Brit. J. Psychiat. (1982), **140**, 410–415

Season of Birth in High and Low Genetic Risk Schizophrenics

ERIC SHUR

Summary: Hypotheses which have been proposed to account for the unusual seasonal birth pattern observed in schizophrenic populations are discussed. These competing hypotheses were tested by retrospectively studying season of birth in 975 schizophrenics divided according to family history of psychiatric illness. Information was obtained from case notes, item sheets, and questionnaires sent to general practitioners. The results were inconclusive, but there was a trend for high genetic risk cases to be born less often in the first quarter of the year. Although no clear support could be provided for one or other season of birth hypothesis, it is tentatively suggested that a seasonal constitutional damage factor may be responsible for the excess of births described in schizophrenic populations in the early months of the year.

Schizophrenics show an unusual seasonal birth pattern compared to normal populations. A significant excess of births in the early months of the year has been demonstrated for schizophrenics in England and Wales (Hare *et al*, 1974), Eire (O'Hare *et al*, 1980), Scandinavia (Videbech *et al*, 1974; Dalen, 1968, 1974; Ødegård, 1974) and the United States (Torrey *et al*, 1977). This is not due to any known statistical or demographic artefact (Dalen, 1974; Hare, 1975), and other hypotheses have been proposed to account for the findings. The 'genetic gain' hypothesis proposes that schizophrenic genotype confers 'robustness' which protects against allergies or infections which may cause mortality in the early months of the year, thus allowing preferential survival of infants with schizophrenic genotype who are born in winter (Huxley, 1964; Buck *et al*, 1977; Jones and Frei, 1979). Secondly, the 'season of conception' hypothesis states that parents of schizophrenics conceive more often in the summer months, thus producing an excess of schizophrenics born in the early months of the year (Hare, 1976; McNeil *et al*, 1976). This could be because of unusual reproductive habits, or for biological reasons. Thirdly, the 'constitutional damage' hypothesis states that birth in the early months of the year is associated with constitutional damage (e.g. obstetric complications or viral infections) which predispose to the later development of schizophrenia (Dalen, 1974; Hare, 1976; McNeil and Kaij, 1978).

The genetic gain theory predicts that schizophrenics *at high genetic risk* for the disorder should demonstrate an excess number of births in the early months of the year. Now, if we assume that in any individual, a constant amount of 'stress' (both genetic and environmental) is required to exceed the threshold for the production of schizophrenia, then in each individual the quantities of genetic and environmental stress should be *inversely* related. Therefore, environmental factors should be more marked, on average, in the life histories of schizophrenics for whom hereditary predisposition is low or absent (Kinney and Jacobsen, 1978). Using this argument, the constitutional damage hypothesis would predict that schizophrenics *at low genetic risk* for the disorder should demonstrate excess seasonality of birth. Season of conception probably depends on biological and non-biological factors and therefore is more difficult to test.

Kinney and Jacobsen (1978) studied season of birth in 34 schizophrenic adoptees and found a significant excess of low genetic risk patients born in the early months of the year, although their whole sample did not show an unusual birth pattern. This small study was interpreted as supporting the hypothesis of constitutional damage.

In order to test these competing hypotheses, I carried out a retrospective controlled study of season of birth in 975 schizophrenics, divided according to genetic risk.

Methods

All patients with a primary diagnosis of schizo-

phrenia (International Classification of Diseases Diagnosis 295.0–295.9), who had been admitted to The Maudsley and Bethlem Royal Hospitals between 1967 and 1978, were identified (patients born outside the United Kingdom, Eire, Europe and the USA were excluded) and their date of birth was noted. At the time of discharge from hospital the psychiatrist responsible for the care of the patient completes an *item sheet* which codes certain information about the patient, including family history of psychiatric disorder. Patients were classified as being at high or low genetic risk for any psychiatric disorder (APD) according to whether or not they had a first or second degree relative who had ever attended a psychiatric clinic or hospital or had a history of suicide. The case notes of all high risk cases were scrutinized in order to obtain more information about disorder in the relative. Where this was unclear, general practitioners were sent a questionnaire requesting more information. On the basis of information from item sheets, case notes and general practitioners, patients were classified into 4 groups without knowledge of their dates of birth:—

(1) *Genetic risk unknown:* no information about relatives obtained.

(2) *High genetic risk (SCZ):* when a definite or probable diagnosis of schizophrenia could be made in first or second degree biological relatives.

(3) *High genetic risk (APD):* when any psychiatric disorder had been diagnosed in first or second degree biological relatives.

(4) *Low genetic risk:* when no known psychiatric disorder was present in first or second degree biological relatives.

Of 1212 schizophrenics identified, date of birth was not known in three. Of the remaining 1209, 173 (14 per cent) were foreign born and excluded. This left 1036 cases among whom the family history was unknown in 61 (6 per cent). Of 975 cases in whom genetic risk was known, 598 (61 per cent) were classified as being at low genetic risk. Of 377 high genetic risk cases, questionnaires were sent in 247 and returned in 127. There were 285 high risk cases with psychiatric illness other than schizophrenia in biological relatives and 92 with schizophrenia in biological relatives. This is shown in the figure.

The genetic risk groups were then compared with each other and with control data from the 1971 Census of England and Wales or live birth figures from the Registrar General (1972) for season of birth.* The genetic risk groups were matched for age and social class, and the control population was matched for age.

Results

The distribution of all schizophrenic births was remarkably similar to expectation: no trend towards an excess of schizophrenics born in the early months of the year was noted. When compared with live births in England and Wales, patients with schizophrenic relatives were born less often in the first quarter of the year by 28 per cent. Those whose relatives had suffered other psychiatric disorders were born less often in that quarter by 16 per cent. These differences were not statistically significant.

The season of birth of high genetic risk patients is compared with that of low genetic risk patients in the Table. Patients with schizophrenic relatives were born less often in the first quarter of the year by 29 per cent: those whose relatives had suffered other psychiatric disorders showed a deficit of births in that quarter of 13 per cent. This finding is likely to occur by chance in fewer than 10 per cent of trials but the overall difference was not statistically significant.

Discussion

Characteristics of the population

The present study found an average annual admission rate of 101 schizophrenics for the Joint Hospitals. The rates were lower for the earlier triennia and increased over the later triennia of the study. Hare (1971) found an annual rate of 104 for patients diagnosed as suffering from schizophrenia or paranoid psychoses for the years 1967–69. If we exclude patients with a paranoid psychosis and take into account the increasing rates over the later triennia of the study, then the annual rate found in this study agrees with Hare's report very closely. Although the sample in the present study appears complete, it may not be representative of the schizophrenic population of Great Britain, because of the social characteristics of the population of Camberwell and the continuing specialist referrals to the Joint Hospitals.

Fourteen per cent of patients were born outside the UK, Eire, Europe and the United States. This is higher than the general population where less than 10 per cent are foreign-born (Lipsedge and Littlewood, 1979). Since immigrants from the West Indies, Asia and Africa are much more likely to be admitted to hospital with schizophrenia than their English-born

* In theory it is best to use live-birth rather than Census data, since differential mortality rates may occur in the groups studied. In practice there is very little difference between the data from these two sources. Unless otherwise stated, expected figures are based on live births. (Registrar General's Tables. Statistical Reviews for England and Wales for 1970. Vol. II, HMSO 1972).

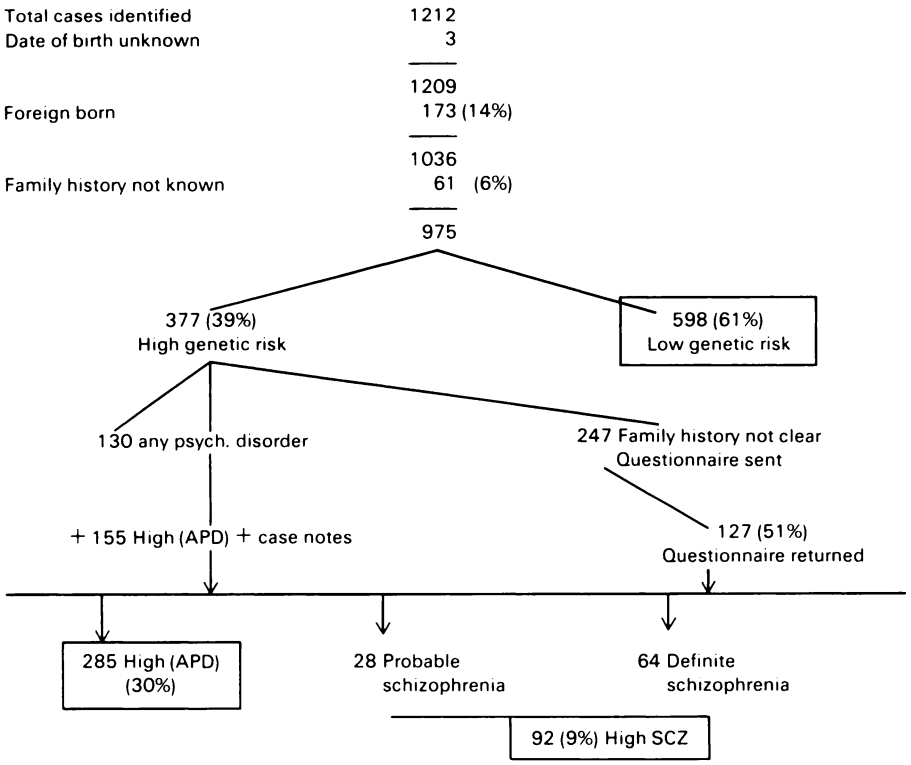

FIG.—Breakdown of 1212 schizophrenics admitted to the Joint Hospitals between 1967 and 1978.
High (APD) = Positive family history of any psychiatric disorder.
High (SCZ) = Positive family history of schizophrenia.
For explanation, see text.

countrymen (Lipsedge and Littlewood, 1979), this finding could be explained in terms of the high immigrant population of Camberwell.

Five hundred and ninety-eight (61 per cent) of the patients had no known family history of psychiatric disorder. Of 377 (39 per cent) patients with a family history of psychiatric disorder, 92 had a family history of definite or probable schizophrenia. Notwithstanding the possibility of under-reporting, this figure is higher than that found in Iowa (Tsuang *et al*, 1980), where probable schizophrenia was found in 5.3 per cent of biological relatives of 375 probands. In the Iowa study, only first-degree relatives were diagnosed using operational criteria. This probably accounts for the difference, but both figures are lower than those expected from earlier morbid risk studies (Slater and Cowie, 1971). Morbid risk studies concern lifetime expectancy for schizophrenia, while in the present study younger relatives may not yet have reached the end of the risk period for the development of schizophrenia at the time of data collection. The figure of 9 per cent found in the present study seems compatible with reports in the literature and is probably an accurate reflection of the proportion of schizophrenics in Camberwell who have a biological relative suffering from the same disorder.

It is notable that 285 schizophrenics (30 per cent) had biological relatives with psychiatric disorders other than schizophrenia. Some patients could have been misclassified as High risk (APD) when in fact they could have had relatives with schizophrenia. Alternatively, this could reflect a genetic loading of the 'spectrum' type (Kety *et al*, 1975). It is also possible that family or social stresses of a non-specific kind could be operating to produce both schizophrenia and other psychiatric disorders in certain families.

Season of birth in the whole population

No unusual season of birth was demonstrated for 975 schizophrenics admitted to the Joint Hospitals between 1967 and 1978. This finding was disappointing, especially as it makes interpretation of season of

https://doi.org/10.1192/bjp.140.4.410 Published online by Cambridge University Press

TABLE

Season of birth of high and low genetic risk patients. Comparison by quarter of year

Quarter of year	High (APD) Observed	Expected	Observed/ Expected (%)	Low Observed	Expected	Observed/ Expected (%)	2×2 Table chi-square 1 d.f.	P
1	81	93.5	87	161	148.5	108	3.7	0.054
2	101	97.5	104	151	154.5	98	0.3	0.6 > P > 0.5
3	108	97.5	111	144	154.5	93	2.5	0.2 > P > 0.10
4	87	88.5	98	142	140.5	101	0.1	0.8 > P > 0.7
Total	377	377		598	598		6.6 3 d.f.	0.1 > P > 0.05
	High (Schiz.)			Low				
1	17	24	71	161	154	105	2.97	0.1 > P > 0.05
2	28	24	116	151	155	97	1.12	0.3 > P > 0.2
3	24	22	109	144	146	99	0.2	0.7 > P > 0.6
4	23	22	105	142	143	99	0.10	0.8 > P > 0.7
Total	92	92		598	598		4.3 3 d.f.	0.3 > P > 0.2

d.f. = degrees of freedom.
P = probability.

birth data among the different genetic risk groups difficult.

The reason for my failure to refute the null hypothesis of season of birth of schizophrenics is not clear, but several possibilities exist:—

(*a*) *Size of the sample*
Previous studies have been made on populations 5–30 times the size of that in the present study and have found excesses or deficits of 6–13 per cent of the expected distribution in certain seasons of the year. With large numbers, these small differences have turned out to be highly statistically significant. However, the present study fails to find even a trend in the expected direction. Thus sample size seems unlikely to account for the present negative finding.

(*b*) *Population bias*
Because of the characteristics of the population of the catchment area (Camberwell) and the specialist referrals to the Joint Hospitals, it may be that this population of schizophrenics is unusual. Nevertheless, it seems unlikely that the present population is biased with respect to season of birth.

(*c*) *Diagnostic practice*
It could be argued that the diagnostic practice of Maudsley psychiatrists is more rigorous or in other ways idiosyncratic compared to that of other psychiatrists, especially those in other countries. This could produce a different population to those studied, for instance, in North America, but again it is difficult to see how this would affect season of birth.

(*d*) *The control population*
Selection of appropriate controls is vital to the interpretation of season of birth data, since the expected values are calculated from the control population. Approximately two-thirds of the schizophrenics in the present study were aged between 21 and 40 years at the time of admission. This means that the majority of patients will have been born between 1936 and 1960. I have used average live-birth figures for these years for England and Wales. The present study included

patients born in Eire, Scotland, USA and Europe, but these accounted for only 14 per cent of the population, 62 per cent of whom were born in England. Ideally, it would have been best to compare season of birth of patients and controls for each quinquennium; however, the number of persons born in each quarter for the years 1936–60 remains remarkable constant between quinquennia. It therefore seems likely that the control population is appropriate.

The genetic risk groups

The genetic risk groups show, by and large, close agreement with chance expectation in season of birth, except that high genetic risk patients (whether their relatives suffer schizophrenia or any other psychiatric disorder) are born less often in the first quarter of the year. Although the differences are not statistically significant, the deficits are of the order of 13–29 per cent which is greater than the 6–13 per cent described in other schizophrenic populations (e.g. Hare *et al*, 1974; Hare, 1975; Torrey *et al*, 1977; Parker and Balza, 1977). Thus, although no conclusive support can be provided for one or other season of birth hypothesis, some points are suggested:—

Firstly, the birth pattern of low genetic risk cases most closely resembles that described in schizophrenic populations. This suggests that a seasonal environmental damage factor may be responsible for the excess schizophrenic births in the early months of the year and is in agreement with the findings of Kinney and Jacobsen (1978).

Secondly, schizophrenics with a genetic loading for psychiatric illness, and more specifically for schizophrenia, demonstrate a birth pattern which differs most (but not significantly) from that of normal and other schizophrenic populations. This may reflect a constitutional trait in parents of high genetic risk cases leading to unusual patterns of childbearing, either for biological reasons or because of idiosyncratic reproductive habits.

In order to produce excess seasonal births of schizophrenics possible environmental damage factors must occur with an increased frequency in the early months of the year. Moreover, they must be linked in some way to the pre-, intra- or perinatal period, and be capable of producing damage of a kind which can result in the later development of schizophrenia.

Studies examining the incidence of obstetric complications (OC) in schizophrenics (McNeil and Kaij, 1978; Moskalenko, 1980) have shown that schizophrenics are significantly more likely to have suffered low birth weight, prematurity, jaundice and hypoxia than controls, and that OC are associated with low IQ, early onset and a poor prognosis. Moreover, stillbirths, fetal and infant mortality and perinatal asphyxia occur preferentially in the early months of the year in several European countries (Dalen, 1974). Several viral illnesses also occur seasonally and rubella, measles and varicella-zoster have peaks in the winter and spring. Virus-like agents have been implicated in the causation of chronic illnesses of the central nervous system and recently Tyrrell *et al* (1979) have demonstrated a virus-like agent in the cerebrospinal fluid of 18 of 47 patients with schizophrenia and only 1 of 25 with medical or surgical conditions. Increased levels of cerebrospinal fluid antibodies to common viruses have also been found in black schizophrenics in the United States (Albrecht *et al*, 1980). It is possible that infection with an agent which occurs more commonly in the early months of the year is contracted at or around the time of birth. At the time of infection or years later, critical areas of the nervous system could be damaged in such a way as to produce schizophrenia. OC and viral infections seem possible candidates for causing critical brain damage in a seasonal way, thus producing an excess of schizophrenics born in the early months of the year.

In considering season of conception, both biological and non biological factors need to be taken into account. In animals, including some higher primates, conception and reproduction vary markedly with the season of the year and seem to be strictly controlled by seasonal rhythms of gonadotrophic release which are entrained to the light-dark cycle (Van Horn, 1980; Lincoln and Short, 1980). It is tempting to explain the sinusoidal birth pattern observed in normal populations on this basis and it is possible that a genetic predisposition to schizophrenia could in some way accentuate these rhythms of seasonal reproduction. Alternatively, a schizoid trait affecting reproductive habits could be at work.

In conclusion, it seems that season of birth studies in schizophrenic populations will have to take account of the possible heterogenesis of the disorder, as well as the multiple factors responsible for the shape of birth curves. This will make the task of the epidemiologist even more difficult in the elucidation of clues as to the aetiology of schizophrenia.

Acknowledgements

This work was supported in part by grants from the Mental Health Foundation and The Maudsley and Bethlem Royal Hospitals. I would like to thank Dr Robin Murray for his drive, patience and ideas, and Dr E. Hare for his constructive criticism and supply of the Census figures. His many papers were an inspiration. Thanks to Mrs Ryan and Mrs Liddle for their secretarial assistance, and to Mr Nortei Amoboe for his help with the computing.

Finally, I would like to thank Stuart Checkley for his interest and support.

References

ALBRECHT, P., TORREY, E. F., BOONE, E., HICKS, J. T. & DANIEL, N. (1980) Raised cytomegalovirus-antibody level in cerebrospinal fluid of schizophrenic patients. *Lancet*, *ii*, 769–72.

BUCK, C., SIMPSON, H. & WANKLIN, J. M. (1977) Survival of neices and nephews of schizophrenic patients. *British Journal of Psychiatry*, **130**, 506–8.

DALEN, P. (1968) Month of birth and schizophrenia. *Acta Psychiatrica Scandinavica*, **203**, 55–60.

—— (1974) *Season of Birth. A Study of Schizophrenia and Other Mental Disorders*. Amsterdam: North Holland/ American Elsevier.

HARE, E. H. (1971) *The Bethlem Royal Hospital and the Maudsley Hospital Triennial Statistical Report, 1967–1969*.

—— (1975) Season of birth in schizophrenia and neurosis. *American Journal of Psychiatry*, **132** (11), 1168–72.

—— (1976) The season of birth of siblings of psychiatric patients. *British Journal of Psychiatry*, **129**, 49–54.

—— PRICE, J. & SLATER, E. (1974) Mental disorder and season of birth: a national sample compared with the general population. *British Journal of Psychiatry*, **124**, 81–6.

HUXLEY, J., MAYR, E., OSMOND, H. & HOFFER, A. (1964) Schizophrenia as a genetic morphism. *Nature*, **204**, 220–1.

JONES, I. H. & FREI, D. (1979) Seasonal births in schizophrenia. A southern hemisphere study using matched pairs. *Acta Psychiatrica Scandinavica*, **59**, 164–72.

KETY, S. S., ROSENTHAL, D., WENDER, P. H., SCHULSINGER, F. & JACOBSEN, B. (1975) In *Genetic Research in Psychiatry* (eds. R. R. Fieve, D. Rosenthal and H. Brill), pp 147–65. Baltimore and London: John Hopkins University Press.

KINNEY, D. K. & JACOBSEN, B. (1978) Environmental factors in schizophrenia: new adoption study evidence. In *The Nature of Schizophrenia: New Approaches to Research and Treatment* (ed. L. C. Wynne, R. L. Cromwell and S. Matthysse), pp 38–51. New York: Wiley.

LINCOLN, G. A. & SHORT, R. V. (1980) Seasonal breeding: Nature's contraceptive. In *Recent Progress in Hormone Research* (ed. R. O. Greep), **36**, 1–43.

LIPSEDGE, M. & LITTLEWOOD, R. (1979) Transcultural psychiatry. In *Recent Advances in Clinical Psychiatry* (ed. K. Granville-Grossman), 3. Edinburgh: Churchill Livingstone.

MCNEIL, T., KAIJ, L. & DZIERZYKRAY-ROGALSKA, M. (1976) Season of birth among siblings of schizophrenics. *Acta Psychiatrica Scandinavica*, **54**, 267–74.

—— —— (1978) Obstetric factors in the development of schizophrenia. In *The Nature of Schizophrenia* (ed. L. C. Wynne, R. L. Cromwell and S. Matthysse). New York: Wiley.

MOSKALENKO, V. D. (1980) On the interpair differences in ontogenesis, premorbid state and severity of schizophrenia in twins. *Zhurnal Neuropatologii I Psikhiatrii Imeni* (*Moskva*), **80**, 78–83.

ØDEGÅRD, O. (1974) Season of birth in the general population and in patients with mental disorder in Norway. *British Journal of Psychiatry*, **125**, 397–405.

O'HARE, A., WALSH, W. & TORREY, F. (1980) Seasonality of schizophrenic births in Ireland. *British Journal of Psychiatry*, **137**, 74–7.

PARKER, G. & BALZA, B. (1977) Season of birth and schizophrenia—an equatorial study. *Acta Psychiatrica Scandinavica*, **56**, 143–6.

PASSOMINICK, B. & KNOBLOCH, H. (1966) Seasonal variation in complications in pregnancy. *Obstetrics and Gynaecology*, **12**, 110–12.

REGISTRAR GENERAL'S TABLES (1972) Statistical reviews for England and Wales for 1970. Vol. II, HMSO.

SLATER, E. & COWIE, V. (1971) *The Genetics of Mental Disorders*. London: Oxford University Press.

TORREY, E. F., TORREY, B. B. & PETERSON, M. R. (1977) Seasonality of schizophrenic births in the United States. *Archives of General Psychiatry*, **34**, 1065–70.

TSUANG, M. T., WINOKUR, G. & CROWE, R. R. (1980) Morbidity risks of schizophrenia and affective disorders among first-degree relatives of patients with schizophrenia, mania, depression and surgical conditions. *British Journal of Psychiatry*, **137**, 497–504.

TYRRELL, D. A. J., *et al* (1979) Possible virus in schizophrenia and some neurological disorders. *Lancet*, *i*, 839–41.

VAN HORN, R. N. (1980) Seasonal reproductive patterns in primates. In *Progress in Reproductive Biology* (ed. S. Karger), pp 181–221. Basel.

VIDEBECH, T., WEEKE, A. & DUPONT, A. (1974) Endogenous psychoses and season of birth. *Acta Psychiatrica Scandinavica*, **50**, 202–18.

Eric Shur, M.B., B.Ch., M.Phil., M.R.C.Psych., *Research Worker and Honorary Senior Registrar, Maudsley and Bethlem Royal Hospitals, London, SE5*

(*Received 26 May; revised 4 November 1981*)