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INVITED COMMENTARY:
CURRENT ISSUES IN OBSTETRICS AND GENETICS

Gastroschisis—an overview

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Gastroschisis is an increasingly common malformation with unique fetal complications. Although it is usually an isolated defect, gastroschisis has a significant mortality rate of 5–10%. Complications include bowel damage, but growth retardation, oligohydramnios and fetal distress in labour are also common. There have been recent data that may help explain some of these observations, which will be reviewed in this article.

DEFINITION AND EPIDEMIOLOGY

Gastroschisis is a para-umbilical defect of the abdominal wall (almost always right sided) resulting in the evisceration of abdominal contents into the amniotic cavity. The defect is usually small (less than 4 cm in length) through which various segments of bowel may be extruded and other abdominal organs, such as the fallopian tubes, may also be herniated (Pinzon and Barr, 1955). Unlike exomphalos, the exposed bowel loops are not protected from the amniotic fluid by a covering of peritoneum and the blood supply to the herniated organs is more likely to be interrupted. This can produce intrauterine and neonatal complications, including bowel torsion, atresia, necrosis and short bowel syndrome.

The prevalence of gastroschisis is usually quoted as 0.5–1 cases per 10 000 births, but the incidence has increased in many parts of the world over the last 2–3 decades (Penman *et al*., 1998; Rankin *et al*., 1999; Suita *et al*, 2000). The most striking epidemiological association with gastroschisis is young maternal age, especially less than 20 years of age (Tan *et al*., 1996; Penman *et al*., 1998). In England the incidence of gastroschisis doubled in a decade to 1.35 per 10 000 births and in the South West the incidence has been as high as 4.4 per 10 000 births (Figure 1). The rising teenage pregnancy rate in England over the past 20 years cannot fully explain this trend. However, there is increasing epidemiological evidence that environmental factors, such as cigarette smoking and drug abuse, which are more common in teenage pregnancy, may be important (Penman *et al*., 1998). In a study of the rising incidence of gastroschisis in teenagers in Western Australia 46% of the population studied admitted to cigarette smoking and 19% to regular recreational drug use (Nichols *et al*., 1997). Gastroschisis is also significantly associated with poor maternal education, low socio-economic status, more than one elective termination of pregnancy and a short interval between menarche and first pregnancy (Torfs *et al*., 1998, 1994).

AETIOLOGY

Animal models suggest that radiation damage at the pre-implantation stage may increase the incidence of gastroschisis (Hillebrandt *et al*., 1998). Very rare familial clusters have been reported suggesting an autosomal inheritance pattern with variable expression (Torfs *et al*., 1998; Rankin *et al*., 1999; Suita *et al*., 2000) but these are exceptional. The incidence of chromosomal abnormalities is probably not increased with a diagnosis of gastroschisis. Over an eight-year period in one fetal medicine centre 235 fetuses with abdominal wall defects were diagnosed. The karyotype was abnormal in 36% ($n = 116$) of the fetuses with exomphalos but in none of the 26 fetuses diagnosed with gastroschisis (Nicolaides *et al*., 1992). Since gastroschisis is almost always right sided it has been suggested that it may be caused by disruption of the right terminal branch of the superior mesenteric artery (which is located in the extraembryonic coelom of the body stalk) resulting in ischaemia and necrosis and so a secondary paraumbilical defect (Hoyme *et al*., 1981). Another possible explanation is that failure of the right umbilical vein to involute into the abdominal cavity between 28 and 32 days' gestation may result in vessel compromise and paraumbilical necrosis of the mesoderm and ectoderm resulting in a full thickness abdominal wall defect.

DIAGNOSIS

In cases of gastroschisis the malformation should usually be suspected on routine second trimester ultrasound. Also, as there is an increased passage of alpha-fetoprotein (AFP) from the fetus into the amniotic

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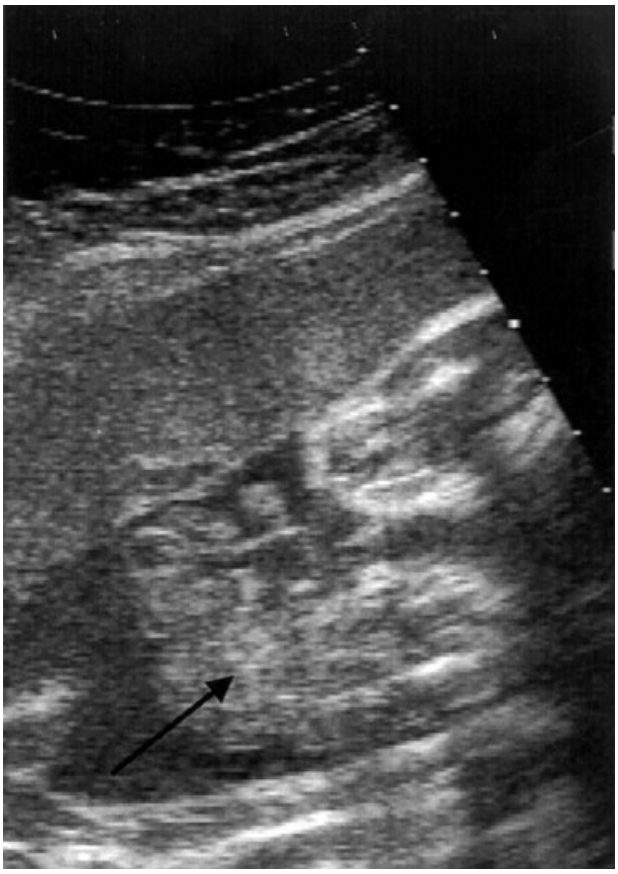

Figure 1—Incidence of gastroschisis in the South West of England (per 10 000 births) by year of last menstrual period 1987–1995. The increased incidence in 1995 was statistically significant ($p = 0.0009$). (Printed with permission from British Journal of Obstetrics and Gynaecology)

fluid, and hence the maternal circulation, an elevated maternal serum AFP often occurs in these pregnancies. The prenatal detection rate of gastroschisis has been estimated at between 76–90% but in regions with a good routine ultrasound programme it now approaches 100% (Axt *et al*., 1999; Forrester and Merz 1999; Walkinshaw *et al*., 1992). Detection is made after careful inspection of the anterior abdominal wall and the amniotic cavity because the loops of bowel are not always obvious next to the defect especially in later pregnancy or with reduced amniotic fluid (Langer *et al*., 1993). Gastroschisis may be distinguished from exomphalos by the herniation being next to a normal cord insertion and the absence of a covering of the defect (Fogata *et al*., 1999) (Figure 2). Polyhydramnios may be associated, probably in cases with reduced bowel motility or bowel obstruction, but oligohydramnios is a much more frequent finding and this is associated with a high incidence of intrauterine growth retardation which occurs in up to 60% of affected fetuses (Axt *et al*., 1999). There is no significant association with chromosomal abnormalities and so invasive testing is not usually offered because of this finding alone. Amyoplasia and arthroryphosis may occasionally occur with gastroschisis: mobius anomaly and hypoplasia of the

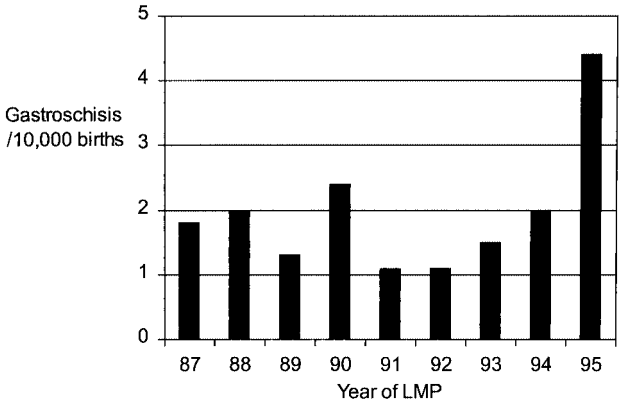

Figure 2—Ultrasound scan of fetus with gastroschisis. The loops of exposed bowel are shown (arrow)

pectoral, deltoid and biceps muscles should be excluded on scan (Robertson *et al*., 1992).

COUNSELLING

After diagnosis the patient should be informed of the 5–10% incidence of fetal or neonatal death and long-term digestion problems associated with short gut syndrome. The prognosis for an isolated gastroschisis may be worse than for an isolated exomphalos because of the bowel protection in the latter malformation. Therefore, termination of pregnancy should be mentioned as an option in cases of gastroschisis. However, this is rarely chosen because of the much lower rates of other associated syndromes/abnormalities (Mann *et al*., 1984; Nicolaides *et al*., 1992). If the pregnancy is to continue, serial ultrasound examinations are recommended to detect gut complications, assess fetal well-being and plan delivery. The cases that survive to the end of pregnancy and into the neonatal period may be a self-selected group with a good prognosis. For this reason, combined with our inability to predict some fetal complications, the prognosis and counselling given to women at 20 weeks should be guarded. A consultation with a paediatric surgeon should be made to give the parents a better insight into the surgical management of gastroschisis.

COMPLICATIONS

Although 90–95% of infants with gastroschisis survive, the condition may be associated with severe complications for the fetus. As pregnancy progresses in gastroschisis the bowel usually becomes coated in an inflammatory fibrous peel resulting in thickening of the bowel wall, matting of the intestines, decreased bowel motility and obstruction. Morrison *et al*. (1998) demonstrated that the amniotic fluid in cases of gastroschisis contained inflammatory cells and significantly elevated levels of the pro-inflammatory cytokine, interleukin-8 compared to controls (Morrison *et al*., 1998). A chick model of gastroschisis suggests that bowel inflammation

occurs due to the effects of the amniotic fluid on exposed bowel loops and worsens with gestational age due to the increased concentration of the surrounding fluid (Tibboel *et al*., 1986). Therefore, a vicious circle may occur: the exposed bowel becomes inflamed due to contact with the amniotic fluid and releases an inflammatory exudate into the amniotic fluid which increases in concentration with gestational age and further aggravates the bowel.

The cause of the increased frequency of CTG abnormalities and meconium staining has been intriguing (Crawford *et al*., 1992). In a study of 115 cases of gastroschisis between 1980 and 1996 in the South West of England, the infants with intestinal atresia had a significantly higher birth weight and fewer CTG abnormalities than those with patent bowel (Dixon *et al*., 2000). We hypothesized that bowel atresia, and so obstruction above the level of exposed loops of bowel, may significantly protect the fetus from growth retardation and CTG abnormalities in labour, perhaps due to the prevention of protein, salt or fluid loss across exposed bowel loops. Also, we found that staining of the amniotic fluid occurred just as often in fetuses with bowel atresia, so meconium could not have been passed to produce the characteristic green/black colour (Dixon *et al*., 2000). This suggests that the liquor staining in these pregnancies is the result of bile vomiting. Therefore, staining of the liquor in gastroschisis should not necessarily be taken to indicate meconium passage as a result of fetal hypoxia.

Compared to controls, chick embryos with gastroschisis were smaller and with reduced levels of sodium, chloride, amino acids and glucose (Lopez de Torre *et al*., 1991). A recent study from our unit showed that there was a significant decrease in fetal cord blood serum protein but a rise in amniotic fluid protein in fetuses affected with gastroschisis compared to normal controls or those with exomphalos (Carroll *et al*., 2001) (Figure 3). These studies support the hypothesis that *in utero* protein and fluid loss from the bowel to the amniotic fluid may account for the raised incidence of growth retardation, oligohydramnios and intrauterine death that occur in these pregnancies. The resultant hypovolaemia could also explain the high incidence of CTG abnormalities that occur in labour in gastroschisis.

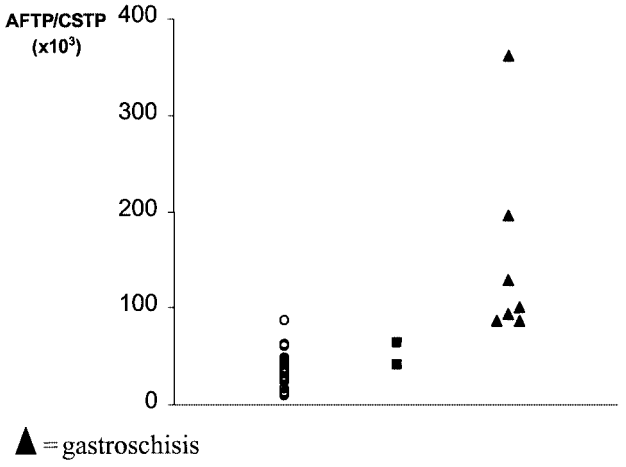

Figure 3—Amniotic fluid/cord serum totals protein ratio. Relationship between amniotic fluid total protein (AFTP) concentration in controls (open circles) and cases of gastroschisis (filled triangles) and exomphalos (filled squares) plotted in relation to gestational age

FETAL THERAPY

Due to the possible secondary effects of severe oligohydramnios (pulmonary hypoplasia, limb compression and cord compression) two cases of gastroschisis with associated oligohydramnios were treated with serial transabdominal amnioinfusion of saline (Dommergues *et al*., 1996). The authors felt that the treatment may have reduced the complications of severe oligohydramnios and prematurity and it was observed that bowel peel and matting were minimised. In a retrospective study of 20 cases of gastroschisis the most significant poor prognostic factors were prematurity and the degree of inflammation of exposed bowel. Prematurity was most likely in the infants with severe bowel inflammation and heavily stained fluid. The amniotic fluid of the most severely affected fetuses contained higher concentrations of interleukins and TNF-α than gestation-matched controls (Luton *et al*., 1999). These cytokines may mediate bowel injury and possibly stimulate premature delivery (Morrison *et al*., 1998) Hence, the investigators proposed that amniotic fluid exchange would improve the prognosis in gastroschisis, and cases treated by amnioinfusion had a significant improvement in the success of surgical repair compared to those not treated in this way (Luton *et al*., 1999).

MANAGEMENT

Growth scans are difficult to interpret as the abdominal circumference is usually decreased in gastroschisis as a result of some bowel being outside the abdomen. However, careful evaluation of the amniotic fluid volume can detect if oligohydramnios develops and Doppler assessment can be used to assess placental function. With such monitoring, delivery is often delayed until 37–38 weeks (Crawford *et al*., 1992).

Premature onset of labour is common and there is a high incidence of CTG abnormalities during labour (Crawford *et al*., 1992). These CTG effects may be due to oligohydramnios producing cord compression. However, abnormal CTG tracings are often associated with normal Apgar scores so in pregnancies with this malformation they may not indicate 'asphyxia' during labour (Dixon *et al*., 2000). These may be due to the haemodynamic effects of fluid and protein loss across the fetal bowel to the amniotic fluid during pregnancy.

It is now rare for a case to be delivered without the abnormality having been prenatally diagnosed. To enable the best outcome for the fetus with gastroschisis it is vital that there is a team of obstetricians, neonatologists and paediatric surgeons with sufficient experience. Although controversy still exists over the obstetrical management of the fetus with gastroschisis, there is no clear evidence of any advantage of elective Caesarean section over vaginal delivery (Rinehart *et al*., 1999).

NEONATAL MANAGEMENT

A senior neonatologist and neonatal nurse should be present at the delivery and the paediatric surgeons promptly informed of the delivery of a baby with gastroschisis. To limit fluid and protein loss and prevent hypothermia, a silastic bag is immediately placed over the exposed abdominal contents. Handling of the bowel is minimised to prevent vascular compromise and nasogastric decompression, intravenous fluids (albumin/saline infusion) and broad-spectrum antibiotics are commenced. Any metabolic acidosis is corrected and, if possible, surgery is performed within 4 h of delivery.

The type of repair performed is relative to the degree of bowel inflammation, bowel matting and size of the abdomen relative to the extruded bowel that is present at delivery. Bowel in good condition may be replaced into the abdomen and primary fascial closure performed (Bianchi and Dickson, 1998). Delayed closure involves temporary coverage of exposed bowel with a silastic/dracon abdominal pouch and early parenteral nutrition.

After repair, bowel motility may be a problem particularly in the first week and parenteral feeding in the short term is required. Although long-term prognosis after successful surgery is excellent, morbidity is more likely when bowel obstruction, sepsis, delayed nutrition and closure complications occur. Mortality is associated with gut injury, late repair and the development of necrotizing enterocolitis (Snyder, 1999).

Long-term follow up studies suggest that those surviving initial surgery have an excellent prognosis. In one follow-up study of 23 subjects with neonatal repair for gastroschisis less than 10% had problems with bowel adhesions requiring further surgery with the remainder in excellent health (Davies and Stringer, 1997).

SUMMARY

The rising incidence of gastroschisis is of concern and further epidemiological studies are needed to understand the environmental factors that may be responsible. Greater understanding of the pathophysiological consequences of gastroschisis on the fetus may allow better *in utero* treatment options, reduction of IUGR and prematurity and improved post-operative outcome. Multicentre trials of amnioinfusion are currently being considered.

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