Comparative L.E. Cell Investigations with Patient's own and Normal Subject's Leucocytes

Case No.	Initials	Lupus Erythematosus Cell <i>In vitro</i>						<i>In vivo</i> Plasma Transfer Experiment
		Patient's Own Leucocyte	Normal Subject's Leucocytes S.L.E. Plasma in ml.					
			0.25	0.5	1.0	2.0	3.0	
1	T.J.	++++	0	0	0	0	0	N.T. (1)
2	K.E.	++++	++++	++++	++++	++++	++++	T. (2)
3	V.M.	++++	0	0	±	±	±	N.T. (4)
4	M.K.	++	0	0	0	0	0	(0)
5	P.J.	++++	0	0	0	±	±	N.T. (4)
6	K.L.	++++	++++	++++	++++	++++	++++	(0)
7	O.P.	++++	++++	++++	++++	++++	++++	T. (20)
8	B.I.	++++	0	0	±	±	±	N.T. (8)
9	T.I.	++++	++++	++++	++++	++++	++++	T. (9)
10	K.K.	++++	0	0	0	0	±	N.T. (3)
11	S.M.	+++	0	0	0	0	0	N.T. (2)
12	P.J.	++++	0	0	0	0	0	(0)
13	K.F.	++++	++++	++++	++++	++++	++++	T. (4)
14	H.K.	+++	0	0	0	0	0	N.T. (2)
15	P.J.	++++	++++	++++	++++	++++	++++	T. (4)
16	P.F.	++++	0	0	±	±	±	N.T. (4)

± = Examinations showed in some cases presence in others absence of L.E.-cell. T. = Transferable. N.T. = Not transferable. Figures in parentheses indicate number of experiments.

S.L.E. plasma of non-transferable type considerably fewer L.E. cells were seen when a normal subject's cells were added than when the patient's own leucocytes were added, even when more plasma (2 and 3 ml. respectively) was used. At the same time, we failed to produce L.E. cells with smaller amounts (0.25 and 0.5 ml.) of S.L.E. plasma. *In vitro* investigations were carried out at different times on several occasions with plasma of these five S.L.E. patients, but we failed to find L.E. cells in some cases when a normal subject's leucocytes were added—even when as much as 3 ml. of plasma was used.

The L.E.-cell phenomenon could not be produced with the plasma of five S.L.E. patients out of a total of 16 when a normal subject's leucocytes were added (no transfer experiment was completed with the plasma of two S.L.E. patients). Significantly fewer L.E. cells could be detected when the plasma of a further five S.L.E. patients was treated with a normal subject's cells than when the patient's own leucocytes were added. But when the plasma of five S.L.E. patients which proved to be transferable was treated *in vitro* with leucocytes from normal subjects (on several occasions and at different times) the L.E.-cell phenomenon was always observed—as it was in Case 6, in which no plasma transfer experiment has been completed. The number of L.E. cells produced (compared with the total number of leucocytes) was the same whether the patient's own or a normal subject's leucocytes were added *in vitro* to samples of plasma from these six S.L.E. patients. The L.E.-cell phenomenon came into being in all six cases when only as little as 0.25 ml. and 0.5 ml. of plasma was used.

Ten of the 16 S.L.E. patients were systematically observed by us for a period of years. L.E.-cell examinations were frequently made on different occasions—six times at least. In six of these 10 patients (Cases 1, 4, 5, 10, 14, and 16) no L.E. cells could be found by Zinkham and Conley's method on several occasions, even when the patient's own leucocytes were used. Plasma transfer experiments were completed on five of six S.L.E. patients; all five proved to be non-transferable. In the other four S.L.E. patients L.E. cells could always be found (Cases 6, 7, 9, and 13); in three of these four patients *in vivo* plasma transfer experiments were completed, and all three proved to be transferable. [We wish to make it clear that comparative *in vitro* investigations were made only in those

cases in which the L.E.-cell phenomenon could be produced with the patient's own leucocytes.]

Summary

Comparative *in vitro* investigations using the leucocytes of S.L.E. patients and of normal subjects provided evidence that a difference existed between the transferable and non-transferable type of L.E. plasma factor. In the latter type L.E. cells could be produced *in vitro* only when the patient's own leucocytes were used; they could not be produced—or could be produced only in very small numbers—with the leucocytes of normal subjects.

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Medical Memoranda

Case of Listeria Meningitis

Neonatal meningitis due to *Listeria monocytogenes* is rare enough to raise difficulties in diagnosis and treatment. Human listerial infection may be more common than generally supposed, and papers reporting cases from Great Britain support this view (Edmunds, Nicholson, and Douglas, 1957; Mair, Mair, Stirk, and Reid, 1957; Barrow and Pugh, 1958; Turner, Dawson, and Pryce-Jones, 1958).

CASE REPORT

The patient, a white male infant, was born by spontaneous vertex delivery after an uneventful full-term gestation. Birth weight was 6 lb. 14 oz. (3,120 g.). Progress was normal for the first 10 days; he then had loose bowel motions and became febrile. He was admitted to the 7510th U.S.A.F. Hospital, Wimpole Park, two days later.

On the day of admission he appeared lethargic and showed opisthotonos. The temperature was 100.4° F. (38° C.); there were no other physical signs. Lumbar puncture and blood culture were performed. The cerebrospinal fluid was turbid and contained 2,400 leucocytes per c.mm. (90% polymorphonuclear), the sugar was 26 mg. and protein 440 mg./100 ml. The Gram film showed a moderate number of

Gram-positive bacilli, mainly extracellular in position, at first thought to be *Haemophilus influenzae*, in view of the ease with which they could be decolorized, but subsequently identified as *Listeria monocytogenes*. Similar organisms were isolated from the blood culture after 48 hours' incubation. The organism was resistant to penicillin but sensitive to tetracycline, erythromycin, streptomycin, chloramphenicol, and sulphonamides. The haemoglobin was 17.5 g./100 ml., white-cell count 15,800/c.mm. (36% polymorphonuclear leucocytes, 60% lymphocytes, 4% monocytes).

Treatment was started with intravenous fluids. Crystalline penicillin, 400,000 units intramuscularly, chloramphenicol, 75 mg. intramuscularly, and sulphadiazine, 150 mg. subcutaneously, were given six-hourly. Penicillin was stopped on the second day and the chloramphenicol and sulphadiazine were given orally after three and five days respectively. Intravenous fluid was discontinued after two days.

The child made an excellent response to treatment. On the third day he was afebrile and started to gain weight; there were no abnormal physical signs five days after admission, and chloramphenicol and sulphadiazine were discontinued.

Lumbar puncture was repeated at the end of the third week of the illness, the C.S.F. was sterile, the sugar 44 mg. and protein 150 mg./100 ml. Further progress was interrupted by a mild chest infection, but the child was discharged apparently well and gaining weight after five weeks in hospital.

Morphology.—The organism on first isolation was a small, short, Gram-positive rod resembling a diphtheroid bacillus. Some V forms were present. It could be easily made to appear Gram-negative by decolorization with acetone. Filamentous forms appeared after repeated subculture.

Cultural Characteristics.—Growth occurred fairly well on a variety of solid media. On blood-agar incubated at 37° C., slightly opaque, smooth domed colonies, less than 1 mm. in diameter, were visible after 18 hours. After 48–72 hours the colonies were 2–3 mm. in diameter, milky in appearance, and with fimbriate edges. A narrow zone of clear (beta) haemolysis was present around the colonies on blood-agar. The presence of a soluble haemolysin was confirmed by the method of Webb and Barber (1937). On blood tellurite, minute black colonies were just visible in 18 hours; no growth was apparent on MacConkey's medium after 36 hours. After repeated subculture "rough" colonies (Barber, 1939) could be distinguished.

Motility.—The tumbling motility said to be typical of *Listeria monocytogenes* could be seen in glucose-broth cultures grown at room temperature for 18 hours.

Biochemical Reactions.—The organism produced acid but not gas from maltose, glucose, xylose, and salicin within 36 hours and from lactose and sucrose in five days. Dulcitol and mannitol were not fermented. Urea was not split on Christenson's medium; hydrogen sulphide and indole were not formed. There was no growth in Koser's citrate, the methyl-red test was positive, and the Voges-Proskauer reaction negative.

Antibiotic Sensitivities.—Strips of filter-paper, soaked in solutions of antibiotics, incorporated in nutrient agar, were used for testing antibiotic sensitivities. Organisms of known sensitivity were used as controls.

Production of Monocytosis in Rabbits.—The conjunctival sac of one eye of each rabbit was infected with a swab

dipped in an 18-hour glucose-broth culture. The blood monocytosis in two rabbits is shown in the Table. After recovery from the conjunctivitis, the rabbit conjunctival test was performed on one rabbit and local immunity demonstrated (Julianelle, 1941).

Serology.—A rabbit antiserum of a titre of 1/2,000 to a known strain of *Listeria monocytogenes* agglutinated a formalized suspension of the organism at 1/1,000.

Serological Investigations of the Patient's and Mother's Serum.—No agglutinating or complement-fixing antibodies to formalized suspensions of the organism were detected on sera taken from the patient on the 11th and 25th days of the illness or in the mother's serum 37 days after delivery. The patient's serum gave a negative Paul-Bunnell reaction. Dr. D. G. Ingram determined the immuno-conglutinin titre of the patient's and the mother's serum. No activity was detected in the mother's serum, but the second serum from the patient showed a significant rise in titre compared with the first, indicating that an antibody response had occurred.

COMMENT

Listeria monocytogenes has been confused with streptococci, pneumococci, diphtheroids, and *E. coli*. In this case, as in that described by Selinger and Becker (1955), the ease with which the organism could be decolorized led to a provisional diagnosis of *H. influenzae* meningitis. Penicillin therapy was therefore discontinued. Fortunately, treatment with chloramphenicol and sulphadiazine was remarkably effective.

Though this case is an exception, resistance to penicillin seems to be uncommon. Of six cases described in Great Britain within the last three years the organism was found to be sensitive to penicillin in five, and in the United States *Listeria monocytogenes* appears to be more often sensitive to penicillin than to chloramphenicol (Dedrick, 1957).

We thank Captain Thomas L. Evans, U.S.A.F., for the clinical details of this case, and Dr. D. G. Ingram, late of the department of pathology, University of Cambridge, for determining the immuno-conglutinin titre and supplying the antiserum.

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Arthrodesis of the Great Toe

Keller's operation is still the most frequently performed operation for hallux valgus and rigidus. The results are often good, but they are not reliable. In my view the main reason for this is that metatarsalgia is often not relieved. In the normal foot the weight taken by the forefoot is divided mainly between the metatarsal heads and the tip of the great toe. The other toes take a relatively small proportion of the weight. In a severe hallux valgus the great toe deviates so far laterally that its tip takes only a little weight and the metatarsal heads

Monocytic Response in Rabbits to *Listeria Monocytogenes*

Date	Rabbit 1		Rabbit 2	
	Total W.B.C./c.mm.	Monocytes/c.mm.	Total W.B.C./c.mm.	Monocytes/c.mm.
3/2/59	10,000	750	6,000	450
4/2/59, conjunctival inoculation	8,000	760	7,000	630
6/2/59	9,000	1,350	9,000	990
8/2/59	11,000	1,760	8,000	1,840
10/2/59	15,000	2,850	8,000	1,680
12/2/59	10,000	1,200	8,000	1,400