The distribution and effect of *Chlamydia trachomatis* in CBA mice inoculated genitally, intra-articularly or intravenously

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Abstract. A "fast" egg-killing human strain of *Chlamydia trachomatis* was inoculated into normal CBA and congenic CBA/nu mice, which have an impairment of T-cell function and do not produce anti-chlamydial antibodies. The mice were inoculated by the intra-uterine, intra-articular, or intravenous routes. Some of the mice were first treated with progesterone, which allows successful chlamydial infection of the mouse genital tract when the organisms are introduced genitally. Mice were sacrificed up to 27 days after inoculation. Homogenates of joints, genital tract, spleen, liver, kidneys, eyes and lungs were prepared and tested for chlamydiae in cycloheximide-treated McCoy cell cultures.

Chlamydiae were detected in the genital tracts and spleens, but not in the joints, of mice inoculated via the intra-uterine route. They were found in the joints and spleens of mice inoculated intra-articularly, and were detected also in spleens and, from the 4th to 6th day after inoculation, in joints of mice given the organisms intravenously. These results were obtained irrespective of whether or not the mice had received progesterone. The numbers of chlamydiae in the spleens and joints of the nude mice were larger and they persisted longer than in the corresponding immunocompetent animals, although this was not true for chlamydiae in the genital tract of mice inoculated via the intra-uterine route.

Compartmentalisation of chlamydiae was evident although the spleen was infected consistently irrespective of the route of inoculation and, as mentioned, chlamydiae were found transiently in the joints following intravenous inoculation. This suggests that chlamydiae might also enter the human joint. However, the observations in mice have not, so far, been helpful in establishing the mechanism of human arthritis thought to be chlamydial because none of the mice given chlamydiae extra-articularly developed arthritis either in the presence or the absence of antibody.

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Introduction

Sexually acquired reactive arthritis (SARA) develops in 1%–2% of patients after non-gonococcal urethritis (NGU). In addition, extensive genital tract infection, especially in women, may be associated with sacro-iliitis and spondylitis, and arthritis is well-recognized also as a complication of lymphogranuloma venereum. It is known that *Chlamydia trachomatis* is the cause of almost half the cases of NGU and that it is a triggering factor in the development of SARA in about the same proportion of patients (Keat et al. 1983). The exact mechanism by which arthritis occurs in these patients is, however, not known. The development of a small-animal model of arthritis caused by *C. trachomatis* would be of value in understanding this problem. Progesterone treatment of female CBA mice has enabled us not only to infect the genital tract of these animals with a “fast” egg-killing strain of *C. trachomatis* (Tuffrey and Taylor-Robinson 1981) but also to produce a polymorphonuclear leucocyte response in the genital tract (Tuffrey et al. 1982). In view of this, we considered it worthwhile to determine whether the chlamydiae were confined to the genital tract of the CBA mice or distributed more widely and, in particular, whether they reached and invaded the joints. In addition, we have looked at the distribution of the same strain of *C. trachomatis* given intravenously and the fate of these organisms when inoculated intra-articularly.

Materials and Methods

*Mice.* Seven-week-old female CBA/Ca and congenic CBA/nu mice, bred and maintained in the specific-pathogen-free unit at the Clinical Research Centre, were used. After inoculation, the nude mice were kept in an isolator, which had filtered inlet air, and were removed only briefly for experimental procedures.

*Chlamydia* strain. The “fast” egg-killing human strain of *C. trachomatis*, designated SA-2f, was used. This strain has been identified as an LGV-2 serotype (Wang and Grayston 1971).

**Inoculation of mice.** Chlamydiae were inoculated either into the uterus, or into the knee joints, or intravenously. Since mice inoculated genitally received the progesterone preparation Depo-Provera, additional progesterone-treated animals were included in the groups inoculated via the other routes. Progesterone-treated mice were anaesthetised and inoculated genitally as described before (Tuffrey and Taylor-Robinson 1981) by introducing 0.1 ml of a suspension containing $10^5$ inclusion-forming units (i.f.u.) of strain SA-2f through a 30-gauge needle directly into the uterus. For intra-articular inoculation, the hind legs of progesterone-treated or untreated mice were depliated before 0.05 ml of a suspension containing $5 \times 10^4$ i.f.u. was introduced through a 30-gauge needle into each joint. Mice serving as controls were inoculated only with the sucrose-phosphate transport medium, which contained 10% fetal calf serum (2SP). Other groups of mice were inoculated with 0.1 ml containing $10^5$ i.f.u. through a tail vein.

Detection of *chlamydiae.* Vaginal swabs were obtained from each mouse 7 days after genital inoculation to confirm infection. Vaginal swabs were also taken from the mice in