# THE MECHANISM OF DEATH IN, AND THE TREATMENT OF, SEPTIC ABORTION

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The tragedy of maternal deaths is steadily decreasing and sepsis in institutional confinements is a very slight factor. In Cape Town, in 1960, maternal deaths in obstetrical institutions under the control of the University of Cape Town were 8, and sepsis was a factor in 1 case.[1] In 1961 there were 12 maternal deaths, none of them due to sepsis. In 1962 there were 7 maternal deaths and in only 1 was sepsis a factor. These figures agree with a world-wide tendency—puerperal and intrapartum sepsis is no longer the dreaded cause of death that it used to be. On the other hand, a review of the deaths in the Department of Gynaecology at Groote Schuur Hospital during the period January 1960 to March 1963 indicate that 13 followed abortion (in which sepsis was an important factor) out of 63 from all causes. Because sepsis was a major factor, a critical analysis was made retrospectively to determine all the causative factors that culminated in the deaths of these patients. At the same time, an assessment of the treatment of such cases has been made. Thirteen cases are reviewed.

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## REVIEW OF CASES

### *Method of Induction*

It is very difficult to obtain an admission of 'induction' of abortion from a patient. This statement is endorsed by Woodard,[2] who analysed a large series. In only 4 of the 13 was an admission of interference obtained and even then the

evidence was doubtful. The interference took the following forms:

(*a*) Taking 'Wonderkroon' and herbs, followed by a hot bath.
(*b*) Syringing with an unknown material.
(*c*) Syringing with a sodium bicarbonate solution.
(*d*) Self-inducement with fingers (doubtful).

In another case the deceased patient's employer said her maid was visited by a midwife friend.

*Clinical Syndrome*

Unfortunately, no figures were available to indicate the time period between the interference and the admission to hospital. The gestational age of the pregnancies was between 7 weeks and 20 weeks, with an average of 13 weeks. Six of the 13 patients were pulseless and of the remaining 7, 5 had pulses of over 120 beats per minute on admission.

General abdominal tenderness was noted in 4 patients.

All these patients appeared extremely ill on admission. Eleven of the 13 were severely shocked, with blood pressures below 80 systolic, and in 6 blood pressures were unrecordable. Of the remaining 2, 1 died one hour after admission and the other collapsed and died after the expulsion of the foetus.

The haemoglobin was above 10 G. per 100 ml. in 9 patients. Of the 4 who had haemoglobin readings under 10 G. per 100 ml., in only 1 the haemoglobin was very low, i.e. 4 G. per 100 ml. In the other 3 the readings ranged between 8 and 10 G. per 100 ml. The patient with the haemoglobin of 4 G. per 100 ml. had been bleeding for 7 days after the passage of the foetus.

Oliguria was recorded in 5 of the 13 patients.

In view of the high haemoglobin estimations and the low blood-pressure readings, it appears that haemorrhage is not the most important factor in causing the shock and often the death of these patients. Septicaemia is probably a more important factor, and the terms vasogenic, septic or bacteraemic shock have been applied to such cases. The most important sign of incipient shock following infection is the insidious drop in blood pressure. Obviously, in established septic shock the blood pressure has already dropped.

*Postmortem Findings*

Postmortem data were sorted, and the following pertinent factors emerged:

1. 3 patients had perforations of the uterus.
2. 7 patients had peritonitis. In 5 of these there was blood-stained fluid in the abdominal cavity.
3. 4 patients had pulmonary oedema.
4. 6 patients had fluid in the pleural cavity.
5. Renal damage was found in 3 patients; in 1 it was reported as necrosis of the convoluted tubules.

In 1 patient features typical of cardiac failure were found.

In 4 of the 10 patients in whom septicaemia was diagnosed, *Clostridium welchii* were isolated. Other organisms isolated included *Staphylococcus aureus* on 2 occasions and coliforms on 1 occasion.

Of the remaining 3 patients in whom septicaemia was not diagnosed, 1 had features of cardiac failure, in another pulmonary infarction was diagnosed and in the third retroperitoneal blood clots amounting to 350 ml. were found. This last-mentioned patient was put on a pitocin drip and collapsed immediately after expulsion of the foetus.

It is interesting to note that in 1 patient gross bilateral suprarenal haemorrhages were found together with other evidence of septicaemia such as a septic spleen. This finding supports the view of certain people[3] that bacteraemic shock resembles closely the picture in the adrenal-insufficiency syndrome, or Waterhouse Friderichsen syndrome. This may be the pathogenesis of septic shock, although it has been demonstrated that a normal cortisol level exists in these shocked patients. It may well be that this picture of adrenal haemorrhages represents the extreme of the septicaemic picture.

MECHANISM OF DEATH IN SEPTIC SHOCK

Bacillary septicaemia with acute peripheral vascular collapse and renal shutdown is usually secondary to infection by bacteria of any of the three groups of *E. coli, Pseudomonas aeruginosa* and *Proteus vulgaris*. The organisms liberate a powerful endotoxin, which may cause profound vasomotor collapse, renal failure with marked metabolic acidosis, and haemorrhagic necrosis in various organs. The clinical syndrome is manifested by shock (*not accounted for by blood loss*), tachycardia and, possibly, acute pulmonary oedema or a haemorrhagic diathesis. That the acute renal insufficiency seen in *Cl. welchii* and *E. coli* septicaemia is secondary to acute tubular necrosis, according to Woodard,[2] is a view held by a number of authorities.

Septic shock is a potentially lethal complication in patients with severe bacterial infections. Weil and Spink have reported a 65% mortality in 43 such cases.[4] The exact mechanism of the shock, which usually occurs 8 – 36 hours after the onset of fever, has not been fully elucidated.[5]

Weil and his associates[6] have shown that shock produced in dogs by the injection of endotoxin is due largely to diminished cardiac output and is not related to loss of arteriolar tone or diffuse injury of the capillary bed or primary failure of the myocardium. Endotoxin injection causes obstruction to venous outflow from the liver, resulting in portal hypertension and pooling of blood in the splanchnic venous bed and portal system. This, in turn, leads to decreased cardiac output and a fall in blood pressure. The lowered aortic pressure leads to decreased coronary blood flow, resulting in myocardial ischaemia and, ultimately, cardiac failure.

Kuida *et al.*[7] have shown that a rise in pulmonary pressure follows the injection of endotoxin in the cat, but there was no rise in left atrial pressure. This is due to pulmonary vascular constriction leading to pulmonary oedema, resulting in diminished venous return to the left side of the heart and a further diminution of cardiac output. If this same vascular abnormality occurs in humans it would account for the tachypnoea, cyanosis and pulmonary oedema frequently observed in bacteraemic shock. In this series of 13 autopsies, 4 showed pulmonary oedema.

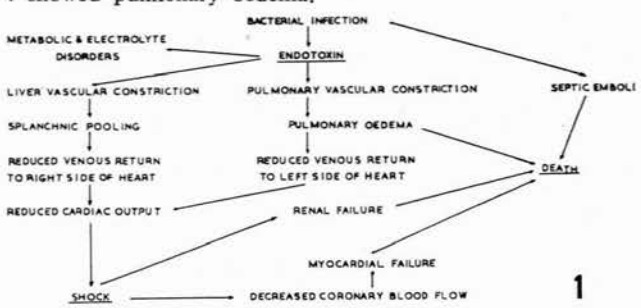


*Fig. 1.* See text.

The major physiologic and pathologic alterations occurring in endotoxin shock[4] are shown in Fig. 1. The cardiovascular system is thrown into a vicious cycle, the end result frequently being *irreversible shock and death*. If, through vigorous treatment, the cardiovascular instability is corrected, death may still occur several days later from irreversible renal damage in the form of bilateral renal cortical necrosis or acute tubular damage resulting from the period of hypotension and ischaemia.

Although the cardiovascular and renal complications are the most serious, various tissues and organs are damaged by the protracted general hypoxia during the state of shock. These include the brain, gastro-intestinal tract and liver; in this series of postmortems, evidence of damage in these organs was found in patients who suffered from shock.

The haemorrhagic phenomena (congested organs and blood-stained fluid) encountered in several of the autopsies may be explained, where *Cl. welchii* were isolated, on the basis of afibrinogenaemia or hypofibrinogenaemia associated with infection by the organism. The mechanism of the afibrinogenaemia is uncertain. Pritchard,[8] in 1956, believed it to be

due to liver damage from haemolysis. Clark and Ellison,[9] in 1959, theorized that it may be due to release of a thromboplastin-like substance from the decidua or to a fibrinolytic toxin produced by the organisms. Only 6 cases have been discussed in the literature, noting the association of *Cl. welchii* infection and diminished fibrinogen states, but many cases of haemorrhagic phenomena have been described. These latter were attributed to liver damage from the organism's toxin. Another theory, which could explain the hypo- or afibrinogenaemia, is that of intravascular clotting. This idea came from reports of incompatibility reactions to transfusions. Shinowara[10] isolated a lipoprotein from the erythrocyte fraction of blood which he called 'thromboplastin cell component' (*TCC*). Unlike tissue thromboplastin his TCC requires the presence of plasma and calcium to activate prothrombin. The mechanism may be as follows: The haemotoxin of *Cl. welchii* causes haemolysis of the red blood cells, and the red blood cell factor thus liberated in the presence of thromboplastinogen and calcium starts the process of clotting by changing prothrombin to thrombin.[11] The degree of clotting and haemolysis probably depends on the number and the virulence of the organisms, and thus this haemorrhagic state does not occur in all cases of *Cl. welchii* infection in abortion. This idea of intravascular clotting supports the work of Hardaway and others (1961),[12] who state that the pathologic physiology underlying endotoxin shock is predominantly initiated by intravascular thrombosis and its sequel. The work was based on observations made after intra-aortic injection of *E. coli* endotoxin in mongrel dogs.

*The Management of the Patients under Review*

All the patients were given blood and 3 were apparently over-transfused, since 1 had to have a venesection and 2 others developed pulmonary oedema.

It appears that in these three patients the assessment of oligaemic shock was not correct. Haemoglobin estimations were not done. Blood may be necessary in all cases, but the amount must be carefully judged. It is most important to distinguish between oligaemic shock and shock following in the wake of sepsis. In the latter, if the patient is to survive, *aggressive* treatment aimed at eradication of the infection and at rapid correction of the circulatory changes must be instituted early.

Critical assessment showed that in 11 severely shocked patients the maximum dosage of cortisone given was 200 mg. In 4 of these it was administered intramuscularly. It does not seem logical to administer dosages intramuscularly in a shocked patient because of the poor peripheral circulation and the uncertainty of absorption. In a further two patients no cortisone was given at all—both of these patients had very low blood pressures (one being unrecordable), with normal haemoglobin readings. One patient received 2 pints of blood and 50 mg. of terramycin in a dextrose-in-water infusion only.

The most usually administered antibiotics were 'chloromycetin', penicillin and terramycin. Their average dosages were chloromycetin 500 mg., penicillin 2·5 million units and terramycin 500 mg. Streptomycin was also commonly administered in a dose of ½ G. Anti-gas gangrene serum was administered in 4 cases.

## DIAGNOSIS

The criteria used for the diagnosis of septic abortion by Perera[13] in the abortion unit of Walton Hospital in Liverpool are similar to those adopted by Stallworthy,[14] namely, that an abortion was regarded as septic when:

1. It is associated with a pyrexia for which no other causes are found.
2. There is evidence of offensive purulent discharge, or
3. There is evidence of pelvic infection.

Bacterial shock must not be misdiagnosed but must be considered with any septic abortion. Shaking chills and vascular collapse without significant blood loss should help establish the diagnosis. All the classical signs and symptoms of shock are present, including hypotension, rapid thready pulse, tachypnoea and pallor. The patient most often appears severely toxic. Positive blood cultures help confirm the diagnosis, but one should not wait for blood culture results before initiating therapy.[5]

## TREATMENT

The principles to be followed in treatment are:

1. Treatment of the shock.
2. Treatment of the infection.
3. Treatment of electrolyte imbalance and renal failure should such failure occur.

It seems only logical that because of the markedly lowered blood pressure and the uncertainty of absorption all medications should be given *intravenously*.

*1. Treatment of the Shock*

*Steroids.* Investigators have shown that the levels of circulating cortisone in patients with septic shock are elevated, and therefore deny the existence of an absolute adrenal-insufficiency state. Superior results have, however, been achieved by Madsen and Tieche[3] with *massive* doses of hydrocortisone. In 21 patients so managed during an 18-month period, there were no fatalities. One of their criteria for diagnosis was progressive hypotension (below 80 mm.Hg systolic), unaccounted for by blood loss. Lillehei and MacLean[15] believe that the reason hydrocortisone has not been used more extensively and effectively in septic shock is that inadequate amounts have been administered. The dosage of the cortisone does not vary so much with the diagnosis as with the degree of acuteness of the disorder. A high initial dose might be indicated in acute fulminating conditions.[16] In Madsen and Tieche's[3] series all patients received massive initial intravenous doses of hydrocortisone and smaller amounts of vasopressors. Their average dose of hydrocortisone was 280 mg. ranging from 100 to 1,400 mg. depending on the severity of the condition.[3] The *maximum* initial dosage in the fatal cases reviewed at Groote Schuur Hospital was 200 mg. of cortisone, which, in 4 cases, was given intramuscularly. Madsen and Tieche[3] believe from their results that hydrocortisone is the most important agent in the treatment of septic shock and that the poor results of others are due to inadequate quantities being administered. It must either be used pharmacologically as opposed to physiologically, or not at all. The error is not to give enough.

The rationale for the use of hydrocortisone is as follows:

1. Steroids alleviate the relative degree of adrenocortical insufficiency supporting the patient in the present stress.
2. Steroids block the intense sympathomimetic effect of the endotoxins.
3. Steroids act on the peripheral vascular bed, restoring vascular tone and potentiating the vasopressors.
4. Steroids decrease the clinical toxicity and permit survival long enough to allow benefit from antibiotics.

Both Jones[5] and Madsen and Tieche[3] recommend an adequate starting dose in critically ill patients of 300 – 500 mg. of hydrocortisone intravenously followed by 500 – 1,000 mg. daily in divided doses for 3 – 6 days. On the 4th day they start giving 'medrol', 4 mg. *q.i.d.* and decrease this dose by 2 – 4 mg. per day. (ACTH 10 u. intramuscularly may be used to supplement this.)

*Pressors.* However important, vasopressors are secondary to hydrocortisone. Vasopressors in judicious amounts will, with hydrocortisone, support the peripheral pressure and increase the return to the heart. It is unnecessary and probably undesirable to restore the blood pressure to normotensive levels.[5] It should be restored only to levels high enough for adequate renal function (30 – 50 ml./hour) which usually occurs at 90 - 100 mm.Hg. The intense vasoconstricting effect of the vasopressors with resulting tissue oligaemia must be guarded against. 'Neo-synephrine' (phenylephrine HCl), 'aramine' and 'levophed' may be used.

Levophed is short-acting and must be given intravenously to prevent sloughing; it is rarely indicated, if ever. Madsen and Tieche[3] used neo-synephrine in amounts of from 20 to 100 mg. per 500 ml. of 5% dextrose in water, with an average initial dose of 46 mg. per 500 ml. of fluid.

*Blood* is given when the abortion is accompanied by severe haemorrhage. Blood in the form of packed red cells is best. The blood should be freshly collected to minimize its extracellular potassium content. If haemorrhage is not a factor, blood is given only to correct pre-existing anaemia. If

cardiac decompensation occurs, rapid digitalization may be life-saving.

*2. Treatment of the Infection*

*Antibiotics.* Blood should be drawn and a cervical smear taken for culture before the initial administration of antibiotics. Antibiotics should be given intravenously and in large doses. With the great probability that the organism is a gram-negative bacterium, one of the broad spectrum antibiotics, tetracycline or chloramphenicol, is recommended. Streptomycin also may be of value, but its use during the hypotensive phase is limited since it is given intramuscularly and absorption therefore may be poor. Its only route of excretion is *via* the kidney and it must therefore be used judiciously when renal output is impaired. At the time of the hypotension, Jones[5] gave the patients an average dose of 3 G. of chloromycetin intravenously per 24 hours. This was maintained until the cessation of intravenous therapy, when 1 G. per day was given orally. Woodard[2] uses streptomycin in an initial dose of 2 G. (½ G. was used in the autopsies reviewed). A good combination of antibiotics for use until the results of blood culture with accurate sensitivity become available is streptomycin and chloramphenicol.

Against *Cl. welchii* infection, Harris and Benjamin[17] used high dosages of penicillin, the most effective being 8 million units daily in divided doses. Penicillin may be given intravenously. Although penicillin is given orally or intramuscularly as a routine, intravenous administration gives a higher titre than is needed, and elimination is complete much sooner than is desirable. This route is therefore used only in instances where continuous infusion is required to maintain an unusually high titre of the drug.[15] Penicillin and streptomycin may be used together in mixed infections, but penicillin with other antibiotics may produce therapeutic antagonism. Harris and Benjamin[17] found the organism was sensitive to most antibiotics but was insensitive to streptomycin in 8 out of 10 cases, and to penicillin in 1 case.

*Antisera.* The suggested dose of antisera to *Cl. welchii* varies; one scheme is 50,000 units intramuscularly 6-hourly for 4 – 6 days.[18]

Because of the danger of serum reaction and uncertainty of its effectiveness, Harris and Benjamin used it only if there was clinical evidence of the activity of the *Cl. welchii* toxins, e.g. gas in tissues, jaundice, or oliguria. On the other hand Woodard[2] believes in treating vigorously with antitoxin if the diagnosis is in doubt. This point remains controversial. Antibiotics should be continued for 7 – 10 days after all evidence of infection has gone.

*Operation.* The following are the views of Perera,[13] of the abortion unit at Walton Hospital. Firstly, no abortion is regarded as complete unless the intact ovum or the foetus followed by an intact placenta is seen by the hospital medical officer. (Patients with incomplete abortion are given ergometrine if there is any bleeding.) The experience in Perera's unit shows that active treatment with immediate evacuation is as safe as passive expectant treatment. Although operative evacuation of an infected uterus is delicate and potentially dangerous, the advantages are considerable, i.e.:

1. The infecting agent is removed.
2. The abortion is properly completed.
3. Shortened period of convalescence.

To minimize the risk of generalized infection, the blood stream should be saturated with antibiotics pre-operatively. Excessive haemorrhage was regarded as the only reason for immediate operative intervention in the presence of pyrexia. In the majority of cases the temperature falls to normal within 24 hours after the operation.

When the infection has spread beyond the uterus, surgical evacuation is withheld until the spreading process has been brought under control with adequate antibiotic therapy. Harris and Benjamin,[16] in a series of cases of *Cl. welchii* infection, did not perform curettage if the diagnosis was known; but if placental tissue was protruding into and through the cervix this was removed with minimal manipulation. More extensive surgery was reserved for patients in whom bleeding was severe or infection was prolonged and worsened despite conservative measures.

*3. Renal Management*

The onset of shock is accompanied by oliguria or anuria, which persists until the blood pressure is at least partially restored to normal levels. Urinary output should be carefully recorded, using indwelling catheters. Fluid administration over a 24-hour period should replace: (a) the insensible loss of 500 – 700 ml., and (b) the estimated amount lost in the urine and that lost by emesis.

Increase the fluid intake by 100 – 150 ml. for every degree of temperature elevation. Overhydration must be avoided since this further complicates the pulmonary oedema that almost always occurs.

Severe electrolyte imbalances, most often metabolic acidosis, are a frequent and serious complication. They can be corrected by administering the appropriate electrolyte solutions, providing adequate renal output has been established.

If renal failure occurs, its management requires careful attention to fluid and electrolyte balance and maintenance of proper caloric intake. Dialysis with use of the artificial kidney has to be undertaken in some cases.

*Suggested outline for the management of septic shock* (After Madsen and Tieche)[3].

1. Draw blood for culture and electrolyte estimation (sodium, chloride, potassium, carbon dioxide). Cross-match blood in case it may be required urgently. Start a 5% dextrose water infusion, using a No. 18 needle.
2. Administer oxygen for cyanosis.
3. Give chloromycetin succinate, 2 G. per litre, initially and thereafter 1 G. per litre.
4. Hydrocortisone (solucortef) 250 – 300 mg. is administered intravenously, *stat,* thereafter:

   1st 24 hours — 200 mg. 4 – 6 hours
   Second day — 100 mg. every 6 hours
   Third day — 100 mg. every 8 hours
   Fourth day — 100 mg. every 12 hours

On the fourth day start 'medrol', 4 mg. four times a day and decrease by 2 – 4 mg./day (ACTH 10 u. intramuscularly may be used as a supplement).

5. Administer phenylephrine hydrochloride (neosynephrine), 50 - 100 mg./500 ml. of 5% dextrose in water, connected with a Y tube so that it may be regulated independently to maintain the blood pressure between 80 and 100 mm.Hg systolic. Chart the blood pressure reading every 15 minutes for the first 24 hours.
6. Give 1,500 ml. of 5% dextrose in water per 24 hours unless renal shutdown is suspected. Examine the lungs frequently for pulmonary oedema.
7. Measure the urinary volume hourly for the first 24 hours. Give potassium after 24 hours if allowed to do so, depending upon the urinary output.
8. Blood chemistry tests should be done daily and adjustments made accordingly.

*It is essential that all drugs are administered intravenously, at least for the first 24 hours.*

SUMMARY

1. 13 fatal cases of abortion are critically reviewed with reference to the postmortem findings and their management.
2. The mechanisms of the shocked states occurring in these patients and the causes of death are discussed.
3. All factors involved in the treatment of these patients are discussed.
4. A scheme for the management of septic shock is given.
5. The intravenous method of administration in shock, and giving of large dosages of drugs are emphasized.
6. It has been emphasized that survival is dependent on early diagnosis and active treatment. These patients require careful vigilant management. In an abortion unit where both medical and nursing staff are prepared and trained to manage such cases, the number of fatalities will be reduced.
7. The different approaches to, and treatment of traumatic (as well as haemorrhagic) shock and shock due to sepsis cannot be overstressed. If a patient suffering from septic shock is transfused rapidly — as must be done in the haemor-

rhagic variety — the result, in all probability, will be catastrophic.

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