Mycoplasma hominis in Abortion

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Brit. med. J., 1967, 1, 338-340

Mycoplasma hominis is found in the human genital tract both in health and in disease, and usually behaves as a commensal. *M. hominis* is commoner in the female genital tract than in the male, and there is evidence that it can cause infection of the genital tract in women (Gotthardson and Melén, 1953; Stokes, 1955; Lemcke and Csonka, 1962). The studies reported here were to investigate any connexion between the presence of mycoplasma in the female genital tract and abortion. In the first investigation a series of aborted foetuses were cultured for the presence of mycoplasma in the foetal tissues. After the isolation of *M. hominis* from foetal tissue it seemed important to establish if this organism could be isolated more commonly from the vagina of patients with abortion than from those having normal pregnancies. A further study was made of a series of patients admitted to hospital with abortion. They were examined for the presence of mycoplasma in the genital tract, and also for antibody to *M. hominis* before and after abortion.

Patients and Methods

Foetuses.—Aborted foetuses from patients admitted to Withington Hospital were collected over a period of several months. The foetuses were carefully opened and pieces of lung and liver tissue taken for culture. The tissue was chopped finely and cultured for mycoplasmas, viruses, and bacteria. Great care was taken to avoid contamination from amniotic fluid or from any tissue that had been in direct contact with the genital tract. At the same time portions of tissue were taken for histological examination. When a growth of mycoplasma was obtained from any foetus a specimen of blood was taken from the mother for antibody estimation.

Patients.—The patients investigated were 70 women admitted to Withington Hospital as cases of threatened or incomplete abortion. On the day of admission a specimen of serum was collected and a swab taken from the vaginal vault. The serum was stored at -20°C . and the swab plated on to mycoplasma agar and on to routine media for the detection of bacterial pathogens. On discharge from hospital these patients were asked to return three to four weeks later for the collection of a second specimen of serum; about half of them did so. These sera and those collected on admission were then tested together.

Methods.—P.P.L.O. agar (Difco) containing 20% unheated human serum, 1/2,000 thallium acetate, and 1,000 units of penicillin per ml. was used for the isolation of mycoplasmas. Horse blood agar was also used; these media were inoculated and incubated at 34°C . for three days before being examined for the presence of mycoplasma colonies. All the strains of *Mycoplasma* sp. isolated in this study were identified as *M. hominis* by the growth-inhibition test of Clyde (1964).

Serological Tests.—The complement-fixation antigen was prepared by the method of Card (1959). The method of performing the complement-fixation test and the growth-inhibition test of Taylor-Robinson *et al.* (1966) have been described elsewhere (Jones and Sequeira, 1966).

Results

Culture of Foetal Tissues.—Tissues from 62 foetuses were cultured and *M. hominis* was grown from the lungs of five of them. The organism was not recovered from samples of liver tissue except in one embryo (Case 5), which was very small, and *M. hominis* was grown from all tissue samples taken. In the latter part of this series the placenta, where available, was also cultured. In two instances *M. hominis* was recovered from the placenta but not from the foetus. Pairs of sera were collected from both these cases, and no rise in antibody titre was demonstrable. No bacterial pathogens and no viruses were isolated from any foetal material examined.

Case Histories where *M. hominis* was Grown from Foetal Tissue

Case 1

A woman aged 22, who had had two previous pregnancies and one miscarriage, was admitted to hospital with a threatened abortion at approximately 25 weeks' gestation. Several days after admission she went into premature labour, and had an assisted breech delivery of a male baby weighing 2 lb. 3 oz. (995 g.). The baby was in poor condition and died after half an hour.

Pathological Findings.—An Ayre's smear taken at the antenatal booking clinic had the appearance associated with the presence of mycoplasmas (Jones and Davson, 1967). **Placenta:** Early third-trimester placenta showed areas of polymorph infiltration in the placental septa. Around a major branch of the umbilical artery a zone of polymorph infiltration was present, and there were necrosis and polymorph infiltration in the basal plate. **Lungs:** The lungs were not expanded; the bronchi were lined with columnar epithelium and contained an amorphous pink exudate in which an occasional polymorph could be seen. Many alveoli were small, with indistinct lumina; the lining cells appeared to be enlarged and vacuolated, and occasional polymorphs were present. No definite evidence of foetal pneumonia was found. **Serum:** Three months after delivery the maternal complement-fixing antibody titre to *M. hominis* was 1/20.

Case 2

A woman aged 21, who had had one previous pregnancy, was admitted when about 15 weeks pregnant complaining of intermittent bleeding for one month. Two days after admission she became pyrexial and had an incomplete abortion. She was treated with antibiotics and curettage, and after one week in hospital was discharged.

Pathological Findings.—**Curettings:** Gravid phase endometrium with polymorphs in the gland lumina. In some areas of decidua the cells had giant vacuoles and irregular outlines, and there were diffuse oedema, polymorph infiltration, and patchy necrosis. **Placenta:** The villi were free from obvious inflammatory foci, but the terminal portion of the umbilical cord was the site of a diffuse cellulitis. The amnion epithelium covering the cord showed focal ulceration. The basal plate was extensively infiltrated with polymorphs. **Lungs:** In the main bronchi, bronchioles, and terminal ducts polymorphs and finely granular exudate were present. Occasional amniotic squames were seen in the ducts. The appearances were those of early foetal pneumonia. **Serum:** The complement-fixing titre to *M. hominis* was 1/10 on admission and 1/80 three weeks later.

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Case 3

A woman aged 44, who had had one previous pregnancy, was admitted with an inevitable abortion of 27 weeks' gestation that became complete soon after admission. The foetus was dead but not macerated. The patient developed only transient pyrexia and was discharged five days after admission.

Pathological Findings.—**Placenta:** Early third-trimester villi with little intervillous fibrin; there was polymorph infiltration of the walls of many vessels in the chorionic plate, extending sometimes to the perivascular mesenchyme. **Umbilical Cord:** This was infiltrated with polymorphs. **Lungs:** A few polymorphs were present in the bronchi; the alveoli were not expanded, and contained a granular exudate and occasional polymorphs. No frank pneumonia. No abnormality was seen in sections of liver, thymus, or pancreas. **Serum:** A sample of serum collected three weeks after her admission had a titre of complement-fixing antibody to *M. hominis* of 1/640; the growth-inhibiting antibody titre was 1/320.

Case 4

A woman aged 24 was admitted with an inevitable abortion of 14 weeks' gestation. The abortion continued spontaneously and she became febrile. Retained products of conception were removed, and she was discharged after five days in hospital.

Pathological Findings.—**Curettings:** Necrotic decidua and foetal villi showed the appearances suggestive of foetal death in utero of some duration. Exudate containing polymorphs was present in the intervillous spaces. **Lungs:** There was no evidence of foetal pneumonia, but an interstitial oedema was a marked feature. No abnormality was seen in liver, kidney, adrenal, or myocardium. **Serum:** Three weeks after abortion the titre of complement-fixing antibody was 1/80 and the growth-inhibiting antibody titre 1/40.

Case 5

A woman aged 42 was admitted complaining of irregular bleeding of a month's duration. She aborted a small embryo sac of about eight weeks' gestation soon after admission. The uterus was curetted and the patient was discharged after five days.

Pathological Findings.—*M. hominis* was grown from a vaginal swab taken on admission from foetal tissues and from the fluid from the intact amniotic sac. **Placenta:** The decidual cells of the basal plate showed rounding of the cytoplasm, and were separated by oedema and scattered polymorphs. The amnion appeared normal, but occasional fibrin deposits were present in the chorionic layer. **Curettings:** Sheets of decidual cells interposed with layers of fibrin and numerous polymorphs; some necrotic areas. **Serum** collected on admission contained no antibody to *M. hominis*, and a second specimen could not be obtained.

Culture and Serology Results from Patients Admitted with Abortion

M. hominis was cultured from 12 (17%) of the 70 patients examined; antibody was found in 20 (29%) (Table I). The complement-fixing antibody titres were in the range of 1/5 to 1/40, and in only one patient was growth-inhibiting antibody detected.

TABLE I.—Isolation of *M. hominis* and Antibody to *M. hominis* in Patients Admitted with Abortion

Patients	No.	<i>M. hominis</i> Grown at Time of Abortion	Antibody to <i>M. hominis</i>	Rise in Antibody Titre
Examined on admission	70	12	20	—
Followed up	36	7	10	3

Second specimens of serum were examined from 36 of these patients, and rises in antibody titre were shown in three, there being no change in the remainder. The pattern of the antibody response is shown in Table II. The titres of complement-fixing antibody did not become very high, but in two patients growth-inhibiting antibody appeared.

TABLE II.—Antibody Response in Three Patients, Showing a Rise in Antibody Titre to *M. hominis*

		First Specimen		Second Specimen	
		C.F.T.	G.I.T.	C.F.T.	G.I.T.
Patient 6	..	< 1/5	< 1/5	1/20	1/5
" 7	..	< 1/5	< 1/5	1/40	1/5
" 8	..	1/10	< 1/5	1/40	1/10

C.F.T. = Complement-fixation titre. G.I.T. = Growth-inhibition titre.

Case Histories of Patients Showing a Rise in Antibody Titre

Case 6.—A woman aged 35, who had had four previous pregnancies, was admitted with incomplete abortion of 14 weeks' gestation. She was pyrexial on admission, and a high vaginal swab taken then yielded a growth of *M. hominis*; no bacterial pathogens were grown. Treatment consisted of antibiotics, blood transfusion, and evacuation of the uterus, and she was discharged after five days.

Case 7.—A woman aged 23, who had had no previous pregnancies, was admitted complaining of lower abdominal pain and vaginal discharge. She was approximately 27 weeks pregnant, and she was having moderate contractions of the uterus on admission. Complete abortion occurred three days later. *M. hominis*, but no bacterial pathogen, was grown from the vaginal swab taken on admission. She continued to bleed after delivery and became pyrexial. Some retained products were removed and ampicillin was given. The temperature gradually settled, and she was discharged after 14 days in hospital.

Case 8.—A woman aged 26, with a history of three normal pregnancies and one miscarriage, was admitted with an incomplete abortion of 10 weeks' gestation. On admission she was slightly shocked and pyrexial. She was transfused, treated with ampicillin, and the remaining products of conception were removed. Culture of a vaginal swab yielded a growth of *M. hominis*. Progress was satisfactory and she was discharged five days later.

None of the aborted foetuses from these patients was available for culture.

Discussion

Mycoplasmas occur as saprophytes or potential pathogens in the genital tracts of man and animals. The isolation of a mycoplasma from an aborted bovine foetus has recently been reported, but the significance of the finding is not yet clear (O'Berry *et al.*, 1966). The isolation of *M. hominis* from human aborted foetuses raises the question of whether this organism can have a primary role in abortion. In the present series of 70 patients admitted with abortion *M. hominis* was isolated from 17% and antibody was present in 29%. These findings can be compared with a *M. hominis* isolation rate of 24% and an antibody incidence of 15% in 100 consecutive antenatal patients attending the same hospital (unpublished data). In the abortion group *M. hominis* was present in the vagina to nearly the same extent as in antenatal patients, but antibody was twice as common. The explanation of this may be that mycoplasma infection is associated with sexual promiscuity (Shepard, 1954), and that a group of patients with abortion could be expected to contain more promiscuous individuals than a random group of antenatal patients.

The clinical course of the mothers with infected foetuses was in no way remarkable; there was pyrexia associated with abortion, and a prompt response to antibiotic therapy. It was possible to demonstrate a significant antibody titre in four of these cases. In placental tissue there was histological evidence of infection sometimes extending to the umbilical cord. Definite evidence of pneumonia was found in one foetus; in others evidence of a foetal tissue response was equivocal.

The presence of *M. hominis* in foetal lung but not in other tissues suggests that the organism may spread from the placenta to the amniotic fluid and then to the foetal respiratory tract rather than via the blood stream. The mycoplasma may invade an already dead or dying foetus in this way without producing

a foetal tissue response. The organism may also be capable of infecting a living foetus, and there is evidence of this in Case 2.

Infection with *M. hominis* probably more commonly extends only as far as the maternal genital tract, contributing to pyrexia associated with delivery. Of seven patients who aborted and who had *M. hominis* in the vagina, three developed a rise in antibody titre (Table II). These patients had a pyrexial illness, and presumably an infection of the genital tract due at least in part to *M. hominis*. The appearance of growth-inhibiting antibody, which does not persist for long in the circulation, is consistent with recent infection (Jones and Sequeira, 1966). It is of interest to note that when mycoplasmas are introduced into the bovine uterus, endometritis and endosalpingitis are produced (Hartman *et al.*, 1964). Mycoplasmas, as opportunists, may be able to produce similar infections in humans when conditions in the genital tract are favourable.

Summary

The isolation of *Mycoplasma hominis* from aborted foetuses, accompanied by significant levels of maternal antibody, is

described. Rises in antibody titre to *M. hominis* were also detected in some patients who had this organism in the vagina at the time of abortion. These findings suggest that infection of the genital tract occurs in association with abortion, and sometimes this infection may involve the foetus. The possibility that such infection may sometimes cause abortion is discussed.

I am indebted to Dr. James Davson for the histological reports, and to Dr. R. W. Burslem and Mr. J. B. Jones, under whose care these patients were admitted.

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Unusual Case of Mercury Poisoning

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Brit. med. J., 1967, **1**, 340–341

Poisoning by metallic mercury is extremely rare. A review of the literature of the past 70 years has brought to light only 27 cases. Most of these were accidental, and many of the more recent ones had followed gas-analysis procedures, where mercury was used as a seal in syringes (Lathem *et al.*, 1954; Schulz and Beskind, 1960; Buxton *et al.*, 1965). Others occurred after injury from broken thermometers (Haubrich and Schuler, 1949), or in those working with mercury (Ekert, 1949), or after the rupture of the mercury-filled bag of an indwelling intestinal tube (Lindenmuth, 1949; Crikelair and Hiratzka, 1953), or as a result of inunction of the skin with preparations containing mercury (Rixford, 1895; Stammel, 1929), or in tattoos (Lane *et al.*, 1954). Suicidal attempts by means of metallic mercury are quoted by Umber (1923), Conrad *et al.* (1957), and Schulze (1958). In all these cases the presence of metallic mercury in the tissues was demonstrated by radiography, the mercury being present either at the site of introduction or in the form of emboli. Out of the 27 cases reported, there were only three deaths.

In view of the rarity of the condition, a case of deliberate self-injection of metallic mercury with subsequent death from mercurial poisoning is presented in detail.

Case Report

An intelligent, healthy female laboratory technician aged 23 deliberately injected her own left forearm with between 1 and 2 ml. of unsterilized mercury. Three weeks later her forearm had become tender, red, and swollen, and symptoms of median nerve damage had developed. X-ray examination confirmed the presence of mercury in the arm. The left forearm was explored, and between

0.5 and 0.75 ml. of mercury was removed. There was obvious damage to the median nerve. After the exploration increasing fever and pulse rate with muscular spasms and rigidity developed. Four days later her temperature had reached 107.2° F. (41.8° C.), and she was unrousable. A lumbar puncture showed no abnormality. She was intubated and put on a respirator. The next day her arm was re-explored, but no more mercury was found. Necrotic tissue was cultured for *Clostridium tetani*, with negative results. X-ray examination of her chest the same day showed mercury emboli throughout both lungs. Her blood urea rose steadily, and she died 31 days after the original mercury injection.

Post-mortem Findings

The whole body was x-rayed before dissection. Residual mercury was seen in the left forearm and hand, and multiple fine globules were present throughout both lungs (see Figs. 1 and 2). A few scattered solitary globules were present elsewhere in the body, but none were seen in the brain.

The body was pale and oedematous. There was necrosis of the median nerve in the left forearm. Dissection under low-power magnification showed multiple fine globules of mercury in and around the median nerve sheath and between muscles. The lungs were oedematous, but there were no other naked-eye abnormalities, and no more mercury was seen.

Histologically extensive epithelial necrosis was found in the renal proximal convoluted tubules, which contained eosinophilic debris. There was exudate around many glomeruli beneath Bowman's capsule, and many distal tubules contained altered red cells. In the heart were multiple foci of inflammatory cells with necrosis of myocardial fibres. The blood vessels in all parts of the brain contained rounded bodies staining purple with haematoxylin and eosin, and giving a positive reaction with the periodic-acid-Schiff stain. There was no obvious damage to the nervous tissue of the brain itself, but many anterior horn cells in the spinal cord showed degenerative changes.

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