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Genetic study of Welsh gypsies

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SUMMARY A South Wales gypsy kindred of Romany origin had a high incidence of phenylketonuria along with other recessively inherited disorders. There was a high degree of consanguinity ($F = 0{\cdot}017$) with an excess of non-specific mental subnormality among known consanguineous matings. Phenylketonuria and a number of other recessively inherited disorders have been recorded from other Romany gypsy populations, but it is uncertain whether this results from a generally high gene frequency for the disorders or from consanguinity and other more local factors.

The language, social structure, and ethnic origin of the gypsies of Britain and other parts of Europe have been extensively studied but genetic observations have been few. The present study of gypsies in Wales originated from the detection of the recessively inherited disorder phenylketonuria in two newborn gypsy children and the discovery that not only were there other cases but that all formed part of a single extensive kindred. Genetic data and blood samples were collected during the years 1972 to 1975. This paper reports details of the kindred, its genetic structure, and the occurrence of phenylketonuria and other genetic disorders within it. A subsequent paper (Harper *et al.*, 1977) will report on blood groups and other genetic markers and discuss them in relation to the possible origins of the Welsh gypsy population.

Methods

Pedigree data were obtained by personal visits to the homes of families. Particular inquiry was made about infant deaths, miscarriages, and stillbirths, and cases of mental retardation. Details of former generations were obtained independently from several older members of the kindred to compensate for the lack of written records. Once initial reluctance had been overcome all branches of the kindred proved willing and consistent informants. In particular the occurrence of consanguineous marriages was not concealed, these being regarded in general as desirable.

The diagnosis of phenylketonuria was established initially by thin-layer-chromatography of heparinised blood samples, giving a semiquantitative estimate of plasma phenylalanine. The diagnosis was confirmed in positive cases by fluorimetric measurement of plasma phenylalanine in an amino-acid auto-analyser. Urine samples were tested by paper chromatography for the metabolite ortho-hydroxy-phenyl-acetic acid. Samples were taken from all individuals known or suspected to be mentally retarded. All children born in Wales since 1968 have been screened at birth for the disorder (Bradley, 1975).

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Results

THE KINDRED

The majority of gypsies of Romany origin living in South Wales were found to belong to a single extensive kindred (see Fig.). There were numerous consanguineous marriages and individuals with recessively inherited disorders, including phenylketonuria (discussed below). The ancestry of the kindred in South Wales derives from the marriage of a Romany individual with a non-Romany Englishman in the early 19th century. Their descendants have maintained a travelling existence in South Wales since that time. The total size of the South Wales Romany gypsy population has been estimated at about 1200, a figure which includes a number of families belonging to primarily English gypsy kindreds at present living in Wales and which is obtained from a government census in 1965. This included a variety of travellers of non-Romany extraction in the estimate, but it is also known to have omitted a number of Romany families, so that the final estimate is likely to be essentially correct.

CONSANGUINITY

Table 1 shows the degree of consanguinity present in the 99 matings documented in the present study: 43

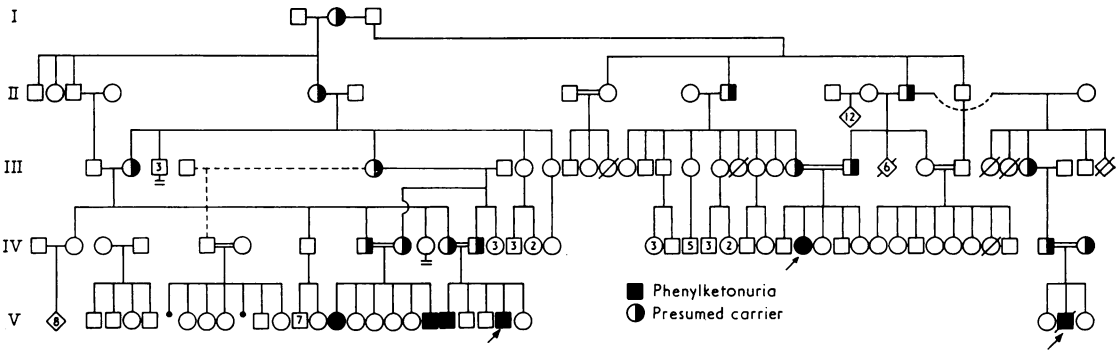

Fig. *Phenylketonuria in a Welsh gypsy kindred.*

represent known consanguineous unions while in only 24 is 1 partner of non-Romany origin. An approximate estimate of the coefficient of consanguinity (F) of the population may be obtained from the contribution of 1st cousin (F-$\frac{1}{16}$) and 2nd cousin (F-$\frac{1}{64}$) matings, which gives an overall coefficient of consanguinity of 0·0122 for the population (Table 2). Since the 32 inter-Romany matings not known to be consanguineous can be presumed to have a coefficient of consanguinity of this value on the assumption that this degree of consanguinity was present in earlier generations, a correction based on this must be added, giving a final estimate of F = 0·0170.

INCIDENCE OF PHENYLKETONURIA

Testing of mentally retarded individuals and newborn infants showed 6 individuals in 4 sibships to be affected with phenylketonuria. In 3 instances the disorder was detected in the newborn period, and appropriate dietary treatment instituted. Diagnosis was delayed till the age of 6 months in 1 member, while 2 older mentally retarded children, previously undiagnosed, were found to be phenylketonuric on testing of the families. The disorder was considered to be classical phenylketonuria with blood phenylalanine levels of greater than 20 mg/100 ml and with metabolites of phenylpyruvic acid in the urine, though the appearance of these was delayed till after 1 month old in 2 individuals.

Table 3 compares the incidence of phenylketonuria and the gene frequency for phenylketonuria in the Welsh gypsy population with that found for all births in Wales during the years 1971 to 1974. For the gypsy population only individuals under 20 years of age are considered, since the disorder is unlikely to have been diagnosed and may have carried a high mortality in groups born previous to this.

There is an incidence of about 1 in 40 of phenylketonuria in the Welsh gypsy population compared with 1 in 16 000 in Wales as a whole. About 1 in 4 of Welsh gypsies would be expected to be a carrier of the phenylketonuria gene compared with around 1 in 60 individuals in Wales as a whole, assuming Hardy Weinberg equilibrium. Correction for consanguinity reduces the frequency of heterozygotes slightly (from 0·264 to 0·257).

OTHER DELETERIOUS AND LETHAL RECESSIVE GENES

Apart from phenylketonuria, 2 other disorders showing autosomal recessive inheritance were identified. One child with a progressive neurological deterioration was shown to have metachromatic leucodystrophy, confirmed by extremely low levels of the enzyme aryl-sulphatase A. A younger sib is

Table 1 *Consanguinity in 99 matings*

Type of mating	*Generation*					*Total*
	1st	*2nd*	*3rd*	*4th*	*5th*	
1st cousin	—	2	9	3	—	14
2nd cousin	—	—	10	12	—	22
Consanguinous (more remote than 2nd cousin)	—	6	—	1	—	7
Inter-Romany (no known consanguinity)	—	—	22	10	—	32
Romany-non Romany	2	2	10	10	—	24
Total	2	10	51	36	—	99

Table 2 *Coefficient of consanguinity (F) of population*

Type of mating	*F*	*No. of matings*	*Contribution to Total F*
1st cousin	$\frac{1}{16}$	14	$14 \times \frac{1}{16} = 0{\cdot}875$
2nd cousin	$\frac{1}{64}$	22	$22 \times \frac{1}{64} = 0{\cdot}33$
Other inter-Romany	0·0122	39	$39 \times 0{\cdot}0122 = 0{\cdot}475$
Overall	0·0170	99	1·68

Table 3 *Incidence of phenylketonuria*

	Welsh gypsies (< 20 years)	*Wales, all newborns (1970-1974)*
Cases of phenylketonuria	6	12
Total population	242	172 785
Incidence of phenylketonuria	0·0247	$6{\cdot}96 \times 10^{-5}$
Phenylketonuria gene frequency (q)	0·157	0·00827
Heterozygote frequency (2pq)	0·264	0·0165
Corrected for consanguinity (F = 0·0170)	0·257	—

subsequently known to be affected. Two sibs were identified with congenital nystagmus without any specific underlying ocular disorder found on ophthalmic examination.

A study of individuals showing non-specific mental subnormality, excluding those with phenylketonuria and other known cases, was made and the incidence in consanguineous and non-consanguineous matings compared. These are shown in Table 4 together with data on infants deaths, spontaneous abortions, and stillbirths, and infertile unions.

A considerable excess of cases of non-specific mental subnormality is shown in the offspring of consanguineous matings (19 cases) compared with the non-consanguineous matings (1 case), a difference which is highly significant statistically ($\chi^2 = 19{\cdot}0$; $P < 0{\cdot}001$). A less significant excess of abortions and stillbirths is also seen in the consanguineous group ($\chi^2 = 5{\cdot}79$; $0{\cdot}01 < P < 0{\cdot}02$) and the phenylketonuric offspring are confined to consanguineous matings. No obvious difference is seen in fertility as measured by total liveborn offspring or in the number of infertile unions.

Discussion

ORIGINS OF GYPSY POPULATIONS

The origin of the gypsy populations of Europe appears, both on historical and linguistic grounds, to be from Northern India, and this is supported by blood group studies to be discussed in a subsequent paper (Harper *et al.*, 1977). British gypsies are thought to be descendants of a number of groups who travelled across Italy and France, reaching Britain in the late 14th century, from which the first historical evidence derives.

In Wales the gypsy population appears to consist of 2 major groups. The most extensively documented is that of North Wales, in particular the Wood kindred, for which accurate genealogies have been compiled by Sampson (1926) extending to the mid-17th century. This group was found by Sampson to be speaking the pure Romany language at the beginning of the present century, and it formed the source of his philological studies (1934). The second group, principally inhabiting South Wales and with no immediate relation with that of North Wales, forms the subject of the present study and derives, as discussed above, from the marriage of an English (Shropshire) gypsy with a non-Romany individual in the early 19th century. The Romany language is spoken in South Wales only by older members of the gypsy community.

CONSANGUINITY

Genetic studies of gypsies, in contrast to sociological and linguistic studies, have been few in number. Avcin (1969) assessed the consanguinity of a Yugoslav gypsy population by means of isonymy and found that over 70% of the population of some villages bore the same surname. No attempt was made to estimate the coefficient of consanguinity by means of genetic relationships.

The coefficient of consanguinity ($F = 0{\cdot}0170$) found in the present study is extremely high, approaching that seen in such extreme isolates as the Hutterites ($F = 0{\cdot}0216$; Mange, 1964) and greatly exceeding that for stable rural British communities such as Warkworth, Northumberland ($F = 0{\cdot}0063$–$0{\cdot}0072$; Rawling, 1973). Nevertheless, endogamy is not complete: about a quarter of the marriages during the past 3 generations were with individuals of non-Romany origin.

The principal genetic effect of consanguinity is to increase the expression in homozygous state of those disorders and characteristics showing autosomal recessive inheritance, and examples of this in the Welsh gypsy population are seen in the high incidence both of non-specific mental subnormality and of specific disorders such as phenylketonuria among the offspring of consanguineous marriages. Previous studies on gypsies have not noted a high incidence of mental subnormality, but Avcin (1969) found a high prenatal and neonatal mortality of 25 to 28%, though he did not analyse his data for consanguineous marriages separately.

There are several reports of phenylketonuria in other gypsy populations (Blehova *et al.*, 1959;

Table 4 *Comparative data in consanguineous and non-consanguineous matings*

	Consanguineous Unions	*Non-consanguineous Unions*	*Total*
Total number of unions	43	56	99
Sterile unions	4	8	12
Total live births	129	149	278
Abortions and stillbirths	11	3	14
Infant deaths	4	1	5
Non-specific mental subnormality	19	1	20
Phenylketonuria	6	0	6

Table 5 *Recessively inherited disorders recorded in gypsy populations*

Disorder	*Country*	*Source*
Phenylketonuria	England	Carter and Woolf (1961)
		Barton (personal communication)
	Wales	Present study
	Czechoslovakia	Blehova *et al.* (1959)
Galactokinase deficiency	Switzerland	Gitzelmann (1967)
	Austria	Thalhammer *et al.* (1968)
Citrullinaemia	Germany	Passarge (1975)
Menkes syndrome (X-linked)	Holland	Van de Kamp *et al.* (1975)
Seckel syndrome	England	Siggers (personal communication)
Wilson's disease	England	Shaw (personal communication)
Congenital nystagmus	Wales	Present study
Metachromatic leucodystrophy	Wales	Present study

Carter and Woolf, 1961), but it is uncertain at present whether our finding in Welsh gypsies reflects a generally high gene frequency for the disorder in gypsies or whether it is simply a feature of Welsh gypsies. This is of practical importance since, while all newborn children in Britain are tested for the disease, the gypsy population is particularly likely to be missed owing to its travelling mode of life. In our particular kindred it is in fact possible that the gene is derived from a non-Romany source, since the only ancestor common to all cases of the disease is a woman who was not herself of gypsy origin. Out of the phenylketonuria genes present in the 6 confirmed cases 11 could be derived from this individual, the line of presumed descent being indicated by the half-shaded symbols in the Figure.

There is no evidence that the high incidence of phenylketonuria in the present kindred is of Irish origin, though intermarriage with Irish individuals has occurred. It should also be noted that while a high frequency of phenylketonuria is characteristic of Irish-Scottish (Goedelic) Celts and those areas influenced by them (Saugstaad, 1975) it is at relatively low frequency in the Brythonic Celts of Wales, Cornwall, and Brittany (Harper, 1976, and in press).

The available data on other recessively inherited disorders recorded in gypsies are shown in Table 5. The unpublished observations were given in reponse to a request for information on genetic disorders in gypsies (Harper and Williams, 1975) and it remains to be seen whether the incidence of the disorders is high in gypsy populations generally. Careful distinction must be made in these instances between true gypsies of Romany origin and other itinerant groups, often referred to as gypsies by the public. Thus the Scottish 'tinkers' with goitrous cretinism resulting from dehalogenase deficiency (Hutchison and McGirr, 1956) were of Irish not Romany origin, while the family with phenylketonuria reported by Klein (1946) and mentioned by Carter and Woolf (1961) are reported as being 'tramps' and 'Bohemians' but not specifically as gypsies.

The authors would like to make a plea for further study of genetic disorders in Romany gypsy populations while their identity remains distinct.

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