CLOSTRIDIUM WELCHII INFECTION IN GYNAECOLOGY*

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Although *Bacillus welchii* is a rare cause of postabortal or puerperal infection, the dramatic course and high mortality are of paramount importance to the gynaecologist or obstetrician. The most important determining factor in the production of an actual infection would seem to be the presence of traumatized or dead muscle tissue, which augments enormously the pathogenicity of the organism. The majority of serious puerperal infections therefore follow criminal abortion or traumatic operative delivery.

Incidence

Clostridium welchii is a normal inhabitant of the intestinal tract of humans as well as the lower mammals. It is therefore abundantly present in soil, and has indeed often been found in the floordust of the labour ward and on the hands of attendants.[1] It is reported to be present in the vagina of 5% of healthy women: Sadusk and Manahan[2] isolated the organism in 9·1% of their patients.

In a survey conducted at the Karl Bremer Hospital in 1963, *Cl. welchii* was found to be present in cervical smears in 8·9% of 115 patients seen over a period of 3 weeks at the gynaecological outpatient department.

It is quoted in the literature to be the causative organism in 2% of puerperal infections.

Bacteriology

The *Bacillus welchii* (*Clostridium perfringens*, Gas-bacillus) was isolated in 1891 by Welch. It is approximately 5 $\times 1{\cdot}3\mu$ in size, with centrally situated oval spores in short, non-motile and encapsulated Gram-positive rods. It is a saccharolytic and proteolytic anaerobe, fermenting sugars to produce an inflammable mixture of carbon monoxide. carbon dioxide and hydrogen. Cultured anaerobically in milk it gives the well-known 'stormy fermentation or clot' by disruption of the coagulate, plastering it against the sides of the tube. It thrives on dead, necrotic lacerated tissues.[3]

Pathology

B. welchii causes necrosis of tissues with rapidly spreading oedema. Its action is essentially saccharolytic and the damaged tissues are then invaded by putrefactive organisms resulting in true gangrene.[4]

Gas-gangrene is described as a clinical entity and not a specific disease by Boyd:[5] its cause is a particular opportunity rather than a particular infection. The opportunity is lacerated tissue, especially involved muscle which would be grossly swollen, pale and inelastic, but would change colour to brownish red, when gas bubbles would appear and the consistency become puttylike. When putrefaction is added to gas formation, the tissues become green or black and the part crackles on palpation. The smell is that of a corpse. Placental tissue obtained at curettage is usually a grey, soft, friable paste, sponge-like in character.

At postmortem 1 or more of the following features may be found.

1. Peritonitis with bloodstained fluid in the abdominal cavity.

2. Pulmonary oedema with fluid in the pleural cavity.

3. The typical signs of cardiac failure and other evidence of septicaemia such as a 'septic' spleen.

4. Gross suprarenal haemorrhage has been found which seems to support the view of some that the shock in *B. welchii* infection resembles closely the picture found in the adrenal-insufficiency syndrome of Waterhouse Friederichsen.

5. A haemorrhagic necrosis can be found in various organs and the acute tubular necrosis may be the reason for renal insufficiency seen in these cases.

6. Where the shock has been of the irreversible type, there may be bilateral renal cortical necrosis as a result of the ischaemia, secondary to the shock.

Pathogenicity

B. welchii was the cause of 75% of gas-gangrene in World War I when it led to the concept of surgical debridement. The clinical features are largely due to the effects of 2 of the toxins which it produces; a myotoxin which causes disintegration of protein with gas production and a haemotoxin which destroys red blood cells. Different series in the literature illustrate its pathogenicity in the gynaecological field: (Toomb and Michelson, in 1928, in England, in a series of 45, had 50% mortality;[6] Hill, in 1936, in Australia, in a series of 30, had 63% mortality;[1] Kadner and Anderson, in 1950, in America, in a series of 31, had 55% mortality;[7] and Mahn, in 1955, in Chile, in a series of 75, had 73% mortality.[8])

Butler[9] investigated the virulence of *B. welchii* and found over 600 strains of clostridium, though only 5% produced severe infections.

In our series of bacteriological cultures done on the curettings of 164 incomplete abortions we found 85 cases where no cultures were obtained, and 79 from which mixed flora were cultured (including 17 that also showed a positive *Cl. welchii* culture). The occurrence of the organisms cultured is compared with a comparable series from the Sloane Hospital in New York where Negroes represent approximately 72% of all admissions, compared to the 70 - 75% of Coloured admissions at the Karl Bremer Hospital.

Karl Bremer Hospital (164 cases)		*Sloane Hospital* (251 cases)	
E. Coli	34	Enterococci	66
Cl. welchii	17 (10·3%)	E. Coli	60
Enterococci	16	Staph. aureus	32
Klebsiella	16	Bacillus proteus	24
Paracolon	11	Staph. albus	23
Alpha-haemolytic Strept.	8	Strept. viridans	21
Staph. aureus	8	Diphtheroids	12
Prot. mirabilus	7	Streptococci	11
Beta-haemolytic Strept.	5	Anaerobic Strept.	3
Candida	2	**Cl. welchii**	3 (1·2%)
Pseudomona aeruginosa	2	Paracolon	3
		Klebsiella	3

CLINICAL PICTURE

Cl. welchii has often been cultured in cases where it was of no consequence, but true infection with the organism produces a most serious condition.

Hill, in one of the best known studies available,[1] divided his cases into postabortal and puerperal series and recorded respectively in each series a mortality of 59% and 75%. He described 4 main clinical types: (1) cases with marked jaundice and gross blood destruction, (2) cases with jaundice but lacking serological or urinary evidence of blood destruction, (3) meta-

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static gas-gangrene, and (4) miscellaneous and presumptive cases.

Douglas *et al.*,[10] in a much later study, grouped the clinical forms as follows:

1. *Cl. welchii* in the vagina with no signs or symptoms of infection.
2. Localized uterine infection in the form of endometritis.
3. Pelvic and peritoneal spread where a parametritis with or without gas formation existed.
4. Bloodstream infection: (*a*) bacteraemia, (*b*) septicaemia, and (*c*) metastatic gas-gangrene.

The clinical picture of *Cl. welchii* infection is very characteristic. After an abortion, especially when criminally induced, the onset of fever, chills and lower abdominal pain, often associated with vomiting and occasionally diarrhoea, herald the onset of this syndrome, which develops with amazing rapidity in 2 - 3 days.

The pulse rate is disproportionally rapid in relation to the fever—usually 110/min. or faster—with a low pulse pressure and a temperature of 100 - 101°F. The blood pressure is often found to be in the region of 70/50 mm.Hg.

As a result of haemolysis, jaundice develops early—particularly of the face and torso and less on the arms and legs. Because of the concurrent vascular collapse, cyanosis becomes apparent—more easily observed in the peripheral parts of the extremities. The conjunctiva turns to a chocolate colour, the skin to a bronze colour, the urine to a portwine colour, and the blood serum to a typical Burgundy colour. The patient has cold, clammy extremities, superficial breathing, and is extremely restless but usually mentally alert—as so aptly put by Stallworthy 'with the imminence of death the eyes still bright and the mind fully conscious'.[11]

These symptoms of haemoglobinaemia and haemoglobinuria, jaundice and rapidly progressive anaemia in a postabortal patient who appears seriously ill, are almost pathognomonic of *Cl. welchii* infection.

COURSE AND COMPLICATIONS

The entire process may develop so rapidly that the patient goes into peripheral circulatory failure, cardiac and renal failure with pulmonary oedema, and subsequent death within hours.

1. *Acute Renal Insufficiency*

Postabortal oliguria is sometimes very prominent. O'Donell,[12] reporting on 19 such cases, concluded that the renal failure may depend on a nephrotoxic substance liberated from dead or dying placental tissue which initiates renal ischaemia. He did not, however, implicate *Cl. welchii*. In the largest single series of 22 cases (reported by Hill), renal failure occurred in 5.

Woodard[13] and a number of other authorities hold the view that the acute renal insufficiency seen in *Cl. welchii* septicaemia is secondary to acute tubular necrosis.

2. *Secondary Anaemia*

This develops rapidly owing to haemolysis. Cases have been recorded[3] where the red-cell count fell by over 2 million/ml. within the course of 6 hours.[27] Ictero-cyanosis can mask the anaemia clinically and a red-cell count alone can demonstrate it and reveal the degree thereof.

3. *Afibrinogenaemia*

Afibrinogenaemia has been reported by Lutz,[14] and may well explain the haemorrhagic phenomena encountered. The mechanism is uncertain: Pritchard[15] believed it to be a result of liver damage from haemolysis; Clark and Ellison theorized that it may be due to a thromboplastin-like substance released from the decidua; and Shinowara[16] mentioned the theory of intravascular clotting caused by a lipoprotein isolated from the erythrocyte fraction of blood, which he called thromboplastin-cell component.

4. *Metastatic Gas-gangrene*

Although a rare type, this should also be mentioned. The myotoxin of the *Cl. welchii* is probably the causative factor, and the onset of excruciating pain in distant muscles heralds this phenomenon.

The course of the disease depends on the clinical type and complications. However, although initial shock, cardiac failure and septicaemia may be vigorously combated, the patient may still die several days later from irreversible renal damage.

The average survival period in the series of Hill was 6 days—the longest 9 days and the shortest 16 hours after interference. Fortunately modern concepts in treatment have improved the prognosis.

DIAGNOSIS

If the above symptoms present in any postabortal or puerperal patient, they should arouse suspicion of a *Cl. welchii* infection.

1. Laboratory investigations can be time-consuming, and since good results depend on early treatment, a clinical diagnosis is as essential as is the early institution of specific therapy.

2. A cervical Gram-stained smear revealing classic Gram-positive rods, is almost conclusive proof.

3. Aerobic and anaerobic cultures must be undertaken in all suspected cases.

4. Culture of, and sensitivity tests on, swabs from the cervical canal and products of conception should be routine procedure in all cases of abortal and puerperal sepsis.

5. Bilirubin and serial blood-urea estimations should be done.

6. Blood count and especially a white-cell count is of value. Ramsay[17] states that the white-cell count usually tends to be over 15,000 in *Cl. welchii* infection, while infection with other organisms invariably result in lower counts.

7. X-ray examination may diagnose metastatic gas formation or physometra, although it is rare to detect gas in tissues during life.

THERAPY

Early vigorous therapy is essential.[18] A regime of treatment providing for electrolyte disturbance, shock and infection is called for. Blood replacement is usually imperative and it should be borne in mind that the differential diagnosis between septicaemia and blood-transfusion reaction is sometimes difficult: positive blood cultures and vaginal cultures will help to differentiate this.

Antibiotics

These should be administered intravenously, and most authorities recommend a combination of broad-spectrum antibiotics including streptomycin, chloramphenicol and erythromycin.

In the survey conducted at the Karl Bremer Hospital, it was found that *Cl. welchii* was sensitive to the antibiotics tested, as follows: chloramphenicol 16, erythromycin 15, tetracycline 12, penicillin 10, novobycin 4, and streptomycin 2.

Chloramphenicol should be administered in doses up to 4 G daily and penicillin up to 10 million units daily. In renal failure not more than 3 G of chloramphenicol should be given daily.[26, 27]

Steroids

The use of corticoids is controversial. One hesitates to give them in overwhelming septicaemia, but for the peripheral vascular collapse, the use of corticoids may be an important adjuvant. The tendency seems to be towards massive dosage, and cortisol in doses up to 500 mg. daily is advocated. The patient should be 'weaned' from the corticoids, gradually at the end of therapy. Madsen and Tieche[19] advise:

Solucortef 300 mg. intravenously, *stat.*
Solucortef 200 mg. 6 hourly, first day.
Solucortef 100 mg. 6 hourly, second day.
Solucortef 100 mg. 8 hourly, third day.
Solucortef 100 mg. 12 hourly, fourth day.
Medral 4 mg. 6 hourly, fourth day started, and
Medral by 2 - 4 mg. per day, decreased.[29]

Pressor Agents

Blood pressure should be restored to levels high enough for adequate renal function. 'Neosynephrine', 'levophed' or 'aramine' may be used. Neosynephrine, 20 - 100 mg. per 500 ml. of 5% aqueous dextrose solution is used by Madsen and Tieche.[19]

Blood Replacement

Blood in the form of packed red cells is preferable. Fresh blood is best since it minimizes the extracellular potassium administration which is concomitant with the use of stored citrated blood.

Antitoxin

The dosage and use is also controversial, but in suspected cases it should be used in high concentration—100,000 units daily being the recommended dose.[21, 28]

Electrolyte Balance

This should be maintained at all costs and extracorporeal haemodialysis can be life saving.[19, 20] The urinary output should be accurately measured. Three litres of intravenous fluid can be allowed in 24 hours, unless renal shutdown is suspected, in which case 400 ml. should be allowed for insensible loss and the volume of the urinary output added.

Surgical Therapy

Evacuation of products of conception from the uterus is advised under cover of antibiotics.[20, 21] No particular time limit is proposed for emptying the uterus. Curettage, if indicated, is performed where possible when the patient is relatively afebrile. There seems to be a tendency in the recent literature towards advising early emptying of the uterus even if the patient is still febrile.[22-24]

Even more radical surgery in the form of hysterectomy and bilateral salpingo-oophorectomy is strongly advised in the appropriate cases.[25]

High-pressure Oxygen Therapy

With the advent of this new concept it seems as if we are on the threshold of a vast new field in the therapy of *Cl. welchii* infection. At present the lack of facilities will limit the practical appliance, but in the not too distant future the provision of adequate recompression chambers will surely be provided for. 'Flooding the anaerobic phlegmon with plasma containing oxygen at a high partial pressure makes for cessation of the growth of the anaerobic organisms within the tissues able to be reached by this plasma'.[30] Of the 6 cases with surgical gas-gangrene resulting from *Cl. welchii* so treated at the Karl Bremer Hospital, only 1 patient did not survive and died of bronchopneumonia. The wound in this last case, however, had healed. Although the clinical experience in so limited a number of cases is difficult to evaluate, experimental work seems to justify the optimism with which this new development is regarded.

It should be emphasized that the more vigorous the therapy, the less will be the chance of a catastrophe.

SUMMARY

The incidence, bacteriology, pathology, pathogenicity, clinical picture and current treatment of gynaecological *Cl. welchii* infection are briefly summarized.

A survey is presented of the prevalence of *Cl. welchii* cultured in cervical smears and uterine curettings of incomplete abortions at the Karl Bremer Hospital during 1963, stressing the 10·3% incidence and the marked sensitivity to chloramphenicol.

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