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LISTERIOSIS AND HUMAN ABORTIONS—INCLUDING A BRIEF
REVIEW OF LITERATURE

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Introduction

In the last two decades *Listeria* has created a great interest and awareness for its varied clinical manifestations amongst human and veterinary microbiologists as well as in clinicians of both fields. Report of first human isolation from the blood of a patient with an illness resembling infectious mononucleosis was made by Nyfeldt (1929). Isolation from human cases of meningitis in 3 infants and one adult was recorded by Burn (1936) for the first time.

The human infection is usually sporadic though reports of epidemics have been recorded in several countries. Seeliger, Emmerling and Emmerling (1968) presented records of 2004 human cases comprising different clinical forms of listeriosis from Germany alone between 1950 and 1966, thus showing the importance of this infection.

The relationship between *Listeria monocytogenes* and repeated human abortions has been clearly established. Well documented but isolated reports of cases have been recorded by authors from various countries.

In India, to date, there are only 5 reports of isolation of *Listeria monocytogenes* from cases of genital listeriosis. These were reported from Bombay (Krishna *et al* 1966), Manipal (Kasinthan and Rao 1973), Delhi (Bhujwala *et al*, 1973; Bhujwala and Hingorani

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1975) and Nagpur (Jagtap and Hardas 1975). Contrary to these reports, authors like MacNaughton (1962), Ruffalo *et al* (1962), Jessen and Bojsen Møller (1963), Rabau and David (1963), Potel (1963) and Dhawan and Dhall (1963) failed to isolate *Listeria monocytogenes*.

This paper describes the result of a pilot study on "Genital listeriosis in South Kanara District", that is being carried out since last 3 years.

Material and Methods

A total of 40 cases with a history of repeated abortions were selected for the study. All the usual common causes of abortion like syphilis, brucellosis, toxoplasmosis, Rh incompatibility, etc. were first ruled out. Deep cervical swabs and

10 ml of sterile blood were collected from each patient. For control purpose, vaginal swabs from 40 healthy women without any history of abortion were also collected. The blood was inoculated onto tryptose-broth, and the swabs onto blood agar and tryptose broth. The plates were incubated at 37°C in 10% CO₂ atmosphere. The broth was refrigerated at 4°C for a maximum period of 3 months and subcultures were carried out from these once in a week, onto solid media. *Listeria* has the unique property of growing at this low temperature of 4°C; thus it out-numbers the other saprophytic commensals of cervix and vagina.

A course of antibiotic treatment as detailed in Table 1 was given to patients when *Listeria monocytogenes* was isolat-

TABLE I
Details of Cases Positive for Genital Listeriosis

Case No.	Age	Brief past history	Treatment given	Follow-up study
1.	24	Ist, 2nd and 3rd pregnancies—premature and macerated foetus—8 months old 4th pregnancy—premature child, 8 months old, alive for 2 days only 5th and 6th pregnancy—eclampsia around 8th month 7th pregnancy—premature—macerated foetus—8 months old	(i) Penidure LA-12 lakhs 2 injections (ii) Resteclin-250 mg 8 hourly x 8 days	Gave birth to a normal child 14 months after treatment.
2.	30	5 abortions	Advised a course of Tetracycline treatment for 14 days	Not done (case referred) from Andhra Pradesh).
3.	24	Ist pregnancy—normal male child, alive 2nd pregnancy—I.U.D. around 8th month 3rd, 4th, 5th, 6th and 7th—abortion around 3rd or 4th month	(i) Streptopen ½ gm. BD x 7 days (ii) Tetracycline 250 grms 6 hourly x 5 days	Delivered a normal male child 9 months after treatment.
4.	35	Ist pregnancy—normal female child, alive 2nd, 3rd and 4th pregnancy—abortion around 3rd month	(i) Streptopen ½ gm. BD x 7 days	Still under observation.

ed from cervical swabs. This was given for a period of 7-14 days till the repeat cultures became negative. Attempts were made to make a follow-up study of the positive cases—only 3 cases could be followed.

Results

Out of the 40 women with a history of repeated abortions, *L. monocytogenes* was isolated from 4 cases, all from cervical swabs only, blood cultures being uniformly negative in all the cases. From the control group, no listeria organisms could be isolated from any one of the 40 cases. Brief details regarding the 4 positive cases is presented in the Table 1.

The identification of the isolates was done according to the procedures outlined by Killinger (1974). The organisms were gram positive cocco-bacilli, showed tumbling movement at 22-25°C and gave characteristic fermentation reactions. They killed mice on intraperitoneal inoculation and produced severe keratoconjunctivitis in young rabbits when instilled into the eyes (Anton test). Serotyping of the strains was not carried out due to the non-availability of the antisera.

Discussion

In humans, listeriosis presents protean manifestations. Seeliger (1961) distinguished 9 clinical forms of the infection in man of which listeriosis of CNS and perinatal listeriosis are the most common forms. However, the most frequent isolations, according to Killinger (1974), were from purulent meningitis, meningo-encephalitis and septicemia.

Apart from these, the organism may affect the throat or give rise to a septicemic disease resembling typhoid fever, and may cause generalised lymphadenitis (Wilson and Miles 1975). The other important lesion which has drawn the atten-

tion of many workers is the localization in the genital organs of both sexes. In the male, the quantity and quality of the semen is affected (Toaff *et al* 1962). In the female it can cause repeated or habitual abortions, stillbirths of macerated fetuses and "infantiseptica granulosa"—a condition first described by the Germans. (Reiss, Potel and Krebs 1951).

In contrast to the severity and bad prognosis of neonatal listeriosis, the concomitant infection of mothers of the affected babies is usually very mild or altogether symptomless. (Seeliger 1961). In most of the cases the mothers may develop a mild flu-like symptoms with mild fever during the last trimester of pregnancy (Killinger 1974).

Serological test for detection of listerial antibodies was not attempted by us, since it is known that even normal individuals possess antibodies in titres of 1/160 and above (Seeliger 1961; Osebold 1965; Bodnar *et al* 1972 and Bhujwala and Hingorani 1975).

The source and mode of infection in man is not fully explored. Seeliger and his colleagues (1965) suggest that man becomes infected through soil contaminated food. According to Gray (1963) *Listeria monocytogenes* has been isolated from 35 different species of mammals, fowls, ticks, fish, crustaceans, stream water, mud, sewage and silage and it occurs in all continents except Antarctica. *L. monocytogenes* has properties which enable it to survive in the soil and can endure relatively high and low temperatures, features which explain its widespread prevalence (Hoeprich 1958). It is believed that the organism attacks the weaklings, particularly newborn infants, elderly persons suffering from some underlying disease and women under the stress of pregnancy. Oral route of trans-

mission was evidenced by Bojsen Møller (1972) who has isolated it from the stool specimens of normal population. Persons in direct or indirect contact with animals, including those who drink infected raw milk or eat raw meat or eggs are most liable to be infected, (Potel 1958; Gudkova *et al* 1958 and Gray 1963) thus suggesting a zoonotic infection.

A brief mention must be made regarding the treatment of Genital listeriosis. Rappaport *et al* (1960) treated successfully 25 mothers with genital listeriosis with 1 million units of penicillin and 1 gm. sulphamethoxy pyridazine (Lederkin) daily for 14 days. Krishna *et al* (1966) gave the same treatment to 18 of their patients and oxytetracycline (1 gm daily for 7 days) for another 3 patients. Tetracycline (14 days treatment) was administered to their 3 cases by Bhujwala *et al* (1973). Later the same authors (1975) treated another 11 patients with Erythromycin and one more with Methicillin since that particular strain was found resistant to Erythromycin.

Two of our patients, received 2 doses of penidure-LA 12 lakhs and 1 gram. tetracycline for 8 days. Third patient was given streptopen 1 gram daily for 7 days. The fourth patient received streptopen 1 gram daily for 7 days and tetracycline 1 gram daily for 5 days. Seeliger and Matheis (1969) regard ampicillin as the drug of choice for all forms of listerial infections. Next to ampicillin comes the tetracycline. It is worthwhile to point out at this juncture that strains resistant to either one or more of the drugs like sulphadiazine, penicillin, ampicillin, tetracycline, or chloramphenicol have been reported. (Bhujwala and Hingorani 1975). One of our isolates was resistant to penicillin

and chloramphenicol. In view of this it is suggested that the treatment may be initiated after studying the antibiogram of the isolate. Irrespective of the choice of the antibiotic, the treatment should be started before conception or during early pregnancy (first trimester) since treatment may not be fruitful if given during late pregnancy (Rappaport *et al*, 1960).

The primary isolation of listeria from contaminated clinical materials presents some problems. Picking up the colonies of *Listeria monocytogenes* from amongst other commensal bacterial colonies needs practical skill and meticulous care, otherwise they can be very easily mistaken for and ignored as diphtheroids. The small cocco bacilli sometime appear like diplococci. At times they may be confused for *H. influenzae*, because of the ease with which they get decolourised. (Seeliger and Cherry 1957). The phenomenon of "cold enrichment" (refrigeration at 4°C) upto 3 months is very helpful to isolate the organisms from highly contaminated specimens like vaginal or cervical swabs (Gray and Killinger 1966). Thus a very systematic search for listeria has to be made in all human abortions in order to arrive at the correct diagnosis.

Summary

1. A pilot study was undertaken to investigate into the incidence of habitual abortion due to *Listeria monocytogenes* in humans. Out of the 40 cases with bad obstetric history studied, 4 were positive for *Listeria monocytogenes* and 2 of the cases which were followed up gave birth to normal full term child after antibiotic treatment.

2. The need for carrying out the antibiotic sensitivity tests of the isolates before initiating the therapy is stressed.

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