CLOSTRIDIAL INFECTION OF THE UTERUS—
A REVIEW TREATMENT WITH
HYPERBARIC OXYGEN

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Post-abortal and puerperal infection due to Clostridial organisms have been reported periodically ever since H. M. Little's paper appeared in 1905.

Hyperbaric oxygen has been proved to be of great therapeutic value in Clostridial infections (Brummelkamp, Boerema and Hoogendyk, 1963; Brummelkamp, 1964, 1965) but we feel that its use for uterine infections has not been sufficiently emphasised.

Since the establishment of an adult hyperbaric oxygen chamber at Whipps Cross Hospital in January 1964, three cases of Clostridial uterine infection have been treated.

Incidence
The incidence of true Clostridial infection of the uterus is very difficult to assess since Clostridia can be cultured from the genital tract in about 5 per cent of normal women (Holtz and Mauch, 1962) and from the vagina of 19-29 per cent of patients following abortion or prolonged and assisted labour (Bysshe, 1938; Ramsay, 1949; Salm, 1944). When found in the vagina these organisms are usually simple contaminants. Ramsay (1949) reported an incidence of severe Clostridial infection in eight of 1,430 cases of septic abortion during a 10-year period. The incidence of severe post-abortal gas gangrene in Australia appears to be higher. Hill (1936) gave an incidence of twenty-two cases among 3,049 women admitted to the Women's Hospital, Melbourne, over a two-year period. Over that same period there were eight cases of severe puerperal sepsis.

Pathogenesis
Russell and Roach (1939) postulated that the following factors were necessary for the development of clostridial uterine infection.

(i) The organism must be introduced into the uterus from without, or in rare instances the organism already present in the vagina or cervix must be carried into the uterus.

(ii) Dead tissue must be present at the time the organisms are introduced.

(iii) The injured tissue, or pabulum must remain in the uterus for a sufficient time to permit incubation of the organisms.

(iv) Damaged maternal tissue must be exposed to the bacteria.

Clinical Description
Once clinical infection of the uterus has occurred, the disease is frequently classified as to the extent of tissue involvement. There have been many classifications (Bysshe, 1938; Doehner, Klinges and Pisani, 1960). Russell and Roach (1939) classified the infection into the following categories:

(i) Local clostridial infection.

(ii) Emphysema of the uterine wall.

(iii) Bacteraemia
    (a) Generalised septicaemia
    (b) Metastatic Clostridial infection.

(i) Local infection. Here the infection is limited to the uterine contents and superficial layers of the decidua. The majority of these cases are mild, and with cleansing of the uterine cavity the prognosis is usually good. However, Hill (1936) states that occasionally severe infection occurs associated with intravascular haemolysis. Russell and Roach (1939) have found that physometra may be present in these

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cases but is largely a matter of obstructed drainage.

(ii) Emphysema of the uterine wall. Gas formation in the uterus is associated with severe endometritis, myometritis, and frequently peritonitis. These patients are usually very ill and present a similar clinical picture to that of generalised septicaemia. Blood culture is usually positive. There is tenderness in the lower abdomen and the uterus is often enlarged and sensitive to pressure. Crepitus of the uterus may be found on manipulation. Localised peritonitis when present is associated with lower abdominal distension, rebound tenderness, and absent or tinkling bowel sounds.

Heim (1933) claims that if there is no evidence of peritonitis the infection is probably limited to the uterine contents and superficial layer of the decidua.

(iii) Bacteraemia. Generalised septicaemia is characterised by shock, acute haemolysis, jaundice, and usually a fatal outcome. Septicaemia is rare in other forms of Clostridial infection. Some patients survive the acute haemolytic phase and develop acute renal failure.

Mahn and Danuono (1955) gave an excellent description of this condition. Symptoms developed within forty-eight hours after septic abortion in 85.3% of their 75 cases and in the more acute cases within twenty-four hours. Rigors, vomiting and diarrhoea characterised the onset, and was rapidly followed by a subnormal temperature, hypotension and tachycardia. All cases developed jaundice which gave the skin a bronzed or occasionally greenish appearance. The urine was mahogany coloured. In 94.6% of cases the urine output fell to less than 200 ml. daily. The mortality in their series was 73.3/%, 9.4% dying within twenty-four hours of the onset of symptoms. The main causes of death were acute renal failure and cardiovascular collapse. Generalised peritonitis was present in 5.5% of these fatalities.

Metastatic gas gangrene is rare, and the course rapidly fatal. Localised abscess formation is followed by rapid collapse and death.

Investigations

In the severe cases, acute intravascular haemolysis is associated with a rapidly falling haemoglobin, bilirubinaemia, haemoglobinemia and methaemalbuminaemia. The urine contains an excess of urobilinogen and free haemoglobin. Except for the mildest cases there is a polymorphonuclear leucocytosis, the neutrophils showing a shift to the left and degenerative changes. Mahn and Danuono (1955) state that the changes in the blood picture appear early, often before the blood cultures become positive.

Bacteraemia may be associated with infection of the decidua, uterine muscle or peritoneum. The recovery of clostridial organisms from the blood stream, as stressed by Hill (1936), does not constitute clinical infection unless associated with other features of the disease, since they may be recovered following abortion or curettage in non-suspect cases.

Cultures of products of conception, uterus, swabs from the cervical canal or even the urine may be positive for Clostridia, but on occasions bacteriological proof is not obtained and diagnosis can only be made on the overall clinical picture.

Doehner, Klinges and Pisani (1960) stress the use of lower abdominal X-ray for detection of uterine emphysema. They describe a case in which the diagnosis was made on X-ray before the condition was suspected clinically. The gas was arranged in an onion-peel fashion within a mass which probably represented the uterus.

We now report three cases of uterine clostridial infection treated with hyperbaric oxygen.

Case Histories

Case No. 1

Patient, 21 years, had a lower segment Caesarian section for disproportion following a trial of labour lasting ten hours. Twenty-four hours later she became drowsy with a temperature of 104°, pulse 150/min. There was no abdominal tenderness and no vaginal loss. Culture of a high vaginal swab yielded a pure growth of Clostridium Welchii. Intramuscular soluble penicillin and polyvalent anti-gas gangrene serum was given. The temperature fell to normal over the next few days. At no time was there any evidence of intravascular haemolysis or clostridial septicaemia, two blood cultures being sterile. She was discharged 15 days after admission, and at this time the high vaginal swab was sterile on culture.

The week following discharge, she suffered from increasing aching of the left groin which radiated down the left leg and was associated with attacks of numbness. On the day before admission to the hyperbaric oxygen unit she suddenly developed stabbing pain on the right side of her chest; there were no other symptoms.

On admission she looked pale and toxic. Temperature 100.4°, pulse 84/min. blood pressure 130/80 mm.Hg. Nothing abnormal was detected in the respiratory or cardiovascular systems. The uterus was palpable one inch above the symphysis pubis. On vaginal examination the uterus was enlarged but not tender. There was a slight blood-stained, non-foul-smelling vaginal loss. The left leg was swollen with erythema of the skin surrounding a nodular, tender long saphenous vein for six inches below and up to the saphenous opening. Arterial pulses were normal. A diagnosis was made of pelvic thrombo-
Tuberculosis with extension down the long saphenous vein, complicated by pulmonary embolus.

Treatment was started with intramuscular penicillin and ampicillin. High vaginal swab yielded a heavy growth of "toxigenic Clostridium Welchii", a moderate growth of coliforms and Streptococcus faecalis.

In view of the patient's toxic condition and the culture result, she was given a total of fourteen hours hyperbaric oxygen therapy over the next seven days. Her condition improved after four hours therapy but she continued to run a hectic temperature, ranging between 100° and 104° over the next three days. Four days after admission she experienced a further attack of chest pain. Anticoagulant therapy was started but had to be discontinued after a bout of haematuria and detection of blood in the stools. Five days after admission her condition had improved and toxoaemia had subsided. Vaginal swab taken six days after admission grew only occasional coliform organisms; other investigations included three chest X-rays all of which were normal, and two negative blood cultures.

Comment: Thrombophlebitis is only rarely associated with Clostridial infection, but was mentioned by Toombs and Michelson (1928). They commented that the infection spread by way of the veins and was accompanied by frequent chills. The frequent occurrence of anaerobic streptococci in their cases seemed to throw doubt on Clostridia being the causative agent. Bornstein, Weinberg, Swartz and Kunz (1964) commented that the vagina, uterus and contiguous structures were frequent sites for bacterioides and anaerobic streptococcal infections and that these were often complicated by thrombophlebitis, septicaemia and metastatic pulmonary abscesses. In this case, the main infective organism was Clostridium welchii and it is probable that the infection was partially suppressed by the initial therapy. The attacks of chest pain were presumably due to emboli arising from pelvic veins; it is unlikely that these were septic.

It is doubtful whether hyperbaric oxygen had any therapeutic value in this case but might have stopped the development of clostridial septicaemia.

Case No. 2

Patient aged 24 years in the last trimester of pregnancy was admitted with a septic abortion. She gave a history of vaginal bleeding and lower abdominal pain for twelve hours prior to admission; no foetal parts had been noted.

On admission she was in pain but not shocked. The uterus was enlarged to the size of 28 weeks pregnancy and was tender and firm in consistency. Bowel sounds were present; foetal heart sounds were not heard. On vaginal examination the bag of membranes filled the vagina and ruptured during examination, there were lacerations of the vaginal wall close to the vault. She was given blood and started on a course of tetracycline. Later that day the foetus was delivered spontaneously but the placenta was retained. Following this, she became pyrexial, and developed generalised peritonitis, and her urine output was retained. Cecal perforation was noted over the previous twenty-four hours. High vaginal swab grew Proteus and Clostridium Welchii. She was started on intramuscular soluble penicillin and transferred the following day for renal dialysis. On transfer, the blood pressure had fallen to 95/50, pulse had risen to 124/min., and she was jaundiced. The abdomen was distended; the uterus was palpable to the level of the umbilicus and no bowel sounds were heard. HB had fallen to 4.5. On admission to 5.9, the blood urea was 255 mg. %. She was treated with cephaloridine and polyvalent anti-gas-gangrene serum, and on this therapy she became apyrexial within 48 hours. Peritoneal dialysis was commenced two days after her admission. Three days after admission E.U.A. revealed lacerations of the fornices and posterior vaginal wall, the cervix was ragged and necrotic. A foul smelling necrotic placenta was removed which grew coliforms and Clostridium Welchii. Two days post-operatively crepitus was felt over the anterior abdominal wall and she lapsed into coma. Three days post-operatively she started to have major epileptic seizures which were controlled with paraldehyde; she was given artificial respiration and transferred that evening for hyperbaric therapy.

She was admitted to the hyperbaric unit unconscious with a blood pressure 70/30, pulse 120/min. and temperature 101.6°. A total of 13 hours hyperbaric therapy was given over the following 42 hours. During the first five hours therapy she had several epileptic attacks followed by some clinical improvement. After 13 hours therapy repeated epileptic attacks developed, with deepening unconsciousness. It was decided that no further benefit could be obtained from hyperbaric therapy and she was transferred back to the hospital she came from; where she died in coma two hours later.

Necropsy. The uterus contained numerous gas-filled cavities and the veins in the cervical portion were thrombosed. The infection was most advanced at the fundus, where the muscles were necrotic and liquified. Generalized peritonitis was present with bilateral subphrenic abscesses. There was no direct communication between the peritoneal cavity and the vagina, or uterine cavity. A few pneumococci only were cultured from the uterine wall. The kidneys showed tuberculous necrosis. The brain showed marked congestion of the meninges, but no meningeal infection or brain abscesses.

Comment. This patient had severe clostridial septicaemia following septic abortion. The placenta was retained for four days. Two blood cultures were positive for Clostridium Welchii. Abortion was inevitable, and evacuation of the uterus on admission would have been preferable. Clostridium Welchii would probably have been isolated from the uterus at this time and the patient could then have been transferred to a hyperbaric unit. Should oliguria have developed an acute renal failure regime could have been instituted concurrently with a course of hyperbaric oxygen. No clostridia were cultured.
after the course of hyperbaric oxygen therapy and this patient’s life might have been saved if therapy had been given earlier.

The factors producing the epileptic attacks are of interest; they were unlikely to be due to uraemia since the blood urea was 145 mg/100 ml at the time. In spite of peritoneal dialysis the blood pH continued to fall from 7.42 on admission to 7.075 at the time of onset of the fits. In addition, the blood sugar rose from 112 on admission to 1200 mg/100 ml on the day before and the day of onset of the seizures and had fallen to 520 on the day before death. Wynn (1965) thought that the hyperglycaemia was most probably due to a high sugar concentration in the peritoneal dialysis, absorption being facilitated by an inflamed peritoneum. The other possibility was a diabetic acidosis triggered off by severe infection. The hyperglycaemia and acidosis could have been the cause for the epileptic seizures. Maccario, Messis and Vestola (1965) suggest that hyperglycaemia may produce seizures by a combination of hyperosmolarity and a direct toxic effect.

Case No. 3

Patient aged 24 years and 22 weeks pregnant douched herself with carbolic soap in order to induce an abortion. She was admitted to hospital on the same day and the next day she aborted spontaneously and completely. At the time of abortion she became shocked, B.P. falling to 80/50 mm. Hg., and was noted to be jaundiced. The serum contained methaemalbumin and the urine free haemoglobin. A diagnosis of Clostridial infection was made and she was treated with antitoxin and intramuscular penicillin. *Clostridium Welchii* were subsequently cultured from the high vaginal swab, placenta, foetus and blood. She was transferred for hyperbaric therapy on that day.

On admission she was pale, toxic and slightly jaundiced. Her temperature was 95°, pulse 146, B.P. 90/60 mm. Hg. There was a tender rounded mass rising out of the pelvis reaching to two inches below the umbilicus. The rest of the lower abdomen was tender but there was no rebound tenderness and gut sounds were present. It was noted that she had only passed 2 ml. of urine since her abortion about six hours previously.

Over the next 48 hours she was given a total of 12 hours hyperbaric therapy. After four hours therapy she was no longer toxic and her pulse rate had fallen to 100/min. The pelvic swelling remained, but the rest of the lower abdomen was no longer tender. On the second day following abortion she was returned to the hospital from which she came and a total hysterectomy and left salpingo-oophorectomy was performed. The uterus showed the typical yellowish-green tinge of clostridial infection and the left tube and ovary were black and gangrenous. (See Fig. 1 and 2). She remained oliguric, and the blood urea had risen from 78 on the day of abortion to 408 mg/100 ml. She was transferred for haemodialysis and received five haemodialyses over a period of eight days. The patient was oliguric for 21 days and it was a further 28 days before the blood urea had fallen to 82 mg/100 ml. She was discharged home on furadantin, oral iron, and a low protein diet.

She was seen as an out-patient three months after admission when she felt quite well, but her blood urea was still raised to 73 mg/100 ml.
Comment. This case was a typical example of Clostridial septicaemia. The response to hyperbaric oxygen therapy was dramatic and probably saved her life. This patient would have subsequently died, however, from renal failure had it not been for haemodialysis. The persistently raised blood urea and slow return of renal function probably was due to residual vasomotor disturbance. (Finckh, 1962; Finckh, Jeremy and Whyte, 1962).

Diagnosis

Certain clinical features would make one suspect clostridial uterine infection in a pregnant or post-abortion woman. Uterine infection may not at first be obvious and post-abortion cases often deny interference.

Rapidly developing jaundice is characteristic of severe clostridial infections and is associated with a rapid pulse, low blood pressure, increasing pallor, mental clarity and restlessness.

The onset may be characterised by severe uterine or muscle pain and shock for no obvious reason; or the patient may collapse suddenly with no evidence of a cerebral, pulmonary, cardiac or intra-abdominal cause. In severe cases intramuscular haemolysis is common. If the diagnosis is kept in mind, no other condition produces such a characteristic clinical picture.

Blood and tissue cultures confirm the diagnosis.

Early diagnosis is essential and treatment should be started as soon as the condition is suspected.

Penicillin is the drug of choice for clostridial infections and should be given with ampicillin to counteract the gram negative organisms which are so frequently present, Brummelkamp, Boerema and Hoogendyk (1963) advocate deferment of operation until after a course of hyperbaric oxygen therapy. This is perhaps safe in open wounds where the extent of infection is obvious, but for internal infections such as those of the uterus, we feel it is wiser to remove the septic focus by currettage or removal of the foetus and placenta. Cases with severe toxæmia and shock should receive sufficient hyperbaric oxygen to eliminate the toxicity; followed by operation. Hysterectomy may be necessary if the uterine wall is badly infected.

The value of antitoxin in cases of gas gangrene infection has been questioned. It appears to have a place in prophylaxis (MacLennan, 1962), but as MacLennan states it is probable that the toxæmia of gas gangrene is not directly due to the dissociation of toxins. It is unlikely that antitoxin would have effect upon gangrenous areas since they would be inaccessible to circulating antitoxin; it may, however, have effect in cases of clostridial septicaemia. We therefore recommend that polyvalent clostridial antiserum should be given unless the patient can be immediately admitted to a hyperbaric unit. Hyperbaric oxygen dramatically arrests the severe toxæmia and shock so frequently present with clostridial myonecrosis and/or septicaemia. It is unlikely that high pressure oxygen can reach necrotic muscle and therefore it should be used as an adjunct to surgery. Brummelkamp (1964) places his patients in a hyperbaric chamber in which the atmospheric air is compressed to a pressure of three atmospheres absolute. Once at this pressure the patient begins to breathe oxygen through a mask. The total treatment consists of seven two-hourly sessions over a course of three days. He states that toxæmia generally subsides after six hours therapy. We use 100 per cent oxygen at 2.5 atmospheres absolute, the patient being treated in a single-person, transparent chamber. Two-hourly sessions are given and if necessary the patient is decompressed for only half an hour before having further therapy. We have found that severe cases of clostridial infection often require two to four hours high pressure oxygen therapy in order to get them fit for operation. Hyperbaric therapy can then be resumed post-operatively; the total period of therapy generally varying between 12 and 16 hours.

These patients are frequently restless and may need sedation prior to therapy; the only other complication has been earache on compression—this generally subsides if the pressure is kept steady for a few minutes before resuming pressurisation. The eardrums should always be inspected prior to compression. One hundred per cent oxygen under pressure has the advantage over compressed air in that the patient can be decompressed within twenty seconds in an emergency. In compressed air chambers, slow decompression is necessary because of the danger of nitrogen toxicity to the attendant staff.

We do not give blood in the presence of intravascular haemolysis. We have already mentioned that toxæmic shock responds to high pressure oxygen therapy. Haemorrhagic shock should be treated with blood or plasma infusion; rapid correction may prevent onset of renal failure. We do not use hypertensive agents to raise blood pressure, since they produce vaso-
constriction in the infected area (Brummelkamp 1964) and phenylephrine is known to decrease renal blood flow. (Crosley, Clark and Barker, 1951).

Acute renal failure is a frequent complicating factor and must be detected early. At the onset of oliguria an acute renal failure regime should be instituted for twenty-four to forty-eight hours whilst the patient receives hyperbaric oxygen and surgical treatment. Deterioration in patients with renal failure is rapid and peritoneal dialysis or haemodialysis should be started as soon as possible. It is possible to intermit dialysis with hyperbaric therapy if the necessity arises. The advantages of peritoneal dialysis compared with the artificial kidney are that it is simpler, abrupt changes in blood volume can be avoided, and it is easier to correct disturbances of electrolyte or water imbalance. Unfortunately, this method cannot be used when there is peritoneal sepsis or there has been a recent intraperitoneal operation. (Boen, 1961).

**Conclusion**

Three cases of clostridial infection of the uterus have been described.

Rapid diagnosis and correct therapy in logical sequence are the only way to decrease the mortality of clostridial uterine infections. Hyperbaric oxygen therapy is indicated in all severe cases of clostridial infection and dramatically relieves toxæmia and septicæmic shock. This form of therapy cannot remove necrotic tissue and should be used in conjunction with surgery. Necrotic tissue and infected uterine contents should be removed as soon as possible. When the patient’s condition is critical a course of hyperbaric oxygen therapy should be given prior to any operative procedure. Penicillin and ampicillin should be given from the beginning; mixed clostridial antitoxin is unnecessary unless hyperbaric oxygen therapy is not immediately available; under these circumstances it should be given as an interim measure.

Acute renal failure is a frequent complication and generally requires haemodialysis or peritoneal dialysis; rapid diagnosis and institution of correct therapy should diminish the mortality from this condition.

With greater availability of hyperbaric oxygen units prophylactic therapy may be indicated in cases where conditions known to predispose to clostridial infection are present.

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