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Toxoplasmosis

Contact with cats and eating rare meat are normal pleasures, but both are associated with the risk of contracting toxoplasmosis, probably the most frequent zoonosis in Britain today. Fortunately it rarely causes serious disease and most infections are subclinical. Almost half of a group of men and women aged over 60 in a study in London[1] had serological evidence of previous infection, and around one-third of adults in Britain have toxoplasma antibodies in their blood.

Toxoplasma gondii is a protozoal parasite of mammals and birds in all parts of the world. One primary host is the cat, in whose alimentary tract *T gondii* has a sexual cycle leading to the production of oocysts passed in the faeces, thus contaminating soil—in which they can survive for many months. Other species, including man, may be infected by contact with soil. The oocysts are presumed to be swallowed by children sucking their fingers, by gardeners eating food without first washing their hands, or by anyone eating unwashed vegetables such as lettuce. Undercooked meat is another source of human infection. In the United States a family outbreak of toxoplasmosis[2] was thought to be due to eating rare lamb. A study of a group of French children[3] found that those who ate undercooked beef had a significantly higher incidence of toxoplasma antibodies than others who were served adequately cooked meat. When rare lamb was consumed the incidence was even higher—10 times that of a control population.

Toxoplasmosis is one of the infectious mononucleoses, the other two being glandular fever and cytomegalovirus infection. Clinically the most prominent feature is lymphadenopathy, especially of the cervical nodes, with a predominance of mononuclear cells in the peripheral blood. The results of the Monospot and Paul-Bunnell tests are always negative. Only 300 or so cases of toxoplasma lymphadenopathy are notified annually to the Public Health Laboratory Service for England and Wales, but its recognition is important in the differential diagnosis of enlargement of the lymph nodes. Both clinically and histologically toxoplasmosis may be confused with Hodgkin's disease (and, indeed, the two may co-exist).

Latent toxoplasma infection may become active during immunosuppression, providing a further example of an opportunist infection. *T gondii* is an intracellular pathogen which itself can cause depression of cell-mediated and humoral immunity. Primary infections may also develop in the immunocompromised host, especially one with lymphatic or haematological cancer, in whom the nervous system is the most common site of toxoplasma infection, with meningoencephalitis the usual presentation. The most important focal manifestation of toxoplasmosis is a necrotising retinitis producing yellowish white fundal exudates. Toxoplasmosis developing during early pregnancy may infect the fetus, the baby being born with serious lesions including mental subnormality, cerebral calcification, and chorioretinitis. Fortunately, congenital toxoplasmosis is rare in Britain, fewer than 50 cases being recognised annually in England and Wales, but in France one in every 2000 pregnancies is said to be affected.

The diagnosis of toxoplasmosis may be confirmed by culture of the organism from blood or cerebrospinal fluid by inoculation of mice, by histological examination of a lymph node, or by serological tests. Determination of serum concentrations of antibodies is the usual way for the diagnosis to be confirmed. The Public Health Laboratory Service has just published a useful monograph[4] on the laboratory diagnosis of toxoplasmosis, which provides detailed technical information on the various laboratory techniques and also on their interpretation.

Most toxoplasma infections are self-limiting, and treatment is not necessary. The exceptions are patients with eye disease and those who are immunocompromised. Pyrimethamine given together with a sulphonamide for several weeks is usually recommended, but adverse reactions are common. Pyrimethamine, like trimethoprim to which it is related, is a folate antagonist and can, therefore, cause blood dyscrasias. Other drugs that have been tried include co-trimoxazole and the macrolide antibiotic spiramycin (which is used in France for treating infections in pregnancy when folic acid inhibitors are contraindicated). None of these drugs is of proved efficacy.

What about prevention? Fortunately, toxoplasmosis seldom causes serious illness in the non-pregnant and those with normally functioning defences against infection. Though the exact mechanism by which the disease is contracted remains uncertain, simple precautions for those at risk should include not eating undercooked meat and, if possible, avoiding contact with cats' faeces. Handwashing before food, especially after gardening, should be mandatory for those susceptibles if there is a cat in the house. Children's sand-pits should be covered when not in use, though a case could be made for encouraging

infection in childhood to provide immunity to toxoplasmosis for pregnant women.

[1] Fleck DG. Toxoplasmosis. *Public Health (London)* 1969;**83**:131-5.
[2] Masur H, Jones TC, Lempert JA, Cherubini TD. Outbreak of toxoplasmosis in a family and documentation of acquired retinochoroiditis. *Am J Med* 1978;**64**:396-402.
[3] Desmonts G, Couvreur J, Alison F, Baudelot J, Gerbeaux J, Lelong M. Étude épidemiologique sur la toxoplasmose: de l'influence de la cuisson des viandes de boucherie sur la fréquence de l'infection humaine. *Revue Francaise d'Etudes Cliniques et Biologiques* 1965;**10**:952-8.
[4] Fleck DG, Kwantes W. *The laboratory diagnosis of toxoplasmosis.* Public Health Laboratory Service Monograph Series No 13. London: HMSO, 1980.

Children born as a result of incest

After an address to the Medicolegal Society on the crime of incest, Sir Desmond Ackner[1] asked, "To what extent is it a serious eugenic risk if brother and sister marry?" There was no response from his audience. Father-daughter and brother-sister unions result in inbreeding four times as intense as in first-cousin marriages. The surveys of the extra risks of recessive disorders and congenital malformations to the children of first cousins have not, however, given enough information to permit reliable extrapolation to the children of incestuous unions. There are also obvious difficulties in following up closely children born to a random sample of incestuous unions without causing distress to the families.

Nevertheless, three studies have been reported. The largest, a retrospective survey of 161 children, was from Czechoslovakia[2] in 1971. Rare recessive or probably recessive disorders found in the children included homocystinuria, adiposogenital syndrome, congenital ichthyosis, retinitis pigmentosa, and deaf-mutism as well as a high incidence of mental retardation. Fewer than half the children were normal. This study might possibly have been biased by some selection in the sources from which the children were ascertained. The other two studies,[3 4] one from England of 13 live-born children followed up for four to six years and one from Michigan of 18 live-born children followed up for six to 12 years, were prospective, with the children being ascertained during their mothers' pregnancies.

Of the 31 children in these two studies—12 born to father-daughter and 19 to brother-sister matings—only 13 were normal. Two died from recessive disorders (cystic fibrosis and glycogen-storage disease) and one from an almost certainly recessive disorder causing progressive cerebral degeneration and loss of vision. Two of those alive probably had recessive disorders, both with severe mental retardation with cerebral palsy, and one a possibly recessive disorder, severe non-specific mental retardation. Two others had died in the neonatal period, a baby with very low birth weight and another with respiratory-distress syndrome. Two had congenital malformations, a lethal Fallot's tetralogy and a survivor with bilateral cleft lip. Eight other survivors were mildly mentally retarded with IQs in seven ranging from 59 to 76; the eighth, whose IQ score was not available, was in a school for the educationally subnormal.

This increase in recessive disorders—between three and six cases in 31 children compared with an expected incidence[5] in the general population of two or three per thousand—is in line with expectations. It is compatible with a lesser increase in the children of first cousins, and with the average person carrying one or two recessive genes which when homozygous will cause a serious disorder in live-born children. The average person may well carry further recessive genes which when homozygous will cause early death in utero; but there are no good data on this.

A relatively smaller increase in common congenital malformation, two cases in 31 children compared with about 2% in the general population,[6] is also what might be expected. Inbreeding increases the variance of the genetic liability to multifactorial conditions. The increased incidence of mild mental retardation is also noteworthy. It did not, at least in the American series, simply reflect the low level of intelligence of the biological parents. Some lowering of IQ, of less degree, has been found in the offspring of first cousins both from Japan[7] and from Arabs in Israel.[8] New prospective studies are needed from northern Europe and North America of the children of both incestuous unions and first-cousin marriages, making use of modern clinical and biochemical screening for recessive disorders—though these would not be easy to arrange. On the present evidence the risks to the children of father-daughter and brother-sister unions, in contrast to those of first-cousin marriages, seem unacceptable. The risks are probably also unacceptably high in the intermediate case of uncle-niece, half sister-half brother, and double first-cousin marriages—except perhaps in communities where a long tradition of close inbreeding has substantially lowered the carrier prevalence of recessive genes.

[1] Ackner Sir Desmond. The crime of incest. *Med Leg J* 1980;**48**:79-91.
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[3] Carter CO. Risk to offspring of incest. *Lancet* 1967;i:436.
[4] Adams MS, Neel JV. Children of incest. *Pediatrics* 1967;**40**:55-62.
[5] Carter CO. Monogenic disorders. *J Med Genet* 1977;**14**:316-20.
[6] Leck I. Congenital malformations and childhood neoplasms. *J Med Genet* 1977;**14**:321-6.
[7] Schull WJ, Neel JV. *The effect of inbreeding on Japanese children.* New York: Harper and Row, 1965.
[8] Bashi J. Effect of inbreeding on cognitive performance. *Nature* 1977;**266**:440-2.

Colposcopy

When Hinselmann[1 2] first described the colposcope 50 years ago cervical cancer was thought to begin as an invasive lesion in a small focus or nodule. The colposcope was meant to help the human eye identify this first, cancerous spot. For many years descriptions of the instrument and its use were confined to German publications, where a highly specialised and cumbersome colposcopic terminology developed which had little appeal to the English-speaking world.[3] In time Papanicolau's description[4] of exfoliative cytology, and a growing awareness of the widespread, subtle, cellular changes within the cervical epithelium that precede invasive cancer, focused the attention of gynaecologists on cervical cytology rather than on colposcopy. This led to more frequent use of cone biopsy—on receipt of a positive cervical smear gynaecologists wanted the pathologist to differentiate between dysplasia, carcinoma-in-situ, and microinvasive or invasive cancer of the cervix.[5]

In North America[5] and in Britain[6] the investigation and management of patients with abnormal cervical smears have recently taken a new turn with the reappearance of colposcopy as a technique that bridges the gap between Papanicolau-smear screening and definitive histological diagnosis. Coppleson has