Correspondence

Journal of Medical Genetics, 1980, **17**, 157-158

HLA Bw35 antigen and human reproduction

SIR,

That the HLA system plays an important part in the maternal-fetal relationship has been postulated by several investigators.¹⁻⁵ Finn suggested that these antigens might serve as cell surface 'repellents', contributing to the survival of the fetal allograft.⁶ A possible linkage of the HLA locus with differentiation alloantigens has also been suggested by Erickson.⁷ Abnormalities or absence of such antigens could be associated with failures of embryogenesis and birth defects.

Kamidono *et al*⁸ recently reported a high incidence of Bw35 antigen in couples with unexplained infertility. Komlos and co-workers⁹ in 1977 observed that a higher frequency of common HLA antigens was shared by both members of couples who had had repeated miscarriages compared to controls. From their data, it also appears that the incidence of Bw35 in wives (45.4%) is higher than in husbands (35.0%).

Thirty-five couples from Rome who had had repeated miscarriages (number of consecutive miscarriages ≥ 3) were studied. Routine clinical investigations, both morphological and functional, were negative. Eighteen couples with unexplained infertility were also examined.

The distribution of Bw35 antigen in couples with repeated miscarriage, in couples with infertility, and in a control sample from the same population, separately for females and males, is shown in the table. Females with repeated miscarriages or sterility show a higher incidence of Bw35 compared to males and to controls.

Bw35 antigen has been reported in association with thyrotoxicosis (in Japan), subacute thyroiditis,¹⁰

and non-streptococcal (probably viral) glomerulonephritis.¹¹ The present data suggest that this antigen may also be important in human reproduction, and further investigations into its role in the maternal-fetal relationship and intrauterine development are needed.

MARIA PURPURA, ISA COGHI, MARIA NICOTRA,
ERMINIA CARAPELLA, AND E. BOTTINI
*Central Laboratory of Blood Transfusion,
Italian Red Cross;
Departments of Obstetrics and Child Health,
University of Rome; and
Department of Genetics, University of Camerino,
Italy*

References

- Clarke B, Kirby DRS. Maintenance of histocompatibility polymorphisms. *Nature* 1966;**211**:999-1000.
- Billington WD. Immunological processes in mammalian reproduction. In: Adinolfi M, ed. *Immunology and development*. London: Spastic International Medical Publishers, 1969:89-113.
- Cepellini R. Old and new facts and speculations about transplantation antigens of man. In: *Progress in immunology*. New York: Academic Press, 1971:973-1025.
- Amos DB, Bodmer WF, Cepellini R, *et al*. Biological significance of histocompatibility antigens. *Fed Proc* 1972; **31**:1087-104.
- Beer AE, Billingham RE. Immunoregulatory aspects of pregnancy. *Fed Proc* 1978;**37**:2374-8.
- Finn R. Survival of the genetically incompatible fetal allograft. *Lancet* 1975;**1**:835-8.
- Erickson RP. Differentiation alloantigens, histocompatibility loci, and birth defects. *Am J Hum Genet* 1975; **27**:554-7.
- Kamidono S, Mayumi K, Tanikaze S, Ishigami J, Isojima S, Tsuji K. HLA antigens in male sterility and infertile couples (in Japan). In: *Abstract 5th European Congress on Sterility and Fertility*. Rome: Minerva Medica, 1978:196.
- Komlos L, Zamir RJ, Halbrecht I. Common HLA antigens in couples with repeated abortions. *Clin Immunol Immunopathol* 1977;**7**:330-5.
- Svejgard A, Ryder LP. HLA and disease. In: Ferrara GB, ed. *HLA system—new aspects*. Amsterdam: Elsevier, 1977:143-51.
- HLA and disease: a conundrum. *Br Med J* 1976;**2**:546-7.

TABLE Distribution of Bw35 antigen in couples with repeated miscarriages, in couples with sterility, and in a random sample of normal adults from the same population.

		Bw35 Present	Absent	% positive
Repeated miscarriage	Females (A)	18	17	51.4
	Males (B)	9	26	25.7
	Females (C)	7	11	38.9
Sterility	Males (D)	4	14	22.2
	Females (E)	33	72	31.4
Normal adults				
	Males (F)	30	76	28.3

Comparisons: A vs B, $p < 0.03$; C vs D, NS; (A+C) vs (B+D), $p < 0.02$; A vs E, $p < 0.05$; (A+C) vs E, $p < 0.05$.

Multiple polyposis of the colon

SIR,

The paper by Lynch *et al* (*J Med Genet* 1979; **16**: 1-7), proposing that the autosomal dominant gene for multiple polyposis of the colon could sometimes express itself as a solitary adenocarcinoma, brought to mind a family I first saw in 1954. By now 6 of 7

sibs have multiple polyposis of the colon proved at surgery or necropsy. The eldest was the subject of a case report by Carlson and Novacovich (*J Int Coll Surg* 1952; XVIII: 534-40). The father of these sibs died at the age of 70 of cancer of the lung, and had no near relatives with GI cancer. The mother died at the age of 42 of an annular constricting carcinoma of the splenic flexure with metastases to the liver. She had had a purulent peritonitis, and the mucosa of the ileum, ascending and transverse colon showed numerous small ulcerations, 1 to 7 mm in diameter. The descending colon showed one small pedunculated polyp. This woman's mother (IT) died of 'cancer of the rectum' at the age of 45, and was thought by the family to have had multiple polyposis.

It seems very likely that IT carried the multiple polyposis gene even though she did not have multiple polyps, and at the time I looked, unsuccessfully, for evidence that the polyps might disappear once a malignancy had developed. However Professor Lynch's paper supports the idea that the correct interpretation was variable expressivity of the gene for multiple polyposis.

F CLARKE FRASER
Department of Medical Genetics,
Montreal Children's Hospital,
Montreal, Canada H3H 1P3

Prenatal study of X-linked aqueductal stenosis

SIR,

X linked aqueductal stenosis (XAS) is an uncommon but well recognised heritable form of hydrocephalus.^{1,2} The underlying defect is not known. We report the use of ultrasound in the middle trimester of a pregnancy at risk for XAS.

The proband was a woman whose brother had died in the neonatal period of hydrocephalus, as had her sister's son. Necropsies had not been done and a diagnosis of XAS was not certain, but she knew there was a risk of hydrocephalus in male offspring.

Ultrasound examination of the fetus at 17 and 24 weeks' gestation showed biparietal diameters of 3.8 and 5.9 cm, respectively. These values could not be distinguished from controls. An x-ray of the pelvis at 36 weeks' gestation showed a large fetal head, and

a hydrocephalic male infant was delivered by caesarian section. A CAT scan showed stenosis of the aqueduct of Sylvius and confirmed the existence of XAS in this family.

Enlargement of the fetal head in XAS has been noted by x-ray at 32 weeks' gestation as reported by Cassie and Boon.³ Ultrasound examination in the middle trimester did not show the presence of hydrocephalus in the pregnancy of our patient before 24 weeks; enlargement of the fetal head occurred in the last trimester. The physician should not rely on ultrasound in the middle trimester for the prenatal diagnosis of XAS in a pregnancy at risk.

PAUL BENKE AND RICHARD STRASSBERG
Departments of Pediatrics and Obstetrics,
University of Miami School of Medicine,
Miami, Florida 33152, USA

References

- ¹ Bickers DS, Adams RD. Hereditary stenosis of the aqueduct of Sylvius as a cause of congenital hydrocephalus. *Brain* 1949;72:246-62.
- ² Shannon MW, Nadler HL. X-linked hydrocephalus. *J Med Genet* 1968;5:326-8.
- ³ Cassie R, Boon AR. Sex linked hydrocephalus. *J Med Genet* 1977;14:72-3.

John Fraser Roberts's 80th birthday

SIR,

Will you kindly allow me to use your columns for a happy report, an occasion near to the hearts of all clinical geneticists, indeed of all who are involved in the different aspects of genetic advice. John Fraser Roberts was born on 8 September 1899. He started the first genetic advice clinic in this country at the Hospital for Sick Children, Great Ormond Street in 1946, and this has grown from strength to strength.

For his work and for his leadership in medical genetics and genetic counselling we are deeply grateful. May we say how delighted we are at the continued happiness he derives from his work, and may we extend to him our warmest wishes on this happy occasion?

PAUL E POLANI AND COLLEAGUES
Paediatric Research Unit,
Guy's Hospital,
London SE1 9RT.