

## Increase in incidence of gastroschisis in the South West of England in 1995

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**Objective** To describe the incidence of gastroschisis and to identify possible aetiological factors.

**Design** A retrospective case review study.

**Setting** The South West Region of England.

**Population** All known cases of gastroschisis were identified from the regional fetal medicine, ultrasound, pathology and neonatal surgery databases. Datasets to be collected were agreed prospectively and included demographic, past medical, family and obstetric information for all pregnancies conceived between January 1987 and December 1995.

**Results** In the first eight years the incidence was 1.6/10,000 but in 1995 a highly statistically significant rise to 4.4/10,000 was found ( $P = 0.0009$ ). The increased incidence was not associated with changes in maternal age, proportion of primigravidae, use of tobacco or illicit drugs, conception while taking the oral contraceptive pill, or an increase in the number of teenage pregnancies. The median maternal age at last menstrual period for pregnancies with gastroschisis was 20.4 years which was much younger than the national average of 28 years. Thirty-seven percent of these conceptions occurred during the first quarter of the year compared with the expected 25%.

**Conclusions** The incidence of gastroschisis has risen to a higher level than previously reported which, despite a marked association with young maternal age at conception, is not due to an increase in the teenage pregnancy rate. As the average length of inpatient stay in the neonatal intensive care unit for cases with this malformation is approximately four weeks, the rise has considerable cost implications. The increasing incidence may also offer opportunities to determine the cause of gastroschisis.

### INTRODUCTION

Gastroschisis is a fetal malformation characterised by a full thickness defect of the abdominal wall, usually to the right of the umbilical cord insertion through which there is herniation of intrabdominal structures, principally bowel. It is an entirely different malformation from exomphalos, the other major abdominal wall defect, with a high incidence of karyotypic and associated structural abnormalities. Morphologically, the eviscerated bowel in exomphalos is covered by a membrane, whereas the bowel is unprotected in gastroschisis. The free-floating herniated bowel can be seen from the late first trimester onwards and this is the basis of achieving prenatal diagnosis by ultrasound.

The cause of gastroschisis is unknown but vascular disruption during early embryonic development affecting the omphalomesenteric artery has been suggested as

a possible mechanism<sup>1</sup>. While environmental teratogens could precipitate such an event<sup>2</sup>, an interaction between a genetic susceptibility and environmental factors has been postulated to explain the small but significant sibling recurrence rate<sup>3</sup>. A number of studies have suggested an association between gastroschisis and a variety of environmental factors including illicit drug usage<sup>2</sup>, tobacco<sup>4</sup>, alcohol<sup>5,6</sup>, conception while taking the oral contraceptive pill<sup>2,5</sup>, influenza or its treatments<sup>4,5</sup>. Young maternal age at the time of conception has also been a consistent finding of many studies<sup>2,4,6,7</sup>.

The incidence of gastroschisis has been reported to be increasing over the last few years both in the UK<sup>8,9</sup> and abroad<sup>2,4,7</sup>. In a recently published paper, using nationally collected data, the incidence of gastroschisis in the UK was reported to have doubled from 0.65 in 1987 to 1.39/10,000 births in 1993<sup>10</sup>. However, some have suggested that the increase reported is due to more complete ascertainment as a result of improvements in prenatal services and postnatal diagnosis<sup>3</sup>. Furthermore, the rarity of gastroschisis has meant that larger series

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relied on malformation registers where, because data are drawn from multiple institutions, there may be problems of under-reporting as well as inaccuracies in data entry and coding. Therefore there has been continuing controversy as to the magnitude of the rise in gastroschisis.

We had an impression that the number of cases of gastroschisis in the South West of England was rising. This region has the advantage of being geographically well defined with a relatively stable population served by centralised tertiary referral fetal medicine and neonatal surgery services in Bristol. In addition, a detailed study of gastroschisis made in the region between 1981 and 1986 is available for comparison<sup>11</sup>. We were therefore in a good position to provide quantitative information regarding a change in incidence and have attempted to identify possible related factors.

## METHODS

We conducted a case review study of women with a last menstrual period in the years 1987 to 1995 who were delivered of a fetus with gastroschisis, irrespective of the subsequent outcome or whether the abnormality was diagnosed prenatally. Cases of a fetus or newborn infant with any abdominal wall defect were identified by searching fetal medicine ultrasound, pathology and neonatal surgery department records. This was to ensure that no cases were missed or wrongly included as a result of the abdominal wall defect being misclassified. The maternal and neonatal notes were then reviewed and cases accepted for inclusion if a diagnosis of gastroschisis was made at the time of initial operation or at postmortem examination as applicable. The data to be collected were agreed prospectively and included information on maternal age at last menstrual period, month of last menstrual period, oral contraceptive pill use, smoking, alcohol consumption, illicit drug use, marital status and parity as well as demographic, past obstetric, medical, family, present pregnancy and outcome details. The information was collected by reviewing our maternal and neonatal casenotes and where necessary those of the referring hospital. All information was then entered on to a computer to form the South West Regional gastroschisis database.

Since gastroschisis is caused by an event in the first trimester<sup>12</sup> and premature delivery is a common complication of this condition<sup>2</sup>, we used the date of last menstrual period rather than delivery to date the pregnancies. When the last menstrual period date was uncertain, an estimated last menstrual period was calculated from the ultrasound assessment of gestational age. We obtained from the South West Region Health Authorities data on the total number of births per year divided into maternal age bands (< 16, 16-19, 20-34, 35-39, > 39). The

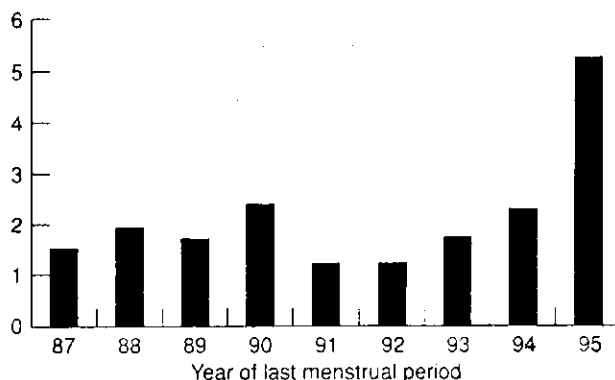


Fig. 1. Incidence of gastroschisis in the South West of England (per 10,000 births) by year of last menstrual period 1987-1995. The increased incidence in 1995 was statistically significant ( $P = 0.0009$ ).

incidence of gastroschisis was expressed as the number of cases per 10,000 births per year.

The statistical assessment of whether the incidence of gastroschisis in 1995 was significantly different from the previous years was by comparison with the Poisson distribution of the mean incidence over the whole study period. The cumulative probability of the 1995 result or greater was calculated. Assessment of  $2 \times 2$  contingency tables was determined using Fisher's exact test. A  $P$  value  $< 0.05$  was regarded as statistically significant.

## RESULTS

In the nine year period of 1987 to 1995, 80 cases of gastroschisis were identified (mean 8.89 cases/year). Twenty of these cases (25%) were conceived during 1995 ( $P = 0.0009$ ) (Fig. 1). The incidence of gastroschisis rose from 1.6/10,000 for the initial eight years of the study to 4.4/10,000 in 1995.

Fifty-four of the 80 cases (69%) were delivered of women in their first ongoing pregnancy. There was a male: female ratio of 0.8. The median maternal age at last menstrual period was 20.4 years which is much younger than average for the region during this time period (28 years). This corresponds to an incidence of gastroschisis of 13.3/10,000 in women younger than 20 years and 1.1/10,000 in those aged 20 years or older (Fig. 2). There was also an association between gastroschisis and the month of conception (Fig. 3), with 30/80 (37%) of cases being conceived during the first quarter of the year while nationally there is only a minimal seasonal variation.

The answers to questions regarding illicit drug use (70/80), alcohol (74/80), tobacco smoking (79/80) and conception while taking the oral contraceptive pill (71/80) were available in most cases. Five women (5/70) reported using a variety of illicit drugs but use of amphetamines in early pregnancy was common in all five. The rates of alcohol usage in pregnancy (14%) and

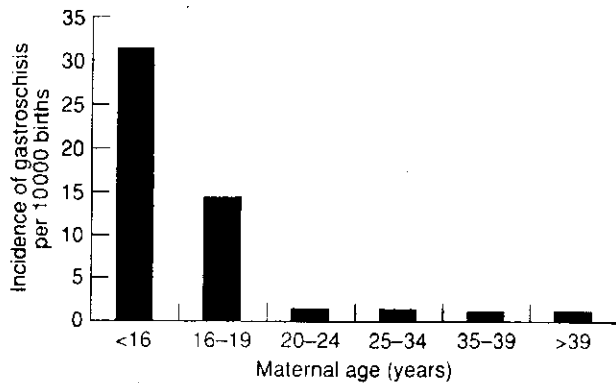


Fig. 2. Maternal age at conception in the 80 cases with gastroschisis, indicating the number of births per year in each of six age range bands (<16, 16-19, 20-24, 25-34, 35-39 >39) and a strong association between young maternal age and gastroschisis is shown.

tobacco smoking (48%) were in line with what was expected for this age group. It was noted, however, that 23 of the 71 pregnancies in which data were available were conceived while taking the oral contraceptive pill.

In order to identify possible confounding variables related to the increase in the incidence of gastroschisis, we compared these factors in cases in 1995 with those in 1987 to 1994 (Table 1). No significant change of maternal age, proportion of primigravidae, illicit drug use, alcohol, tobacco smoking or oral contraceptive use at the time of conception was found.

## DISCUSSION

An established classification of anterior abdominal wall defects was not produced until 1953<sup>12</sup> so it is difficult to gain an accurate picture of the incidence of gastroschisis before this time. A large number of terms were used for gastroschisis and some cases were misdiagnosed as exomphalos with a ruptured sac<sup>12</sup>. The more frequent recognition of gastroschisis led some to the view that it was caused by a new environmental teratogen in the late 20th century<sup>13</sup>. However, this is not likely to be the case since an infant with gastroschisis was described in detail as early as 1733<sup>14</sup>.

The neonatal surgery service for South West England was established in Bristol in the early 1980s. There have been two studies of gastroschisis carried out in our region since then<sup>11,15</sup>. The resulting appreciation of this condition and its management options leads us to the view that we passed the initial part of the ascertainment curve in the region many years ago. We are unaware of any change in management or referral patterns of gastroschisis over the study period and thus believe that the increase observed in 1995 is not due to more complete ascertainment.

Despite the significant fall in the incidence of gastroschisis with advancing maternal age, many texts still

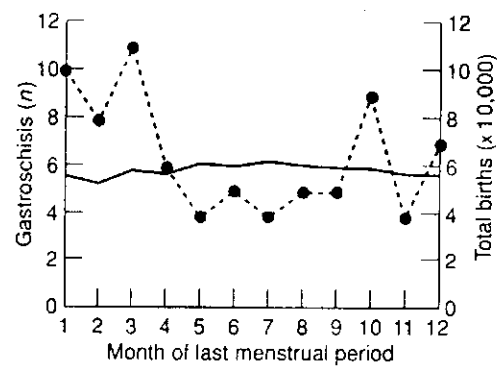


Fig. 3. The relation between month of last menstrual period (LMP) (1-12 = Jan-Dec) and the number of cases of gastroschisis in the study. The solid line indicates UK births per month (10,000s) for 1990, indicating that the higher incidence of gastroschisis in the early months of the year is not the result of variation in total conception rates. ● = gastroschisis.

Table 1: A comparison of data in pregnancies with gastroschisis in 1987-1994 ( $n = 60$ ) with those in 1995 ( $n = 20$ ). Since there was no significant change in any of them (total  $P = 0.0009$ ) it is unlikely that these factors are directly linked to the cause of the increasing incidence of gastroschisis. Values are given as  $n$  total data available unless otherwise indicated.

	1987-1994	1995
Median maternal age (years)	20.4	20.2
Primiparae	42/60	12/20
Gender of infant: male: female	28/32	8/12
Illicit drug use	4/54	1/16
Alcohol	7/55	3/19
Tobacco smoking	31/60	7/19
Oral contraceptive use at time of conception	15/53	8/18

quote an overall incidence regardless of maternal age. This gives a distorted view of the risk of gastroschisis which in this study was more than 11 times more likely in women under the age of 20 compared with those aged 20 years or older at the time of conception. Because of the strong association with young maternal age at conception, the increase in incidence of gastroschisis observed in 1995 could have been due to a rise in the rate of teenage pregnancies. However, in line with the increase in the average maternal age throughout the UK, there has also been a gradual fall in the rate of teenage pregnancies over the study period in this region<sup>16</sup>. No explanation has yet been found for this inverse age-related risk but it may reflect some social/life style exposure to an environmental teratogen.

The rates of alcohol consumption and tobacco smoking among the whole study group were similar to those expected from the general maternity population. The number of women that conceived while taking the oral contraceptive pill was high, but this must be interpreted

with caution in the light of the young maternal age of this population. The higher than expected conception rate for gastroschisis in the first quarter of the year may relate to a cause and a previous suggestion of influenza infection<sup>4,5</sup> is a possibility. No information on minor ailments or their treatment was available in this study. Comparison between the cases in 1995 and the previous eight years showed no significant changes in the rates of illicit drug use, tobacco smoking, alcohol ingestion or conception while taking the oral contraceptive pill. This lack of association with the recent rising incidence suggests that these factors are probably associations rather than a cause of gastroschisis despite previous suggestions.

This paper presents the highest ever reported incidence of gastroschisis. Furthermore, the 1995 incidence represents a threefold increase from the UK national incidence for 1993<sup>10</sup>. The very high incidence of gastroschisis is important for antenatal screening programmes, especially in women younger than 20 years. It is now one of the commonest congenital abnormalities encountered in this age group and so is a common cause of a raised serum alpha-fetoprotein. This recent rise in the incidence of gastroschisis is even more surprising as it occurred while the average maternal age at conception was rising. Since the average length of neonatal care of surviving infants is approximately four weeks, the high incidence of gastroschisis also has considerable cost implications for health services.

The aetiology of gastroschisis remains obscure since none of the previously implicated factors has been found to correlate with the recent rise in incidence. Further research into the cause is urgently required and the increasing incidence may be a useful tool.

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