Anencephaly: a retrospective analysis in Singapore, 1976 to 1980

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SUMMARY Records of 93 cases of anencephaly from three maternity hospitals in Singapore between 1976 and 1980 were analysed. The incidence was 0.54 per 1000 births. No significant correlation between anencephaly and local seasonal conditions could be found for Singapore.

Anencephaly is the commonest type of single monster among fetal malformations. The defect is the result of failure or primary arrest of closure of the cerebral end of the neural tube. This pathological basis was first suggested by von Recklinghausen and confirmed by Sternberg in his study of young human embryos.

The cause of anencephaly is still obscure. Renwick¹ suggested the ingestion of blighted potatoes early in pregnancy as a cause, and Lowe *et al*² implicated the level of calcium in the drinking water as the cause of anencephaly and spina bifida. However, both were found later to be interesting but unproven hypotheses.^{3 4}

Nutritional factors have also been considered as a cause of neural tube defects. A possible link between folate deficiency and these defects in man was first suggested by Hibbard and Smithells,⁵ but other workers have failed to demonstrate this correlation. Smithells and co-workers⁶ suggested that antenatal multivitamin supplements might reduce the recurrence risk of anencephaly. Unfortunately, their study was based on a non-randomised sample and, furthermore, they were unable to pinpoint the lack of which vitamin was likely to have been responsible for the malformation.

There is a higher incidence of anencephalic pregnancies among European populations than among Asian populations (table 1). Elwood⁷ and Carter and Evans⁸ reviewed the incidence of anencephaly in the United Kingdom and found that it was higher in the western and northern areas. It was more frequent in the winter months, especially January and February.

A 5 year review of anencephaly in the major maternity hospitals in Singapore was undertaken to see if there was a correlation between anencephaly and the seasonal conditions prevailing in the country.

Materials and methods

The present study analyses the anencephalic pregnancies recorded among 171 773 consecutive deliveries over a 5 year period (1.1.76 to 31.12.80) in three major maternity hospitals, namely Alexandra

TABLE 1 Incidence of anencephaly.

Place	Incidence (per 1000)	Reference	Year
Aberdeen, UK	1.60	9	1958
Belfast, UK	3.95	7	1970
Birmingham, UK	2.0	10	1972
Dublin, UK	5.10	11	1957
Liverpool, UK	3.10	12	1968
London, UK	1.41	8	1973
Paris, France	0.54	13	1964
Sweden	1.09	14	1968
Rhode Island, USA	1.94	15	1953
India	4.80	16	1978
Taipei, Taiwan	1.15	17	1965
Japan	0.60	18	1958
Thailand	0.21	19	1979
Singapore	0.62	20	1959
Singapore	0.21	21	1964
Singapore	0.25	22	1970
Singapore	0.49	23	1978

At the request of the editor, Dr Tan was asked about the nutritional status of the Singapore population, particularly with respect to vitamin deficiencies. Dr Tan replied as follows: "With reference to your question, I would like to point out that in Singapore multivitamin supplements are routinely provided by the health care institutes, including government maternity clinics and private practitioners, to all pregnant women throughout their antenatal period. Therefore, there is no evidence of vitamin deficiencies in these women during their pregnancies. So far, to my knowledge, no study in Singapore has been carried out to correlate the individual vitamin deficiency and the incidence of anencephaly".

Hospital, Kandang Kerbau Hospital, and Toa Payoh Hospital, in Singapore. The births in these hospitals account for 84.9% of the total births of Singapore in the same period (table 2). Therefore, the results of this study may be taken to approximate closely to the situation in the whole country.

Results

INCIDENCE

A total of 93 cases of anencephalic pregnancy was recorded. The incidence was 0.54 per 1000 births or 1 in 1847 deliveries (table 3).

RACE

The racial distribution of anencephalic pregnancy in Singapore was Chinese 72%, Malays 14%, and Indians 14% (table 4).

MATERNAL AGE

The age distribution of mothers who gave birth to anencephalic infants is shown in table 5. The incidence was highest in those between 25 and 29 years of age.

TABLE 2 *Total birth rate in three maternity hospitals in Singapore, 1.1.76 to 31.12.80.*

Year	No of deliveries		Percentage Three hospitals/Singapore
	Three hospitals	Singapore	
1976	36 782	42 000	87.6
1977	32 762	38 807	84.4
1978	33 475	39 473	84.8
1979	34 592	40 847	84.7
1980	34 162	41 217	82.9
Total	171 773	202 344	84.9

TABLE 3 *Incidence of anencephaly in Singapore, 1.1.76 to 31.12.80.*

Year	Total No of births	No of anencephaly	Per 1000 births
1976	36 782	23	0.63
1977	32 762	15	0.46
1978	33 475	21	0.63
1979	34 592	15	0.43
1980	34 162	19	0.56
Total	171 773	93	0.54

TABLE 4 *Racial distribution of anencephalic pregnancy in Singapore.*

Ethnic group	No of cases	Percentage
Chinese	67	72
Malay	13	14
Indian	13	14
Others	0	0
Total	93	100

TABLE 5 *Maternal age distribution in anencephaly.*

Age (yr)	No of cases	Percentage
15-19	6	6.4
20-24	19	20.4
25-29	46	49.5
30-34	16	17.2
35-39	5	5.4
40-44	1	1.1
45 and over	—	—
Total	93	100.0

PARITY

The distribution of parity is shown in table 6. It appeared to be highest in primigravidae.

SEX OF INFANTS

There were 54 male and 39 female anencephalic infants giving a sex ratio of 1.38:1.

CONDITION AND STATE OF DEVELOPMENT

Among the anencephalic deliveries, 50 were stillbirths and 43 were neonatal deaths. The ratio was 1.16:1.0.

YEARLY INCIDENCE

The distribution of anencephaly in each year was fairly consistent. The incidence in the three hospitals is shown in fig 1.

MEAN MONTHLY INCIDENCE

The number of anencephalic pregnancies occurring in each month was quite consistent. However, the incidence was marginally higher in January and September, and lower in the month following, that is, in February and October (table 7, fig 2).

MONTHLY OCCURRENCE

The occurrence of anencephaly in individual months over the 5 year period is shown in fig 3.

Discussion

The incidence of anencephalic pregnancy in Singapore recorded from 1976 to 1980 in this study was 0.54 per 1000 births. It is in the same range as that of previous reports.²⁰⁻²³

The distribution of anencephaly among the ethnic

TABLE 6 *Parity distribution of anencephalic pregnancies.*

Parity	No of cases	Percentage
1	38	40.9
2	23	24.7
3	20	21.5
4 and over	12	12.9
Total	93	100.0

groups in the present study showed a higher incidence among the Indian population (14%) and a lower incidence in Chinese (72%). The general racial distribution in Singapore is Chinese 76.9%, Malays 14.6%, Indians 6.4%, and others 2.1% (1980

TABLE 7 Mean monthly incidence of anencephalic pregnancy in Singapore, 1976 to 1980.

Month	No of cases	Per 1000 births
January	15	1.12
February	3	0.25
March	4	0.29
April	6	0.46
May	10	0.73
June	8	0.59
July	12	0.83
August	4	0.26
September	14	0.90
October	2	0.12
November	10	0.66
December	5	0.34
Total	93	0.54

FIG 1 Yearly incidence of anencephalic pregnancies in Singapore.

FIG 2 Mean monthly incidence of anencephalic pregnancies in Singapore, 1976 to 1980.

Population Census in Singapore). This finding suggests that a racial predisposition to the disease in Singapore might exist, and other reports have shown a higher incidence among European populations than among Asian populations (table 1). In India, there is a higher incidence of this condition in the population among Sikhs and this tendency is maintained even after their migration to the United Kingdom.¹⁶

Reports on the age distributions of the mothers of anencephalics compared to a control population have variously found an excess of younger women,^{9 20}

FIG 3 Monthly occurrence of anencephalic pregnancies in Singapore.

an excess of older women,¹⁰ or both.¹¹⁻²⁴ In contrast, studies in Oxford,²⁵ in the Liverpool and Bootle areas,²⁶ and in Japan²⁷ did not detect any significant difference in maternal age distribution. In this study, there was a higher incidence of anencephaly in mothers aged between 25 and 29 years. However, no significant difference ($\chi^2=6.004$, $0.50>p>0.10$) has been found when compared to the age specific fertility rates in Singapore (table 8).²⁸

There was a higher incidence of anencephalic pregnancy among primigravidae (40.9%). This happens to agree with the general fertility pattern in Singapore, as population growth in Singapore is well controlled by a family planning programme, and most parents stop at two children. Thus, there is no bias.

The present analysis showed a preponderance of male infants (58.1%), that is, a ratio of 1.38:1 male to female anencephalic infants. In several reports it was noted that female infants predominated.²⁹⁻³¹ On the other hand, in some other studies this has been found not to be so.¹⁷⁻²³⁻³² The results of this study are in agreement with the latter.

There have been conflicting reports over the years as to whether there is a seasonal variation in the incidence of anencephaly. Initial studies revealed a significant excess of winter births in Scotland,³³ in Birmingham,¹⁰ in Belfast,⁷ in Greater London,⁸ and in Oxford.²⁵ In contrast, no seasonal variation has been noted in the United States¹⁵⁻³⁴ or in Sweden.³⁵ Furthermore, the incidence of this disease in certain temperate countries with marked seasonal changes, such as France and Japan, is strikingly similar to the findings in Singapore and Thailand (table 1). The climate in Singapore is rather hot and humid throughout the year. The mean monthly temperature does not vary by more than 1.1°C from the mean annual value of 26.6°C.³⁶ The present study showed no increase in anencephalic deliveries in any particular month of the year in Singapore. Although the distribution was marginally higher in January and September, and lower in February and October, this finding was not statistically significant. It may be

that the number of cases in this study is insufficient to detect seasonal variation.

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References

- 1 Renwick JH. Spina bifida, anencephaly and potato blight. *Lancet* 1972;ii:967.
- 2 Lowe CR, Roberts CJ, Lloyd S. Malformations of central nervous system and softness of local water supplies. *Br Med J* 1971;ii:357-61.
- 3 Clarke CA, McKendrick OM, Sheppard PM. Spina bifida and potatoes. *Br Med J* 1973;iii:251-4.
- 4 Leck I. Paediatric aspects of epidemiology—the frequency of disorders of early life. In: Davis JA, Dobbing J, eds. *Scientific foundation of paediatrics*. Philadelphia: Saunders, 1974:740-1.
- 5 Hibbard ED, Smithells RM. Folic acid metabolism and human embryopathy. *Lancet* 1965;i:1254-6.
- 6 Smithells RM, Sheppard S, Schorah CJ, et al. Possible prevention of neural tube defects by periconceptional vitamin supplementation. *Lancet* 1980;i:339-40.
- 7 Elwood JH. Anencephalus in Belfast: incidence and secular and seasonal variation, 1955-1966. *Br J Prev Soc Med* 1970;24:78-88.
- 8 Carter CO, Evans K. Spina bifida and anencephalus in Greater London. *J Med Genet* 1973;10:209-34.
- 9 Anderson WJR, Baird D, Thomson AM. Epidemiology of stillbirths and infant deaths due to congenital malformation. *Lancet* 1958;i:1304-6.
- 10 Leck I, Record RG, McKeown T, Edwards JH. The incidence of malformations in Birmingham, England, 1950-1959. *Teratology* 1972;1:263-80.
- 11 Coffey VP, Jessop WJEA. A study of 137 cases of anencephaly. *Br J Prev Soc Med* 1957;11:174-80.
- 12 Smithells RW. Incidence of congenital abnormalities in Liverpool, 1960-64. *Br J Prev Soc Med* 1968;22:36-7.
- 13 Frézal J, Kelley J, Guillemot ML, Lamy M. Anencephaly in France. *Am J Hum Genet* 1964;16:336-50.
- 14 Kallen B, Winberg J. Anencephaly in Sweden. *J Pediatr* 1968;41:765-8.
- 15 McMahon B, Pugh TF, Ingalls TH. Anencephalus, spina bifida and hydrocephalus incidence related to sex, race and season of birth and incidence of siblings. *Br J Prev Soc Med* 1953;7:211-9.
- 16 Verma IC. High frequency of neural tube defects in North India. *Lancet* 1978;i:879-80.
- 17 Wei PY, Chen YP. Congenital malformations, especially anencephalus, in Taiwan. *Am J Obstet Gynecol* 1965;91:870-6.
- 18 Neel JV. A study of major congenital defects in Japanese infants. *Am J Hum Genet* 1958;10:398-445.
- 19 Snidvongs W. Stillbirths – five years' experience at Chulalongkorn Hospital. In: Karim SMM, Tan KL, eds. *Problems in perinatology*. Proceeding of 1st Asia Oceania Congress of Perinatology, Singapore, 1979. Lancaster, London: MTP Press, 1979:188-92.
- 20 Searle AG. The incidence of anencephaly in a polytypic population. *Ann Hum Genet* 1959;23:279-88.
- 21 Wong HB. Congenital malformations in Singapore. *Bull K K Hosp* 1964;2:1-6.

TABLE 8 Age specific fertility rates in Singapore, 1976 to 1980 (per 1000 female population)*.

All ethnic groups Age	1976	1977	1978	1979	1980
15-19	16.2	13.4	11.8	11.4	12.2
20-24	107.2	90.3	86.8	85.1	79.9
25-29	160.2	138.9	140.9	139.3	137.3
30-34	95.9	85.2	86.8	88.4	84.5
35-39	33.8	28.7	26.7	27.5	27.2
40-44	8.1	6.9	5.3	5.5	5.7

*Data cited from Fifteenth Annual Report, Singapore Family Planning and Population Board, 1980.

- ²² Vengadasalam D. Anencephaly: a study of 29 cases. *Proceedings of the Obstetrical and Gynaecological Society of Singapore* 1970;**1**:20-3.
- ²³ Woon KY. Anencephaly in Singapore. *J Singapore Pediatr Soc* 1978;**20**:177-82.
- ²⁴ Carter CO. Spina bifida and anencephaly: a problem in genetic-environmental interaction. *J Biosoc Sci* 1969;**1**:71-83.
- ²⁵ Fedrick J. Anencephalus in the Oxford record linkage study area. *Dev Med Child Neurol* 1976;**18**:643-56.
- ²⁶ Owens JR, McAllister E, Harris F, West L. 19-year incidence of neural tube defects in area under constant surveillance. *Lancet* 1981;**ii**:1032-5.
- ²⁷ Imaizumi Y. Anencephaly in Japan: paternal age, maternal age and birth order. *Ann Hum Genet* 1979;**42**:445-55.
- ²⁸ Singapore Family Planning and Population Board. Fifteenth Annual Report, 1980.
- ²⁹ Potter EL. *Pathology of the fetus and newborn*. Chicago: Year Book Medical Publishers, 1962.
- ³⁰ Knox EG. Twins and neural tube defect. *Br J Prev Soc Med* 1974;**28**:73-80.
- ³¹ James WH. The sex ratios of anencephalics born to anencephalic-prone women. *Dev Med Child Neurol* 1980;**22**:618-22.
- ³² Jones WR. Anencephaly: a 23-year survey in a Sydney hospital. *Med J Aust* 1967;**1**:104-6.
- ³³ Edwards JH. Congenital malformations of the central nervous system in Scotland. *Br J Prev Soc Med* 1958;**12**:115-30.
- ³⁴ Dalen P. *Season of birth*. Amsterdam: North-Holland, 1975.
- ³⁵ Sandahl B. Seasonal incidence of some congenital malformations in the central nervous system in Sweden, 1965-1972. *Acta Paediatr Scand* 1977;**66**:65-72.
- ³⁶ Meteorological Service, Singapore. Summary of observations, 1979:3.

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