An Address

ON

PELVIC SEPSIS.

GIVEN TO THE SOUTH-WEST ESSEX DIVISION OF THE
BRITISH MEDICAL ASSOCIATION

BY

A. LOUISE McILROY, D.B.E., M.D., D.Sc.GLAS.,

PROFESSOR OF OBSTETRICS AND GYNAECOLOGY, UNIVERSITY OF LONDON
(ROYAL FREE HOSPITAL).

PELVIC SEPSIS is one of the most important subjects in medicine. It is a danger to life. It is the cause of ill health on the part of many women. It interferes with reproductive function, and leads to more domestic anxiety and conjugal infelicity than almost any other disease.

What are the natural defences of the pelvic organs against infection? Although the reproductive organs consist of a series of canals which potentially lead from the open air to the peritoneal cavity, the structure of these passages is so arranged as to ensure almost complete occlusion. The labia close over the vaginal entrance, and the walls of the latter lie in antero-posterior apposition. The cervical canal is narrow and sealed by mucus. The secretion of the uterine glands, the cilia, the muscular contractions, all prevent the ascent of bacteria. The tortuous condition of the Fallopian tube is an important element in the closure of its lumen. The vagina contains the bacillus of Döderlein, which is a powerful agent against the entrance of infection. When this bacillus is present pathological bacteria are as a rule absent. Dr. Charlotte Houlton, in the Obstetrical Unit at the Royal Free Hospital, made a very comprehensive investigation of the vaginal and cervical discharge during pregnancy. If the *Bacillus vaginalis* was present in numbers puerperal sepsis was less likely to occur than in those cases where the bacilli were scanty or absent. Various other research workers have also found that streptococci are so frequently present in the vagina as to warrant the assumption that these bacteria are protective in function.

With all these methods of defence, how does infection gain an entrance? Mainly by means of the exercise of the reproductive function. In virgins pelvic sepsis is rare, apart from toxic intestinal conditions or tuberculous lesions. The mode of invasion is mainly by the pelvic route by direct infection, as in gonorrhoea, or from infection occurring at the time of labour or abortion. The most important organisms we have to deal with are the gonococcus, the streptococcus, and the *Bacillus coli*. The gonococcus is rarely to be found except in the acute stage, and I do not propose to deal with the subject of venereal disease except to mention that in cases of chronic pelvic sepsis in hospital practice which do not yield to treatment the gonococcus is the chief factor for consideration. Sepsis may gain admission by means of the blood and lymphatics. Septic foci, such as are found in carious teeth or intestinal toxæmia, are a source of infection. The *Bacillus coli* may affect the urinary tract and give rise to pelvic complications. Streptococci or *B. coli* infection of the caecum or appendix may involve the right tube and ovary. The vulva and vagina are not easily infected apart from venereal disease. The cervix may retain bacteria because of its crypts and complicated glands, and a chronic discharge may persist for months or years. Recurrent vascular changes in the endometrium and the formation and exfoliation of the decidua render the uterus liable to attacks of micro-organisms.

Infection during Pregnancy.

In pregnancy infection is not common. The most common infection is by the *Bacillus coli*. It is closely associated with toxæmia and pre-eclamptic manifestations. Urinary symptoms should never be ignored in pregnancy, and bacteriological examinations of the urine should be carried out if toxæmia is present. The presence of albumin is not the only important factor in urinary analysis. Treatment of *B. coli* infection by the oral administration of alkalis, followed by acids and formalin preparations, is

much to be preferred to local applications and douches to the bladder. The treatment of urinary infections in pregnancy is, as a rule, satisfactory. Rest in bed, heat to the abdomen, fluid diet, and non-protein solids, with plenty of fresh fruit and vegetables, give good results. Pregnancy rarely has to be terminated for *B. coli* infection, and only in those cases where there is kidney involvement. The bacilli may persist in the urine for weeks after the patient appears cured. No special clinical significance seems to be attached to their presence in such cases.

General ill health in pregnancy means low resistance to infection at the time of labour. The teeth should be examined as a routine, and attended to when caries or pyorrhoea is present. Even one carious tooth can affect the well-being of a patient. About 70 per cent. of the ordinary hospital patients attending the ante-natal clinics require dental treatment, even though it may merely mean cleaning the teeth and gums. I have never seen abortion occur as the result of dental extraction. On the contrary, many cases of habitual abortion owe the condition to septic mouths. Every focus of infection, such as in disease of the middle ear or skin, should be treated. Defective states of the excretory organs, especially intestinal stasis, and abnormal conditions of the heart and lungs all lower resistance to infection.

If there is a purulent discharge from the cervix a swab should be taken for bacteriological examination. Vaginal swabs are useless. Treatment by antiseptic swabbing of the cervix or by medicated pessaries can be given. Lactic acid pessaries are of benefit, as they stimulate the growth of the vaginal bacillus. Douching is of no value unless carried out by a nurse. It often does more harm than good if left to the patient herself. It inhibits the protective bacteria, and should only be employed for infective discharges. It is quite unnecessary to douche patients during labour or before the application of forceps. A not uncommon cause of puerperal infection is intercourse in the later weeks of pregnancy.

Labour.

Sepsis may be introduced directly by the attendant by means of repeated vaginal examinations, but in the majority of cases the infection is in the patient herself. Lacerated and especially contused tissues may become infected in any part of the body, and the same condition may occur in the pelvic organs. Bacteria which are harmless on an intact mucous surface may easily take on a pathological character when they gain access to tissues filled with blood and damaged cells. Saprophytic organisms invade blood clot or placental tissue which is separated or necrosed, and in some cases they prepare the way for the invasion of pyogenic bacteria. Lacerations are not so likely to occur if the labour is easy and not unduly hurried. An easy labour means less shock, and therefore less lowering of resistance. If the patient is assured that she will not suffer the results are better.

The psychological aspect of labour is of great importance. Fear is often inhibitory in its influence, and causes contraction of the outlet of the pelvis. Shock can be avoided to a great extent by the administration of sedatives in the first stage, sedatives and intermittent anaesthetics in the second stage, and full anaesthesia in primigravidae when delivery is taking place. In domestic practice the medical attendant may be forced to interfere with the course of labour against his better judgement because of the suffering of the patient or the persuasions of her anxious relatives. If the patient sleeps or does not complain of pain the conduct of the labour is much more easy. Chloral hydrate and potassium bromide can be given with safety from the beginning of painful labour and throughout. Morphine is the most efficacious of all drugs, as it hastens the dilatation of the cervix; opoidine, 1/6 to 1/4 grain, is a good preparation of morphine to be given in the first stage. Adaline, 5 to 10 grains, is also useful, and easily administered by the mouth. There is no rule for the repetition of the dose in labour; the dose is regulated by the condition of the patient. The best anaesthetic is gas and oxygen, but it is cumbersome for domestic practice. Chloroform is useful during delivery and at intervals during the later second stage. If the patient is anaesthetized so as to

prevent undue pressure during the delivery of the head, damage to the perineum can be prevented in many cases. In obstetric practice it is not always possible to have an anaesthetist, because of the additional expense. No surgeon would operate under the conditions enforced upon a practitioner in maternity work. Lacerations of the cervix should always be looked for by means of a speculum, and if present stitches must be applied. Tears in the vagina require repair just as much as the perineum. How is this all to be carried out if the light is bad and the patient rolling about the bed? If midwifery practice is to be improved the public must be made to realize that it means more financial responsibility. Skilled medical help in the repair of lacerated tissues will solve to some extent the problem of maternal mortality. Although ante-natal work is doing much to prevent complications in labour, we must direct more attention in the future to the more rational treatment of labour itself and its immediate consequences. If over 60 per cent. of the women of the country are attended by midwives, are these labours to be borne with pain and suffering? Every expectant mother should be seen at least once by a medical practitioner, and I see no reason why he should not arrange for a suitable sedative to be given by the midwife during labour in each particular case. If there is great suffering and an anaesthetic would give relief, this should be an indication for sending for a practitioner, preferably one who has already seen the patient during pregnancy. Pupil midwives should be given some special training in the administration of sedatives. Drugs such as chloral hydrate and potassium bromide could be put up in measured doses and indications taught for their safe administration. Anaesthetics should be given by the medical practitioner as in surgical practice. The obstetric attendant cannot be expected to deliver or operate and give an anaesthetic at the same time. I am not quite sure of the legal aspect of the case, but I could quite well imagine some difficulty arising in the case of a fatal termination from anaesthesia if only one medical practitioner were present.

The practice of making women bear down in labour often results in general and uterine fatigue. Pressing the feet against a board is less tiring than pulling with the arms. Sometimes the squatting position aids the descent of the head.

Third Stage of Labour.

As long as the placenta is in the uterus and no haemorrhage is taking place the uterus should not be manipulated, as irregular contractions may be induced and the edge of the membranes may be retracted upwards towards the cervix, thus causing infection. When the placenta reaches the vagina it can be expelled by gentle massage. If the placenta is adherent and manual removal is necessary, it is not infrequently found that a certain degree of sepsis follows. In cows, if the placenta is adherent, *B. coli* infection is suspected. It may be that a parallel condition exists in human obstetric practice, and that the infection is already in the uterus. To remove an adherent placenta it is better to keep the hand inside the uterus when the placenta is entirely separated and to pull it out by the cord with the other hand. If it is not intact or membranes are left behind, the internal hand can clear the uterus without additional risk of reintroduction. Exploration is unnecessary for retained membranes or small pieces of placenta in other cases, because of the risk of introducing sepsis. The patient should be carefully watched, and if signs of sepsis appear the uterus can be drained or explored. As a rule the uterus expels all retained membranes, and can be aided to do so by the administration of ergogen or pituitrin.

Drainage of the uterus in the puerperium may be aided by sitting up in bed and by exercises. Lochia are retained if the patient lies on her back for any length of time. If the perineum has been lacerated and healing does not take place the stitches should be removed and the perineum cleaned up with antiseptics and sitz baths. As soon as the tissues are clean—usually in about ten days—the patient should be anaesthetized and deep silkworm-gut secondary sutures applied after freshening the granulation tissue with a scalpel. If the perineum is slow in becoming clean, scarlet-red ointment applied for a few days stimulates the

tissues and renders operation possible. Complete union as a rule occurs after suturing, and thus vaginal operations for prolapse are prevented. This method of treatment is most satisfactory, and is carried out as a routine in the Obstetrical Unit in every case where healing has not taken place.

Local Sepsis: Diagnosis and Treatment.

True puerperal sepsis, or septicaemia with blood infection, is not common in hospital obstetric practice, but local sepsis is met with not infrequently. District patients rarely go septic, probably because of their protective organisms. These may be destroyed when a patient comes into hospital, in the process of cleansing.

Local sepsis, in addition to a rise of temperature and pulse, is manifested usually by offensive-smelling intermittent copious lochial discharge. The uterus is tender, and the abdomen is not distended. The main object of treatment is to stimulate uterine drainage and contractions. Ergot, pituitrin, or quinine can be given. Low-pressure vaginal douches are of benefit, also sitz baths. Drainage by means of a wick of gauze with glycerin in the uterine cavity is effective. In some cases digital exploration is necessary to remove pieces of placenta. If pus forms incisions must be made, but with early glycerin drainage cases of pelvic cellulitis have almost completely disappeared. A fresh wick of glycerin gauze is put in daily until the temperature subsides. This method is easier of application than the frequent injections of glycerin as recommended by Dr. Remington Hobbs. As a rule two, or at the most three, applications are sufficient.

Treatment of Acute Sepsis.

In acute sepsis rigors are present in many cases, the lochia dry up, and the abdomen is tender and distended by the paralysed intestine. Streptococci may be found in the blood, usually when the temperature is high. Sometimes the *Bacillus coli* is found, but not frequently. The treatment is more general than local. Antistreptococcus serum in daily doses of 20 to 30 c.cm., or even 40 c.cm., is given. Quinine bilydrochloride intramuscularly, 5 to 10 grains daily, is also given. The two essentials, however, are open air and daily colon lavage. The latter clears away the intestinal toxins, and is the most efficient remedy I know of for sepsis. It helps to prevent the onset of pneumonia. Blood transfusion is of value in some cases. If there is any uterine discharge a glycerin drain may be employed. Vaccines, unless in stock, are difficult to obtain in time for immediate treatment. The Dick serum has not proved itself of much benefit according to the researches of Dr. Salmond and Dr. Turner in the Obstetric Unit at the Royal Free Hospital.

Post-natal care is essential in the prevention of the extension of latent sepsis. The uterus should be encouraged to rise up in the pelvis by making the patient take knee-chest exercises. A pessary may be necessary for a month or two if the uterus is not involuted. If catarrhal conditions of the cervix are present vaginal tampons of ichthylol and glycerin are of use. Operative treatment should not be advised until all other methods of treatment have proved useless and symptoms are present and found to be definitely due to the malpresentation.

Abortion is a very frequent cause of pelvic sepsis, especially if criminal induction has taken place. Drug induction often causes an incomplete abortion, with consequent chronic ill health. As a rule the placenta is retained, and may become foul-smelling with septic necrosis. The patient should be treated as a case of acute sepsis and her resistance raised. Glycerin should be injected into the uterus, and after the acute symptoms have subsided the placenta can be removed by the fingers or ovum forceps. Early removal of the placenta may break down the protective cell barrier in the uterine wall and so turn a local into a general sepsis. Curettage or hysterectomy for puerperal sepsis have been given up by most obstetricians.

Pelvic Sepsis in Gynaecological Practice.

I cannot do more than touch upon one or two points on this subject. Most infections are puerperal or gonorrhoeal in origin. In the treatment of chronic pelvic sepsis the

medical aspect of the question is coming more into prominence than hitherto. The general condition of the patient is more important than the local. Chronic cervical discharge may clear up in many cases with local treatment, but the uterus is frequently the channel for the excretion of toxic products, the result of intestinal stasis or rheumatic affections. Teeth are a source of chronic infection. Dieting, exercise, baths, intestinal lavage, and artificial sunlight all help towards a cure. If there is stenosis of the cervical canal or retained uterine discharge, as in cases of chronic subinvolution with defective uterine contractions, local treatment, such as dilatation, curettage, and drainage, is valuable. Drainage can be carried out by stitching a self-retaining rubber catheter into the uterus for five or six days and injecting a drachm of glycerin with a serum syringe into the tube several times a day. This does not disturb the patient, and can be done by a nurse. Glycerin drainage relieves the pain and uterine spasm of acute sepsis, such as occurs in salpingitis or pyosalpinx. It is used as a preliminary measure to operation, but in many cases of pelvic peritonitis the symptoms subside with drainage, and operative intervention is unnecessary. It is useless operating upon adherent tubes and ovaries if the uterine canal is stenosed. A preliminary dilatation and drainage is necessary. If pus is present in the tubes, and removal or some conservative operation is adopted, drainage of the pelvis is best performed by placing a wick of gauze in the pouch of Douglas and bringing one end out through a vaginal incision. Amputation of the cervix for chronic sepsis may give good results if pregnancy does not occur subsequently, but rigidity from scar tissue may complicate labour. I have seen several cases where Caesarean

section was necessary for this condition. The operation is not a desirable one in the case of young women. Hysterectomy for chronic sepsis is beneficial when drainage has failed, but it is not so frequently employed now that general methods of treatment are available.

The restoration of reproductive function, and not its destruction, should be the aim of the practitioner. A radical pelvic operation should not be performed before treatment of septic teeth or intestinal stasis has been tried. Hysterectomy, if performed, should, when possible, be limited to the supravaginal operation. Panhysterectomy causes contraction of the vaginal vault, with subsequent dyspareunia or difficult intercourse. Hysterectomy not only causes sterility, but gives rise in some cases to domestic unhappiness and infidelity, both on account of its physical and mental consequences. The after-histories of cases when followed up may make one question the advisability of radical operations, which may physically benefit the patient but cause unhappiness in her marital relationships. If the uterus is removed and the ovaries are left, the cervix acts to a certain extent as a channel of excretion.

Tuberculous affections of the pelvic organs should be treated on the same lines as surgical tuberculosis—fresh air and sunlight. The recurrence of menstruation may cause attacks of pain and keep up the activity of the disease. X rays are of value in suppressing menstruation and thus bringing about physiological rest. The dose can be graded to be temporary in its effects.

I have merely touched upon the fringe of the subject of pelvic sepsis. My opinions are perhaps controversial, but they are at least the result of my experience.

"ACTIVATED" (IRRADIATED) FLUORESCIN IN THE TREATMENT OF CANCER.

BY

S. MONCKTON COPEMAN, M.D., F.R.C.P., F.R.S.,
FRANK COKE, F.R.C.S.,

AND

CLAUDE GOULDESBOUGH, M.B., B.Ch.,
RADIOLOGIST TO THE ROYAL NORTHERN HOSPITAL.

(With Special Plate.)

Two years ago (in 1927) we tentatively initiated a method of treatment on cases of inoperable cancer involving the use of a soluble salt of fluorescein, followed by the application of a comparatively small dosage of x rays or radium.

This method, and the results obtained therefrom, formed the subject of preliminary communications by one of us (S. M. C.) to a meeting of the local Branch of the British Medical Association at the Hampstead General Hospital on February 9th, 1928, and to the Chemio-Therapeutic Section of the International Cancer Conference¹ which met in London in July of that year. On the occasion of the London conference we also demonstrated at the Royal Northern Hospital several cases of previously inoperable cancer, which, subsequent to varying periods of treatment, then exhibited no evidences of the malignant disease from which they were suffering when treatment by means of activated fluorescein was commenced.

ACTIVATION OF FLUORESCIN.

Fluorescein ($C_{20}H_{12}O_5$), which may be regarded as the prototype of a long series of acid phthalein dye-stuffs, is formed by heating to a temperature of $190^{\circ}C$. a mixture of phthalic anhydride (1 part) and resorcinol (2 parts). By the introduction of halogen atoms into its molecule most of the fluorescein produced is transformed into dye-stuffs known by the generic term of "eosins." Of these the most important is eosin ($C_{20}H_6O_5Br_2K_2$), well known

by reason of its extensive use in histological investigations. This is the potassium salt of tetra-brom-fluorescein, which is usually marketed rather than the sodium salt, which does not crystallize so well. On the other hand, fluorescein, which is quite insoluble in water, but readily soluble in alkaline liquids, is produced as the sodium salt, under the trade name of uranin. In the course of our investigations we have also made use of the potassium salt, but found it necessary to have this specially prepared.

For some years past it has been known, as the outcome of researches by von Tappeiner and Raab, Noguchi, Salant and Bengis, Pereira, and others, that when lowly organisms such as paramoecia, or embryonic cells, including ova and spermatazoa, are exposed to the action of daylight in the presence of a dilute solution of eosin or fluorescein they are rapidly killed, whereas if protected from light, as when the containing vessel is placed in a dark cupboard, no such lethal effect is produced. Many other dyes, dye-stuffs, and acridine derivatives, in addition to haemato-porphyrin, a derivative of haemoglobin, all of which fluoresce in the presence of light, exhibit similar properties. This fact has been abundantly demonstrated in the case of eosin, most recently by Pereira.

Eosin, and the similar iodine compound erythrosin, have, however, from the clinical point of view, the disadvantage as compared with fluorescein, that, especially if injected intravenously, they are found to be definitely toxic to the animal body, whereas fluorescein appears to be completely non-toxic even if administered in comparatively enormous doses. Thus experiments carried out by W. S. C. Copeman and D. Levi have proved that continuous administration of 1 per cent. fluorescein to mice, over a period of several weeks, in place of water, has no obvious harmful effect; while tadpoles can live in a 1 per cent. solution of fluorescein, if protected from light, for a shorter period of time.

Dr. H. Colwell, radiologist to King's College Hospital, is at present engaged in an investigation on somewhat similar lines with the aid of a grant from the Medical Research Council, but his report has not yet become available.

Recently, in view of suggestions received from Professor Lindemann, F.R.S., of Oxford, we have carried out a series of tests, clinical and experimental, on the action of fluorescein salts of metals other than sodium with, and