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PHYSIOLOGICAL tests show that Horlicks is easily digested, readily absorbed and well utilised. It forms a valuable diet in ulceration of the stomach and duodenum, gastritis, and digestive disorders generally, furnishing adequate nourishment without burdening the weakened digestive powers of the patient. In some cases an emulsion of Horlicks and olive oil is beneficial. The nutritive qualities of Horlicks also make it an ideal diet not only in acute illness and during convalescence, but in the many conditions of ill-health which are favourably influenced by correct dieting.

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Operation: Left lower lobectomy and Lingulectomy following poudrage.

Anaesthetist: Dr. Parry Brown Head and face down position, thoracotomy through bed of 7th rib, upper lobe well stuck. Artery dissected free, ligated and divided; followed by ligature and section of inferior pulmonary vein. Lower lobe bronchus defined and divided. Bronchial stump closed with interrupted thread and oversewn with pleura. Dissection lingulectomy performed and lingula stripped off upper lobe. Pencillin/sulphonamide powder to wound and pleura. 48 hour leak tube.

Progress: Uneventful recovery. Discharged 4 weeks after operation.

(*Medical Bulletin*, 8th June 1946).

PENICILLIN—ITS PRESENT STATUS IN THE TREATMENT OF INFECTIONS.

There are 2 salts of penicillin available for clinical use, the calcium and the sodium salts. These are equally effective and can be used interchangeably. The best route of administration is the intramuscular, and the injections may be intermittent or continuous. The drug may also be given intravenously or topically into the serous cavities, joint cavities or subarachnoid space.

Attempts have been made to delay absorption from local deposits in the muscles by combination with beeswax and peanut oil, or with gelatin and vasoconstrictors. These methods show considerable promise, and when perfected will undoubtedly reduce the number of injections required to maintain an adequate concentration in the blood and tissues.

When large amounts of penicillin are given by mouth at frequent intervals in oil, or in a buffer such as sodium citrate, a sufficient amount is absorbed to influence the course of infections. In gonorrhoea or lobar pneumonia recovery may be observed after the use of 5 to 10 times as much as is needed when penicillin is given parenterally, but at present this method is wasteful, uncertain and extensive.

The dosage depends on the type of infection, its site, the presence of bacteraemia, the age and clinical condition of the patient, and the course of the disease.

There is also a wide variation in the susceptibility of different organisms to the drug. The gonococcus is the most sensitive, so

that 50,000 to 150,000 units will cure 98 per cent of cases of gonorrhoea in 24 hours. The haemolytic *Staph. aureus* is more resistant so that 100,000 to 200,000 units a day for one to 3 weeks or more may be needed. In bacterial endocarditis due to *Strep. viridans* at least 300,000 units a day for 14 to 21 days may be considered the minimum dose.

Generalised infections with bacteraemia:—Such infections due to susceptible organisms such as *Staph. aureus*, *Strep. haemolyticus*, or the pneumococcus, respond well to penicillin. The outlook in individual cases depends to some extent on the source of the primary infection, the age of the patient, the duration when treatment is started, and the accessibility of the infection to surgical treatment. The best results have been obtained in young patients with recent infection given intensive treatment with 120,000 to 240,000 units a day. Less favourable results have been seen in elderly patients with overwhelming infections, bacterial endocarditis, meningitis, or when the infection is associated with some complicating debilitating disease.

In staphylococcus bacteraemia the fatality rate has been reduced to about 10 to 20 per cent, except in bacterial endocarditis where it is still about 75 per cent. In all cases with bacteraemia treatment should be continuous for 2 to 3 weeks.

Infections of the Meninges:—Although penicillin is effective in controlling meningococcal meningitis the response is slower than after the sulphonamides, and it is still necessary to give penicillin both systemically and intrathecally. If a case fails to respond to sulphonamide therapy within 24 to 48 hours of adequate dosage, penicillin should be started at once. The drug is the one of choice in all infections of the meninges due to the pneumococcus, staphylococcus, and the haemolytic streptococcus. Treatment should be started immediately after diagnosis, and all foci of infection in the neighbourhood should be drained surgically at the same time especially when there is associated mastoiditis or lateral sinus thrombosis.

There is some evidence that a combination of sulphadiazine and penicillin may be more effective in pneumococcal meningitis than either drug alone.

Otitis media and mastoiditis:—These cases respond favourably to penicillin. In mastoiditis, simple mastoidectomy followed by closure of the incision and the insertion of a small catheter so that penicillin can be instilled into the cavity for 3 or 4 days is the method of choice. Healing is then rapid and the postoperative course much shortened.

Tonsillitis:—Haemolytic streptococcal tonsillitis responds very promptly to penicillin, but treatment should be continued for 5 to 7 days at least, to prevent relapse. There is a very rapid decrease in

the number of organisms in the throat and it is often difficult to recover streptococci 24 or 48 hours after treatment starts. If the administration is interrupted, however, there may be a relapse and organisms will appear in large numbers in the throat.

Pneumococcal pneumonia:—The pneumococcus is extremely susceptible to penicillin in vitro and penicillin therapy of pneumococcal lobar pneumonia is extremely effective. When patients are treated early, i.e., within the first 24 or 48 hours, there is usually a fall in temperature and pulse rate within the first 24 to 48 hours, and the patient begins to improve subjectively even sooner.

Bacteraemia, if present, disappears promptly, usually after the first injection, and purulent complications are extremely uncommon.

The dosage and duration of treatment vary from one patient to another depending on the clinical response and the severity of the infection. In some mild cases a satisfactory effect has been obtained after 60,000 to 80,000 units a day for 2 days given in doses of 10,000 units every 3 or 4 hours. In other cases, the equivalent of 15,000 units every 2 hours for 12 to 24 hours, followed by smaller amounts or longer intervals may be required for another 2 or 3 days. Treatment should be continued for 2 or 3 days after the temperature has reached normal to avoid relapse, which may be observed if the administration is stopped abruptly after the first 48 to 72 hours. Penicillin is the drug of choice in all cases of pneumococcal pneumonia which do not respond to sulphonamides after 24 hours of treatment, in all cases with persistent bacteraemia, in all cases which show a spread of the process, in all patients showing signs of sulphonamide intoxication or renal irritation, and in all cases of leucopenia or auricular fibrillation, delirium tremens or other complications arising from the infection.

It is well to start with penicillin when the patient is acutely ill or is in a state of shock, or when there is some complicating disease such as renal, hepatic, or cardiac disorder, or when there is leucopenia or a history of sensitivity to the sulphonamides.

Subacute bacterial endocarditis:—When large doses of penicillin are given for long periods, e.g., 200,000 or 300,000 units a day for at least 3 weeks, there will be clinical arrest of the disease for one to ten months in about 55 per cent of the cases. A certain number of patients, however, will die before this treatment has been completed, death being due to the infection, to embolism or to acute heart failure.

Within 24 to 72 hours of treatment in favourable cases, the constitutional symptoms largely begin to disappear, the anorexia disappears, and the temperature may fall. In some other cases there may be a low grade fever for 6 to 8 weeks, while in still others the temperature may not go down until after 2 to 3 weeks.

Within one to five days of the beginning of treatment blood cultures are usually negative and remain so, except for occasional instances when transitory bacteraemia and embolic phenomena occur.

Patechial haemorrhages may continue to occur for 6 to 8 weeks after treatment is started and emboli may occur for up to 2 months. The spleen decreases in size, the leucocytes decrease in number, the anaemia improves, and the clubbing of the fingers may recede.

There are no changes in the signs of valvular disease and the renal lesions are not favourably effected by the treatment. The favourable effects may be obtained with penicillin alone and heparin is not required.

Following clinical arrest the patient may appear to be in normal health for a considerable time, though some patients die of cardiac insufficiency without signs of active infection.

Acute osteomyelitis:—There is now evidence that acute osteomyelitis can be treated satisfactorily without surgical intervention when penicillin is started early in the disease and before abscess of the soft parts or extension of the infection to the joints has occurred. Penicillin must be given in doses varying from 120,000 to 250,000 units a day for 2 to 3 weeks. Since there is a lag between the clinical signs of infection and the development of radiological changes in the bone, it is sometimes found that destruction of the bone appears sometime after all signs of infection have vanished. Under these conditions the lesions in the bone frequently recalcify and complete healing takes place without incision and drainage.

When the infection has spread into a joint, surgical procedures may be carried out to make it possible to instill penicillin locally at least once or twice a day. Where recovery has taken place without surgery the patient should be followed for several months in order to be certain that relapses or recurrences do not occur. In a few cases it may be necessary to drain local abscesses in bone some weeks after the acute infection has subsided. In cases that have been treated very early no signs of bone destruction have ever been seen in X-ray pictures.

In chronic, haematogenous and traumatic osteomyelitis, when sequestra are present, they must be removed surgically in order to obtain satisfactory healing. Primary closure of wounds after sequestrectomy, together with local administration of penicillin, greatly shortens the period of recovery.

Gas Gangrene:—The best results in this disease follow the use of antitoxin penicillin and surgical removal of all necrotic and damaged tissue. Jeffrey and Thomson recommended 15,000 units of penicillin every 3 hours for 3 to 4 days for the control of infection in cases where all the infected tissue can be removed surgically.

Where this is not possible treatment should be continued for 5 to 10 days.

Gonococcal infections:—About 98 per cent of all gonococcal infections of the lower genital tract in men or women can be cured giving 100,000 units of penicillin in 24 hours. The remaining 2 per cent will frequently respond to more intensive and prolonged treatment. No proved case of penicillin resistant gonorrhoea has yet been encountered.

Gonococcal infections complicated by arthritis, prostatitis, salpingitis, epididymitis or endocarditis require much more prolonged treatment.

Syphilis:—Intensive studies of the treatment of early syphilis, neurosyphilis and congenital syphilis with penicillin have been instituted, but final evaluation of the results will not be possible for several years. Preliminary reports indicate that 60 injections of 20,000 units each intramuscularly at 3-hour intervals for 7½ days probably represents the minimum dosage that will be effective in controlling primary and secondary syphilis. In some patients who relapse after this dosage more prolonged and intensive treatment may be necessary. There is some evidence to suggest that the results in neurosyphilis are not as striking as in early syphilis. Late cutaneous and osseous syphilis apparently respond promptly to the drug. So far, there are no reports on the action of penicillin in latent syphilis. Some cases of congenital disease have been treated in which the early results were good.

During the treatment of syphilis with penicillin, Herxheimer reactions have occurred with considerable frequency, characterised by fever, malaise, headache, intensification of the eruption, if present, or painful swelling of the primary lesions and regional lymph nodes. These reactions subside within 24 hours and are not contra-indications to continuing the treatment.

Toxic effects:—About 2 to 5 per cent of patients treated with penicillin develop urticaria, which may occur on the first day of treatment or not until after the end of the course. It may sometimes be extensive and severe, but is generally mild and frequently disappears, even though treatment is continued. When penicillin is given again later to a patient who has developed urticaria there may be reappearance of the eruption. This reaction is not considered to be a contra-indication to continuing treatment or to giving the drug again later in most cases.

Vesicular eruptions have sometimes occurred; the author saw one severe rash of this type appearing within 24 hours of the beginning of treatment especially in areas where there had been severe ringworm infection 4 years previously.

Pain may occur on intramuscular injection, especially if the preparation used is not very pure.

Thrombophlebitis may occur at the site of injection, especially in patient receiving continuous intravenous treatment. It may be associated with chills and fever, and if this is so it is best to change to intramuscular injections. Occasionally patients complain of abdominal cramps with or without diarrhoea and nausea and vomiting have been observed in a few cases. The maximum therapeutic dose of penicillin that can be given safely to man has not yet been determined, but it is known that in one or two cases 4 million units a day have been given without ill-effect.

There are no known contra-indications to penicillin therapy although there may be reasons for giving small initial doses in cases of cardiovascular extragenital syphilis.

Miscellaneous infections:—Some cases of actinomycosis have improved following penicillin therapy, especially when it has been possible to remove infected tissue surgically, or where there has been a super-added infection with *Staph. aureus*. Anthrax with or without bacteraemia responds promptly and a few cases of rat-bite fever due to *Streptobacillus moniliformis* have been treated with good results.

Penicillin is active in vitro against *C. diphtheriae*. A few cases of clinical diphtheria have been treated with antitoxin and penicillin, but with results which are difficult to evaluate. Penicillin will not replace antitoxin, however, and should not be used instead of it, though the combination of the two forms of treatment may be valuable in laryngeal diphtheria or diphtheria gravis, although there is not much evidence at present. The treatment of diphtheria carriers with penicillin has not met with permanent success.

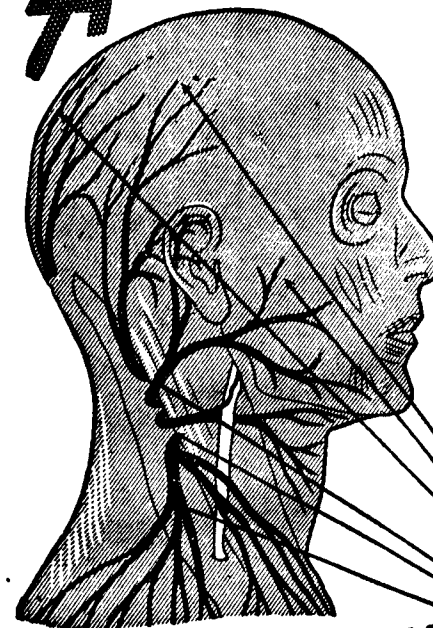
The position of the drug in chronic paranasal sinusitis, chronic infections of the ears, nose and throat, gingivitis and stomatitis remains to be determined.

Prophylaxis:—White and his co-workers have shown that when penicillin is given intramuscularly for a week prior to lobectomy or pneumonectomy and is continued after the infection, the incidence of empyema is greatly reduced. Penicillin may not decrease the incidence of infection in wounds if it is not combined with adequate surgical treatment.

Penicillin failure:—Organisms insusceptible to penicillin are typhoid and paratyphoid bacilli. Dysentary bacilli, *E. coli*, *H. influenzae*, *B. proteus*, *B. pyocynaeus*, *Br. melitensis*, *P. tularensis* and Friedlander's bacillus.

Diseases in which the drug has not been effective include tuberculosis, poliomyelitis, Hodgkin's disease, Histoplasmosis, moniliasis, malaria, cancer, diffuse lupus erythematosus, non-specific iritis and uveitis, pemphigus, toxoplasmosis, blastomycosis, coccidiomycosis, acute rheumatic fever, virus infections, acute and chronic leukaemia, ulcerative colitis, and infectious mononucleosis. (Keefer, Abstracted from the American Journal of the Medical Science, Vol. 210, No. 2, August 1945, Page 147.) (*M. & B. Bulletin*, July 1st 1946).

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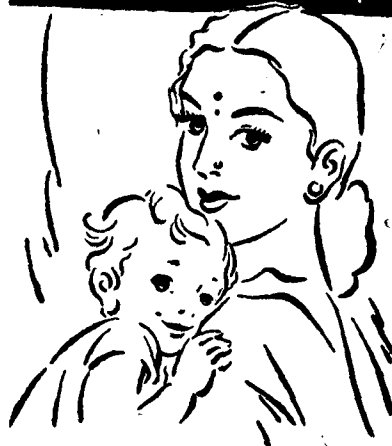
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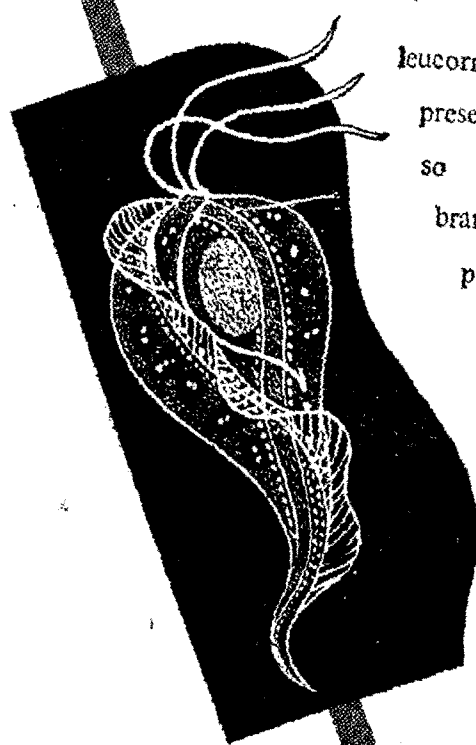
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MEDICO-SURGICAL SUGGESTIONS

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NO. 8

HOW TO HANDLE A CASE OF ABORTION

BY DR. H. V. TILAK, J.P., B.SC. (Bomb.) M.B.B.S. (Bom. & Lon.)
F.R.C.S. (EDIN.)

Professor of Obstetrics & Gynaecology, N.M.C.

Cases of abortion in the first three months, are usually treated, in their earlier stages, by the general practitioner. They can be treated on right lines and the patients can be saved from much worry and prolonged illness if a careful history of each case is taken and a P. V. examination is made early to ascertain the cause of bleeding.

DIAGNOSIS:

In some of the cases the patient may not be even pregnant and the bleeding occurring after a period of amenorrhoea may be due to hormonal disturbances such as Metropathia Hæmorrhagica, or due to the irregular onset of puberty or menopause. The bleeding may occasionally be due to salpingitis, a cervical polyp, Vascular erosion or Cancer. In the case of intra-uterine Pregnancy the per-vaginum examination shows a large, soft uterus and there is no tenderness when the womb is moved from side to side; the palpation of the fornices is particularly easy as the pelvic floor is yielding due to the softening of pregnancy. In the case of an extra-uterine pregnancy the history shows a moderate bleeding, usually dark in colour, but severe pain which may be associated with occasional vomiting and fainting attacks. The vaginal examination will show marked tenderness in the fornices and it may be possible to define a soft tumour by the side of the womb which itself is somewhat soft and large. Extra uterine pregnancy is undoubtedly very rare compared with intra-uterine one but it is this very rarity that puts us off our guard. Doctor Munro-Kerr has emphasized these points very well. In every case of irregular vaginal bleeding during the child bearing age one should keep in mind three possibilities and then proceed to do the vaginal examination whatever may be the diagnosis suggested by the patient or another doctor.

1. Whether the woman is pregnant and if not what is the cause of the non-pregnant bleeding?
2. If pregnant whether the pregnancy is intra-uterine or extra-uterine.

3. If intra-uterine whether the abortion is threatened, inevitable, incomplete or missed?

CAUSES OF ABORTION:

A study of the causes of abortion will help us to apply the treatment intelligently and to keep an open mind as regards evaluation of the various lines of treatment. The large majority of the causes may be grouped as under:

1. Gross morphological defects or abnormalities not compatible with the life of the foetus. Hydatidiform mole may be given as an instance of a gross abnormality.
2. Toxic conditions such as syphilis, Brights disease, Diabetes, severe anæmia, Tuberculosis, alcohol and lead poisoning, fevers and abortifacient drugs given through mistake or intentionally either by mouth, by injection or locally into the womb.
3. Extreme congestion of the decidua due to fibroid, heart disease, prolapse or retroflexion of the womb, laceration and chronic infections of the cervix, chronic constipation, excessive sexual indulgence, etc.
4. Faulty decidual reaction or faulty implantation of the ovum due to defects in the hormones of thyroid and ovary or deficiency of vitamins especially Vitamin E and the anti-hæmorrhagic Vitamin C and K, and salts of Iron and Calcium; this may lead to bleeding into the chorio-decidual space.
5. Pregnancy in an infantile uterus.
6. Trauma, physical or mental and intentional or otherwise.
7. Purely accidental opening of a larger vessel in the decidua due to the eroding action of the chorionic villi and sudden hæmorrhage in the chorio-decidual space. This is sometimes enough to sever the loose attachment of the ovum to the womb in the first two months, i.e., before the placenta begins to develop. This is one of the explanations why abortions are more common in the first two months.

The causes grouped under all the headings except the first do not necessarily cause abortion and many pregnancies go to term. But the tendency to abortion is greater.

PROCESS OF ABORTION:

It is the general experience that nearly half the cases of so-called threatened abortion cannot be arrested whatever the treatment followed. This is explained by a study of the process of abortion which shows that in good many cases the ovum is already dead; i.e. it is a mole. It then acts as foreign body and the uterus tries to expell it. The pain and the bleeding in these cases are only the preliminary signs of an inevitable abortion. In other

cases the ovum is living but bleeding occurs in the chorio-decidual space accidentally due to the eroding action of chorionic villi or due to excessive congestion or defective formation of the decidua. In such cases there is a likelihood of the pregnancy continuing with timely rest and treatment. As however there are no means of knowing, in the early stages, whether the ovum is living or dead we have to give the expectant line of treatment in *all* cases so long as the commonly accepted signs and symptoms of threatened abortion are present viz:—

- (a) Bleeding and pain has started after an amenorrhoea of more than one month.
- (b) The womb is soft and larger than the normal size.
- (c) The bleeding is recent and moderate in amount.
- (d) No part of the ovum is expelled and
- (e) None is felt in the cervical canal.

TREATMENT OF THREATENED ABORTION.

(GENERAL REMARKS)

There is so much difference of opinion on the lines of treatment of such a case that one gets confused about it. All, however, are agreed that such a patient should be put to bed and given a Bromide and Chloral Hydrate mixture to allay her fears. Many recommend Tincture Opil or Morphia to relieve the pain and arrest the process. Others, however, hold that though Morphia relieves the pain it has no effect on the contractions of the uterus and may actually increase it. It is also undesirable in case the pain is due to an undetected ectopic or twisted ovarian cyst as it will mask the symptoms of the true condition and thus delay the right treatment. Projectin is advocated by many as a routine treatment but some Obstetricians think that it has no effect when the abortion has set in and it may convert the condition into a missed abortion if the ovum is already dead. Some obstetricians give Stylboestryol (Female sex Hormone). This Hormone has the property of increasing the tone of the uterine muscle and so it seems to antagonise the action of Projectin which diminishes uterine contractions. Stylboestryol however, is not injurious to the living ovum and it is given in cases of Pregnancy nausea with benefit. It is also known that if this hormone is deficient in the body Projectin will not produce vigorous secretory and decidual phase in endometrium which is so necessary for the proper nidation and nutrition of the ovum in early pregnancy. Finally some obstetricians think that rather than giving medicines that will lessen the tone of uterus, it is better to give those that will maintain it as this will control the hæmorrhage in the choriodecidual space and thus the process of abortion is likely to be arrested. Small doses of Ergot and Nuxvomica are given from this point of view. This much discussion is enough to show that there is no unanimity among the obstetricians

on the question of the treatment of threatened abortion. As I have already stated above, the multiplicity and the diversity of treatments of threatened abortion is partly due to our ignorance of the causes or cause of abortion in a particular case and partly to our ignorance of the condition of the ovum when the abortion starts.

TREATMENT THAT I ADVISE IS AS FOLLOWS:

The patient is confined to bed and a sedative mixture is given. If the pain is severe I give in addition a barbiturate such as luminal or dial. This allays the nervousness, and the recumbent position diminishes the loss of blood. I also give Calcium Lactate and Projestin tablets by mouth. If it is the patient's first conception, I give Stilboestrol in 2 mg. dose with Projestin. If she is anaemic and has suffered from nausea or loss of appetite I give an intravenous injection of Glucose, Vitamin C. & Vitamin B. Recently I am giving injections of Liver Extract & Vitamin K as well. These Hormones. Vitamins and salts are naturally not so effective when the bleeding starts as when given to prevent a possible abortion, as for instance in a case where there is a history of previous abortion. As however these are not toxic and are natural constituents of the body or our food, they cannot do any harm and may do good if the ovum is still living. It is also well known that pregnancy demands a much higher supply of vitamins and Hormones for the healthy growth of the ovum than what is required in the non-pregnancy state. If the patient is constipated I give Liq. Paraffin on the first day and an enema if necessary on the second day. If the womb is retroflaxed no attempt is made to correct the position to put the pessary but I see to it that the bladder is kept empty periodically, by catheterization if necessary, and I ask the patient to lie in Sim's position. The womb usually comes forward in a few days. If it is still retroflaxed and if the bleeding has diminished the patient is put in the knee-chest position and the womb is gently and steadily pushed forward by rectal manipulation. The patient is advised rest for one week after the bleeding stops. If the bleeding persists or increases inspite of this treatment another examination is made and if the cervical canal is found more open than before or a part of the ovum is felt in the canal the treatment of inevitable abortion is begun. If the womb is much larger than what it should be compared to the period of pregnancy and especially when no foetus is felt the possibility of a hydatide form mole should be kept in mind. In some cases of normal pregnancy the bleeding stops for some days and appears again periodically. If the vaginal examination shows the womb growing in proportion to the period of pregnancy no interference is needed as some of these cases go to full term. It is however necessary to keep them under observation as this recurring bleeding may be a precursor of antepartum bleeding either of the

accidental type or due to placenta previa. If the bleeding is scanty or has stopped and a grayish discharge continues and the womb is not only growing but is actually getting smaller than what it was a fortnight or a month ago it should be considered as a case of missed abortion and treated accordingly.

INEVITABLE AND INCOMPLETE ABORTION:

If the bleeding is not severe I give an injection of Morphia and Ergomatrine pituitary extract. In such cases Morphia is excellent as it relieves pain, procures sleep and helps the action of the pituitary extract—also give a hot antiseptic douche and massage the womb bimanually; if any portion of the foetus protrudes from the cervix it is removed. If the bleeding is brisk I pack the vagina in addition to the treatment given above. The ovum usually comes out when the pack is removed in about six hours. If, however, the ovum is not discharged I advise its operative removal as this is the best procedure for preventing further loss of blood, possible sepsis, or subinvolution. Just before the operation I give an injection of Glucose and Calcium Gluconate intravenously and Ergometrine subcutaneously. This hardens the uterine wall, diminishes blood loss during the operation and facilitates the separation of the retained products of conception.

SEPTIC ABORTION:

When this complication arises in the course of an abortion operative interference is dangerous as it is very likely to spread the sepsis. The patient should be put to bed in Fowler position and oxytocic drugs and calcium injections are given to tone up the womb and control the bleeding which is usually not severe. The Sulphonamide group of drugs are given in full doses by mouth or by injection. If the sepsis is not controlled quickly injections of penicillin should be given in addition. If the bleeding is severe or the mole or blood clot is blocking the cervical canal it is gently removed and Glycerine is injected slowly into the womb to favour drainage. This treatment succeeds in a large majority of septic abortions and the mole also gets discharged during the period. If it is retained it should be removed a week after the sepsis is controlled.

MISSED ABORTION:

These cases give history of the signs of pregnancy then bleeding and pain for a few days. The pain and the bleeding cease though she gets occasional blackish discharge. The other signs of continued pregnancy such as fullness in the breasts and swelling in lower abdomen disappear. The patient usually shows no sign of sepsis such as fever or offensive discharge though a dead and shrivelled ovum is retained in the womb. There is therefore no necessity for immediate completion of abortion. I keep the patient under observation for about a fortnight to make sure that is a case

of missed abortion and that the womb is not growing in size. Treatment is then directed to the stimulation of the womb. I give a dose of castor oil and then Ergot in full doses together with still-boestryol in 5 mg. doses. The latter often sensitises the womb to pituitrin which I give after three or four days of this preliminary treatment. The same treatment is repeated again and if the mole is not discharged I advise its operative removal.

(Paper based on the talk given by Dr. H. V. Tilak at the Scientific section of the Silver Jubilee Celebration of the National Medical College on 3rd February 1946 in Bombay.)

ACUTE PLEURISY WITH EFFUSION

BY B. L. CHOPRA,

Divisional Medical Officer N. W. R. Ferozepore.

This disease is generally defined as an inflammatory serous pleural exudate. The most important cause is tubercular focus in the lungs or pleura. The affection commences with dry pleurisy spreading over the visceral and parietal pleura. The fibrinous exudate soon forms a thick rough layer on the surface. As further exudation of the fluid occurs the lung collapses *pari-pasu*. The reaction of the lung this way due to its elasticity continues until the pleural negative pressure is completely abolished. The heart etc., are displaced away from the affected side. If fluid continues to be effused after the lung has retracted to the full extent and negative pressure as said above is completely abolished, a positive pressure is produced. Owing to hilar attachment of the lung, it retracts upwards and inwards allowing accumulation of fluid at the bases and in the axillary region where it reaches its highest level, unless some old adhesions prevent it. The fluid is a clear yellow exudate with a specific gravity between 1010 & 1018. The reaction is alkaline and protein is present to about 4 per cent or over. Microscopically polymorphonuclear cells, lymphocytes and few R. B. C's and sometimes eosinophils and few pleural endothelial cells are seen. The fluid is often sterile but T. B. may be found or if the exudate is injected into guinea-pig it dies from T. B. Lymphocytosis indicates T. B. infection. The amount of fluid varies from a few ounces to over 2 pints.

Clinical Findings:—The effusion may arise insidiously or follow an acute attack or dry pleurisy or may occur as a complication of one of the diseases like rheumatism, oral sepsis, septicamia, typhoid pneumonia or new growths, etc. Artificial Pneumothorax is complicated by serous effusion in about 50 per cent of cases.

The symptoms vary with the mode of onset. There is usually a history of a more or less acute onset with pain but as the disease progresses and surface of the pleura is separated by fluid, pain becomes less and less marked. Sometimes a considerable amount of fluid accumulates without any history of pain. The following is an actual case illustrating the various points mentioned above.

A boy aged 18 years, son of a clerk of D. S. office was admitted into this hospital running a continuous type of temperature with slight cough for 16 days. He stated to have been diagnosed a case of typhoid fever by a private practitioner in the city.

On going carefully into the history of the case it was found that he had severe pain in the right side of the chest for the first few days of his illness and even on admission slight pain was present. Further examination of the patient in this hospital showed that he was dyspnoeic and restless. The clinical findings of the chest were restricted expansion of the right side of the chest, percussion note dull in the right interscapular, infrascapular, intra-axillary and infra-mammary regions. Vocal resonance diminished in these areas and the complete absence of the sound was noticed. The apex beat of the heart found displaced towards the left 6th intercostal space just outside the mammary line.

He was diagnosed as a case of pleurisy with effusion right side, X-Ray was ordered and showed complete opacity of the right side of the lung with displacement of the heart. The patient was put on the usual treatment of;...

1. Saline expectorant with potassium iodide one ounce 3 times a day.
2. Dover's powder Gr. 5 was given whenever necessary.
3. Sleeping mixture with bromide and chloral hydrates was also given, when necessary.
4. Right side of the chest was painted with Liniment Iodide. He was also given Adexoline 10 Mins. twice daily.

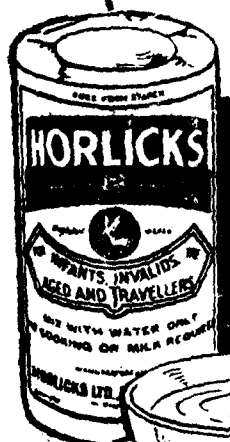
The treatment was carried out for few days and the patient was running continuous type of temperature and there was no change in the level of the fluid. It was, therefore, decided to do paracentesis. Potain's apparatus of the hospital suddenly went out of order and the following technique was devised to draw the fluid out. The patient was given $\frac{1}{4}$ gr. of morphia sulphate half an hour before the operation. He was made to sit up in the bed. The area of the operation was painted with iodine. The skin and the muscles down to the pleura were anaesthetised with 2 per cent Novocaine. One lumbar puncture needle with stiller was introduced into the right 6th intercostal space in the mid axillary line, just above the rib to avoid puncturing the intercostal artery. The 20 cc. record syringe was used for aspiration.

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Pale greenish in colour.

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Albumin + + + +

Microscopically 8 to 10 lymphocytes per field, occasional polymorphonuclear leucocytes and R.B.C.

The other laboratory examinations done may be mentioned here :—

Sputum did not show any acid—fast bacilli on repeated examination.

Blood examination showed increased lymphocyte count to 38 per cent.

Urine examination: No abnormality.

On the 1st sitting about half a pint fluid was drawn, when the patient began to complain of severe pain and it was therefore stopped.

On the next day i.e. on 23.10.45 again, the operation was repeated and the same amount of fluid was drawn off. The dyspnoea was now much less than before, and the pain was nothing much to speak of.

After another week $\frac{1}{2}$ a pint of the fluid was again drawn in the same way.

A week after the 3rd puncture, another attempt was made to draw out the fluid, but nothing came. He was now running intermittent type of temperature, which gradually settled down to almost normal with occasional rise to 99 degree or 100 degree in the evening. He was then put on a course of injections of "Thisin" intramuscularly every other day and after the 3rd injections the temperature settled down to the normal. The lung expansion was satisfactory but the signs of the thickened pleura were still present. He was advised to Waterbury's compound to regain his normal weight.

He was discharged from the Hospital on 12.12.45 and has come to see me twice after that and is regaining his normal weight very rapidly and intends going to college from 1st February.

In this connection it is well-worth mentioning the indication for paracentesis :

1. If the effusion is increasing.
2. When it is of long standing and attended by urgent symptoms.
3. If the absorption is slow. The fluid remaining at the same level for a fortnight or more.
4. When the effusion is bilateral.
5. When albuminous expectoration is present.

The interesting point about this case is rapid and complete cure of this disease by paracentesis and "Thisin" injection as well

as the improvised method of drawing large quantities of fluid as stated above.

My thanks are due to Dr. C. D. Newman for allowing publication of this article.

(*Medical Bulletin*, 29th June 1946).

Extracts.

MENINGOCOCCIC MENINGITIS TREATED WITH SULFADIAZINE AND SULFAMERAZINE.

Sweet and others (*Annals of Internal Medicine*) have treated 207 patients with meningococcic meningitis during a 3-year period, using either sulfadiazine or sulfamerazine. The gross mortality was 10.1 per cent and there was no significant difference in the case fatality rate in patients treated with the two drugs.

The basic treatment for all types of purulent meningitis consists of (1) adequate sedation to keep the patient quiet and comfortable; (2) hydration; (3) sulfonamides, and (4) nursing care. In the above cases morphine in full dosage was the sedative of choice.

An initial oral dose of 6 Gm. of sulfadiazine or sulfamerazine was followed by 1 Gm. every four hours in adults. A proportionately smaller dose was given to children. For severely ill patients the initial dose and a varying number of subsequent doses were given as a 0.5 to 1 per cent solution of the sodium salt of the drug intravenously or subcutaneously. The sulfonamide drug was continued until the patient was afebrile for approximately seven days unless some indication for stopping the drug developed sooner.

Follow-up lumbar punctures were done on the second hospital day and again when discharge was contemplated. If the cell count had not fallen to 30 cells per cu. mm. the puncture was repeated at weekly intervals until the level was reached. At this time the patient was allowed out of bed.

Those who responded poorly to this regime in the first 24 to 48 hours were considered candidates for serum therapy, or, during 1944, for penicillin. Penicillin was administered intrathecally in doses of 10,000 to 20,000 units. This was adjusted to a concentration of 1,000 units per cubic centimeter. The volume of diluted penicillin given always was 5 to 10 cubic centimeters less than the amount of cerebrospinal fluid withdrawn. The penicillin dose was repeated every 12 to 24 hours until satisfactory improvement was noted. The presence of the coma-delirium state and the age of the patient were the factors of the greatest prognostic significance. The older patients responded less well than their younger co-sufferers.

There was no relationship between the concentration of the sulfonamide in the blood and the outcome in meningitis. Careful appraisal of patient and of the findings in the C. S. F. will indicate those patients requiring more vigorous treatment. A total of 91 patients almost 50 per cent of the patients who survived had blood levels of less than 10 mg. per 100 cubic centimeters, and only 24 had levels of 15.0 mg. or above on the day their fever subsided. Nerve palsies were the most frequent complications related to the infection among the patients who recovered. These occurred in 35 patients involving both sensory and motor nerves. Deafness, the most frequent sensory change, was present in 10 patients. The other complications, encountered include 10 instances of arthritis or tenosynovitis and four of purulent conjunctivitis.

Digest of Treatment (1946) March, 678.

AN IMPROVED TECHNIC FOR CIRCUMCISION

The following improved technic has been developed for this purpose in adult circumcisions. This regimen has proved satisfactory to patients and physicians:

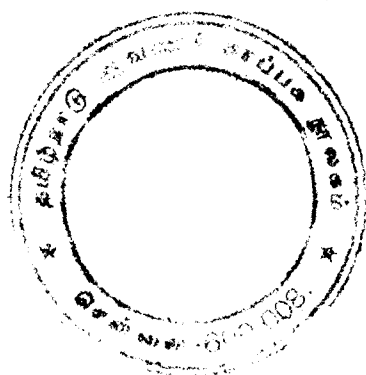
An hour and a half before operation morphine 1/6 gr., scopolamine hydrobromide 1/150 gr., and sodium pentobarbital 1 1/2 gr. are given. If an hour later the patient is alert sodium pentobarbital is repeated. Thorough washing with soap and water for eight to ten minutes is the only local preparation. The local anesthetic is 1 per cent procaine with two drops of 1/1000 adrenalin to each ounce. Ten ounces of the anesthetic solution is sufficient. It is introduced in a subdermic ring (the skin is too thin for endermic infiltration), completely encircling the penis, 1 m. cm. behind the corona. The foreskin is then peeled back. A second ring of infiltration is made under the mucous membrane just behind the corona. The frenulum and its adjacent area are well infiltrated. After two minutes, the anesthesia is tested by needle prick. The first cut is down the frenulum; then pull edges off the diamondshaped defect in the mucous membrane together with No. 000 dermal sutures. Two hemostats are placed on the edge of the foreskin, as it lies in a natural position. Using gentian violet, a line is drawn on the skin 1.5 cm. anterior to and parallel with the coronal ridge. A dorsal slit is made to a point 1.5 cm. anterior to the retroglandular sulcus. From this point, a cut at the same distance, 1.5 cm., and parallel with the coronal ridge is made about the foreskin with scissors. All bleeding points are picked up and tied with No. 00 plain catgut.

A cuff, 2 or 3 cm. in width, is then trimmed from the mucous membrane completely around the penis, to make the skin a bit longer than the mucous membrane.

Interrupted, fine, nonabsorbable sutures are tied very loosely. The edges of the mucous membrane and the skin are turned outward before the sutures are placed to prevent any inversion. Smooth forceps are used.

First three holding sutures are placed so as to divide the circumference into equal parts, ends left long and held by hemostats. The closing sutures, placed close together, are but 2 or 3 mm. from the edges. Finally the holding sutures are cut, the foreskin is retracted under tension as it would be in an erection, any gaps then present are closed. The primary dressing is powdered sulfamylamide and gauze on which has been placed a thick layer of ointment (Nupercain). Against the period of discomfort between the last effect of the local and the first effect of the ointment, the penis enclosed in its ointment dressing is packed in ice for a period of four hours after operation. Postoperative erections are controlled to a degree with pheno-barbital 1-2 gr. and sodium bromide gr. 10 t.i.d. for five days. Patients are kept in bed for 24 to 48 hours to prevent edema. The ointment dressings are used for five or six days. On the seventh day the stitches are removed.

Digest of Treatment (1946) February, 614.



Glycodin Terp-Vasaka Contains active principles of **Vasaka** together with **Terpena Hydrate**, **Codeine**, etc. It has been proved highly efficacious in coughs, colds, bronchitis, asthma, throat and pulmonary tuberculosis and Whooping cough.

COMPOSITION: Each fluid drachm contains:—		
Antimony Tartrate		1/60 gr.
Terpena Hydrate		1/8 gr.
Codeine Phosphate		1/8 gr.
Menthol		1/24 gr.
Syrup Tolu		1/5 Min.
Syrup Vasaka		Sufficient.

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FOR ASTHMA SUFFERERS

Anti-Asthma Liquid, prepared according to a special formula, quickly liquefies and expels the phlegm, clears the air passages and ends irritation.

INDICATIONS:
Asthma, Spasmodic Coughs, Chronic Bronchitis and Catarrhal Inflammation of the Lungs.

ANTI ASTHMA LIQUID

COMPOSITION: Each fluid drachm represents:

Liq. Arsenicalis 1/4 Min.
Tinct. Lobelia Aether 1 1/2 Min.
Tinct. Belladonna 5/8 Min.
Tinct. Euphorbia 1 1/2 Min.
Tinct. Ephedra Vulgaris 20 Mins.
Syrup Vasaka 30 Mins.
Liq. Ext. Kuth 8 Mins.
Potash Bromide 1 1/2 Gr.
Potash Iodide 5/8 Gr.
Sodium Nitrite 1/15 Gr.
Borax ... 1/2 Gr.

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EACH FLUID DRACHM CONTAINS:—

Pot. Bromide	...	10 grs.
Chloral Hydrate	...	5 ..
Tinct. Valerian	...	5 min.
Tinct. Cannabis Indica	...	1 min.
Tinct. Hyoscyami	...	4 ..
Ext. Glycyrrhizae Liq.	1 ..	
Syrup	...	Sufficient.

INDICATIONS:— Neurotic excitability and hysteria; insomnia; epilepsy; infantile convulsions; painful menstruation; chronic alcoholism and all nervous disorders of functional character.

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Elixir Haemoglobin is the prescription of most doctors in cases of anaemia of any origin - due to protozoal infections like Malaria, Kalazar etc., deficiency diseases like Sprue, Rickets, Beri-Beri etc., or in cases of pregnancy, haemorrhage etc.

COMPOSITION: One fluid ounce of Elixir Haemoglobin consists of: Haemoglobin 2 grs., Stomach Extract 1 gr., Liver Extract 2 grs., Organic Copper Salt, Trace, with flavourings and diluents.



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AL. 400.

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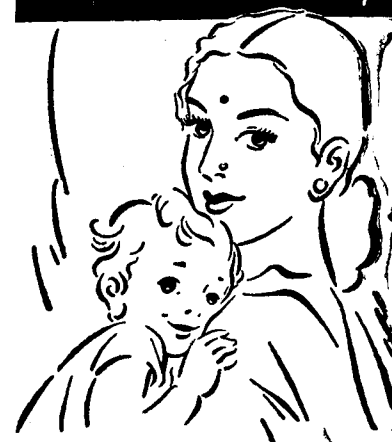
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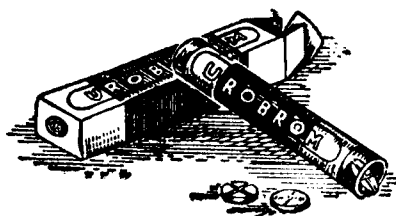
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UROBROM is not a barbituric acid compound and hence it does not act as a hypnotic in the same sense as Luminal, Lupot and other barbituric compounds. UROBROM is Bromisovalerylurea, which is an excellent nerve sedative and hence acts to induce sleep in persons suffering from excitable nerves, worry, over-work, strain and alcoholic excesses, etc., etc.



COMPOSITION:—Each tablet contains Bromisovalerylurea 0.3 G. (5 grs.) corresponds to Bromural (Knoll).

INDICATIONS:—A dependable mild Hypnotic inducing natural restful sleep. The effect lasts for four to six hours and is followed with no 'Hang Over'. The drug is entirely non-habit forming. It should be prescribed in cases of Insomnia due to nerve tensions, over-excitability, emotional shocks, neurosis, seasickness, alcoholic excesses.

DOSAGE:—Adults: 1 to 2 tablets as required. Children: Proportionately less.

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