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## Aluminium sulphate in water in north Cornwall and outcome of pregnancy

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### Abstract

**Objective**—To determine whether the excess aluminium sulphate accidentally added to the local water supply in north Cornwall in July 1988 had an adverse effect on the outcome of pregnancies.

**Design**—Outcomes of all singleton pregnancies in the affected area at the time of the incident (n=92) were compared with those in two control groups: pregnancies in this area completed before the incident (n=68) and pregnancies in a neighbouring area (n=193).

**Subjects**—Mothers in the three groups, among whom there were 13 miscarriages, five terminations of pregnancy, and 336 live births.

**Main outcome measures**—Fetal and perinatal loss, birth weight, gestation, obstetric complications, neonatal condition, and congenital defects.

**Results**—Among 88 pregnancies in women exposed to excess aluminium sulphate there was no excess of perinatal deaths (n=0), low birthweight (n=3), preterm delivery (n=4), or severe congenital malformations (n=0). There was, however, an increased rate of talipes in exposed fetuses (four cases, one control; p=0.01).

**Conclusions**—Because of small numbers it is not possible to say that high doses of aluminium sulphate are safe in pregnancy, but there is no evidence from this study of major problems apparent at birth.

### Introduction

Although normal variation in environmental contaminants is generally assumed to play little part in the genesis of abnormality, animal experiments show that many of the substances to which we are exposed can adversely affect the fetus. The range of harmful substances is wide—from the polychlorinated biphenols to lead, from nicotine to cadmium. Nevertheless, most animal experiments are carried out with high doses, which would normally not be found in a human population, and extrapolation of results to human populations is usually problematical. It is essential therefore to monitor the consequences of any natural human experiments that arise. The tragic events of the toxic oil accident in Spain,<sup>1</sup> the excess mercury causing Minimata disease in Japan,<sup>2</sup> and possibly the Chernobyl accident<sup>3</sup> have provided information that can be used to determine whether high doses of specific pollutants are teratogenic in humans.

On 6 July 1988 a large amount of aluminium sulphate was inadvertently dumped in the Lower Moor water supply in north Cornwall. This water comes from the Lower Moor treatment works on the western edge of Bodmin Moor and serves an area of Cornwall stretching from just south of Tintagel to just north of Wadebridge, including the town of Camelford. Subsequently there were many complaints concerning

effects on health. Although there was little to suggest that women who were pregnant at the time had any worries, there is some evidence from animal experiments that aluminium is a teratogen,<sup>4</sup> that it can cause both fetal and neonatal death, and that after fetal exposure neuromotor development can be impaired.<sup>5,6</sup> Although a study in south Wales showed an association in humans between central nervous system defects and aluminium levels in the household water supply,<sup>7</sup> little further attention had been paid to the effect of aluminium on human malformations.

### Subjects and methods

The population supplied from the Lower Moor source was identified from information supplied by the water authority. A contiguous area supplied from a different treatment works (Bastreet) was selected as a control area. Both supplies are derived from moorland water, and the two populations are similar, both comprising fairly scattered agricultural communities.

Information was gathered on births in the six months before the incident to provide a baseline, and those delivered up to 42 weeks after the contamination; in this way any fetus that may have been exposed at a very early stage (or while the mother was still suffering from high levels of aluminium) would be included even if delivered after term. All pregnancies resulting in a live birth were identified from birth notifications. Miscarriages and terminations were identified by searching hospital records. Stillbirth registrations were scanned. This information was checked against information provided by family doctors and the family practitioner committee. The medical records were examined and information was extracted on to an anonymous form that was used to input data into a computer for analysis.

It was decided not to seek maternal permission to abstract information from the clinical records because it would be likely to raise anxiety and it might result in biases in response from cases and controls. Individual confidentiality was carefully protected. Information was abstracted from the clinical records on to the anonymous forms by one of two clinical assistants employed by the Cornwall and Isles of Scilly Health Authority. The information was then passed as non-identifiable statistical data to Bristol for analysis. The local ethics committees in Cornwall and Plymouth were consulted and gave permission for the study.

Social class coding was based on the occupation of the mother's partner as recorded in the maternity clinical records, using the Office of Population Censuses and Surveys classification. This distinguishes non-manual (social classes I, II, III non-manual), skilled manual (III manual), and semi-skilled and unskilled manual (IV, V) classes.

Comparison of cases with controls used analysis of variance and the *t* test for continuous data,  $\chi^2$  tests for

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categorical data, and Fisher's exact test when expected numbers were small. Comparisons were made of the three groups and also of the exposed group with the other two groups combined. The power of the study was such that we had an 80% likelihood of obtaining odds ratios of 3.0 and 6.0 for low birth weight and major congenital defects respectively at the 5% level.

## Results

In all, 353 pregnancies were studied, 92 of which were in the exposed group. Two pregnancies resulted in twins; these were excluded from the analysis. Table I shows the characteristics of the mothers. It can be seen that there was no significant difference in maternal characteristics or obstetric history. Few mothers had had previous infants with malformations recorded—two in the Bastreet area (one anencephaly, one coarctation) and three in the Lower Moor area (one lissencephaly, one Wolf-Hirschorn syndrome, and one mother with two children with Hunter's syndrome). Among those families that included a male

partner the social class distribution was different between groups, with the exposed group having more fathers in social class III manual and fewer in both social classes IV and V and in the non-manual group ( $p=0.01$ ).

Table II gives details of the pregnancies of the three populations of mothers who delivered a liveborn infant. Among the index cases, 39 women had been exposed in the first trimester. There were no significant differences in the mothers' weights at booking or blood pressure measurements. A higher proportion of women in the Bastreet group showed signs of proteinuria; almost all of these were trace levels, and overall only three women had proteinuric pre-eclampsia. The prevalence of a history of bleeding, urinary infection, or premature rupture of the membranes did not differ between the groups. The Lower Moor mothers were significantly less likely to start labour spontaneously, but there was no difference between the exposed and unexposed groups.

Table III gives details of the infants delivered to the three groups of mothers. On average, the birth weight was higher in Lower Moor than in Bastreet, and there were proportionately fewer low birthweight infants in Lower Moor ( $p<0.01$ ). This was a characteristic of the area, however—there was no difference within Lower Moor between the exposed and unexposed groups. There was no difference in distribution of Apgar scores or admission to special care between the populations. There were two perinatal deaths, both in the Bastreet population.

Slightly more congenital defects were reported in the Lower Moor group. It should be remembered, however, that not all of the fetuses were, at the time of the incident, at a stage of gestation in which the defect could have been formed. Table IV lists all the malformations and deformations that were identified from the termination and neonatal notes. These were assessed (by PL) on the basis of his background knowledge concerning the possibility that the accident occurred at the time in the gestation when it could have been responsible for the defect in the fetus. Eight pregnancies fulfilled the criteria; six among women exposed to aluminium sulphate and two among controls. From the information on month of last menstrual period we estimated that in Lower Moor 88 fetuses and in Bastreet 99 fetuses were in utero at the time of the accident. This gives an incidence of congenital defects of 7% for the index group and 2% for the controls, a difference that was not statistically significant.

Of major interest in table IV is the fact that all six of the defects that could possibly be linked with the Lower Moor incident were mild; five were deformations including four positional talipes. Thus the incidence of talipes among the exposed group was 5%. There was only one case of talipes among the 253 infants in the two control groups (Fisher's exact test,  $p=0.014$ ).

## Discussion

There was no evidence from the data collected that the incident had any deleterious effect on fetal growth or survival. The mean birth weight of the infants of the Lower Moor population was greater than that in the Bastreet area, but there were no significant differences between the exposed and non-exposed groups in the Lower Moor area.

The major finding of an excess in overt malformation rates in the exposed pregnancies is unlikely to have been due to the differences in social class. Other studies have shown that, although malformations of the central nervous system are heavily biased by social class, other types of defect are not.<sup>4</sup> The excess in the malformation rate was entirely due to a significant difference in the

TABLE I—Characteristics of populations of women in north Cornwall exposed to aluminium sulphate during pregnancy (Lower Moor) and those not exposed (Bastreet, Lower Moor)

	Lower Moor			p Value	
	Bastreet (a)	Unexposed (b)	Exposed (c)	3 Groups (a v b v c)	2 Groups (c v (a+b))
Mean (SD) maternal age (years)	27.85 (5.67) (n=183)	27.43 (5.52) (n=63)	27.26 (5.32) (n=88)	0.687	0.474
Mean (SD) maternal height (cm)	163.29 (6.93) (n=161)	161.61 (6.41) (n=62)	162.87 (7.02) (n=88)	0.262	0.955
Percentage (No) of women with parity:					
0	42 (78)	37 (23)	47 (41)	0.400 (df=6)	0.334 (df=3)
1	30 (56)	41 (26)	35 (31)		
2	19 (35)	17 (11)	10 (9)		
>3	8 (15)	5 (3)	8 (7)		
Percentage (No) of mothers with previous:					
Miscarriage	13 (23/184)	18 (52/63)	10 (9/88)	0.415	0.394
Termination	14 (25/184)	10 (6/63)	15 (13/88)	0.619	0.596
Malformation	3 (5/184)	3 (2/63)	5 (4/63)	0.730	0.488
Mean (SD) weight of preceding live birth (g)	3249 (570) (n=100)	3360 (528) (n=40)	3331 (391) (n=47)	0.448	0.498
Percentage (No) of low birthweight babies in previous pregnancies	7 (7/100)	5 (2/40)	0 (0/47)	0.181	0.115
Percentage (No) of mothers unmarried	14 (184)	24 (63)	22 (87)	0.124	0.274
Percentage from social classes†:					
Non-manual	48	34	34	0.016*	0.010**
Manual III	30	43	54		
IV and V	22	23	12		
	(n=136)	(n=47)	(n=67)		

\* $p<0.05$ ; \*\* $p<0.01$ . † Occupation of male partner.

TABLE II—History of pregnancy and delivery

	Lower Moor			p Value	
	Bastreet (a)	Unexposed (b)	Exposed (c)	3 Groups (a v b v c)	2 Groups (c v (a+b))
Mean (SD) maternal weight at booking (kg)	66.81 (11.4)† (n=176)	65.09 (10.1) (n=62)	67.29 (11.7) (n=88)	0.472	0.524
Mean (SD) blood pressure (mm Hg):					
Systolic at booking	118.7 (13.1) (n=179)	122.8 (12.3) (n=62)	119.5 (13.6) (n=88)	0.102	0.868
Diastolic at booking	68.4 (9.3) (n=179)	69.7 (9.5) (n=62)	69.2 (9.6) (n=88)	0.608	0.718
Highest systolic	127.3 (13.9) (n=179)	128.4 (11.8) (n=62)	130.3 (15.1) (n=88)	0.256	0.141
Highest diastolic	79.9 (10.3) (n=179)	77.5 (10.6) (n=62)	78.6 (9.3) (n=88)	0.228	0.550
Percentage (No) with any proteinuria	38 (167/176)	19 (12/63)	30 (26/87)	0.019*	0.588
Percentage (No) with proteinuric pre-eclampsia	2 (3/184)	0 (0/63)	0 (0/88)	0.289	0.569
Percentage (No) with bleeding	8 (15/180)	6 (4/63)	7 (6/88)	0.837	0.761
Percentage (No) with urinary infection	3 (5/181)	2 (1/63)	6 (5/88)	0.317	0.148
Percentage (No) with spontaneous onset of labour	74 (133/179)	62 (39/63)	59 (52/88)	0.023*	0.039*
Percentage (No) with premature rupture of membranes	19 (33/138)	22 (14/63)	17 (15/87)	0.748	0.566
Mean (SD) gestation (weeks)‡	39.58 (2.87) (n=158)	40.30 (1.19) (n=55)	39.97 (2.33) (n=78)	0.148	0.516
Percentage of pregnancies estimated to be <37 weeks	10 (17/171)	2 (1/61)	5 (4/88)	0.053	0.458
Percentage (No) with miscarriage in hospital	3 (6/193)	4 (3/68)	4 (4/92)	0.820	0.749

\* $p<0.05$ . †  $n=176$ . ‡ From date of last menstrual period, excluding women with gestation >44 weeks.

TABLE III—Characteristics of infants (excluding two sets of twins)

	Lower Moor			p Value	
	Bastreet (a)	Unexposed (b)	Exposed (c)	3 Groups (a v b v c)	2 Groups (c v (a+ b))
Mean (SD) birth weight (g)	3280 (584) (n=178)	3483 (482) (n=63)	3330 (490) (n=87)	0.038*	0.931
Percentage (No) with low birth weight (<2500 g)	10 (17/178)	0 (0/63)	3 (3/87)	0.012*	0.301
Mean (SD) head circumference (cm)	34.6 (1.6) (n=160)	34.9 (1.3) (n=59)	35.0 (2.4) (n=81)	0.213	0.299
Sex (% (No) male)	54 (99/183)	52 (33/63)	47 (41/87)	0.562	0.295
Percentage (No) with Apgar score <7 at 1 min	19 (31/162)	17 (11/63)	22 (19/87)	0.750	0.450
Percentage (No) with Apgar score <8 at 5 min	7 (12/162)	3 (2/63)	9 (8/86)	0.344	0.343
Percentage (No) admitted to special care baby unit	9 (16/183)	5 (3/62)	5 (4/87)	0.352	0.461
Percentage (No) with congenital defects†	4 (7/188)	8 (5/65)	10 (9/88)	0.095	0.065
Percentage (No) with other problems	10 (19/185)	8 (5/63)	14 (12/88)	0.502	0.297

\*p<0.05. †Including terminations.

TABLE IV—Infants with malformation or deformation

Case No	Date of last menstrual period	Date of delivery	Congenital defect
<i>Bastreet</i>			
1a	6.7.87	9.5.88	Spina bifida and hydrocephalus
2a	3.8.87	12.4.88	Hare lip, cleft palate
3a	1.10.87	7.6.88	Hypoplastic left heart (died at 4 days)
4a	11.11.87	30.8.88	Birthmark on right side of back
5a	2.1.88	20.10.88	Right hare lip, cleft soft palate
6a*	19.1.88	11.11.88	Minor umbilical hernia (closed surgically)
7a*	15.3.88	29.12.88	Cystic hygroma
<i>Lower Moor—Unexposed</i>			
1b	4.4.87	15.1.88	Extra digit bilaterally (fingers and toes)
2b	?5.87	27.1.88	Urethral opening on top of penis (no action taken)
3b	12.9.87	19.2.88	Spina bifida (termination)
4b	9.10.87	5.7.88	Talipes in right foot
5b	Not known	13.4.88	Anencephalus (termination)
<i>Lower Moor—Exposed</i>			
1c	18.10.87	28.7.88	Hypospadias (plastic surgery required)
2c	16.11.87	19.8.88	Palmar crease in right hand
3c*	29.11.87	31.8.88	Eyelid defect: inverted upper right eyelid (later inverted and flat)
4c*	10.1.88	21.9.88	Right positional talipes
5c*	2.2.88	10.11.88	Bilateral positional talipes (massage only)
6c*	5.3.88	25.11.88	Bilateral positional talipes (no treatment required)
7c*	1.4.88	8.1.89	Extra digit, right hand
8c*	31.5.88	20.3.89	Prominent labia minora (no follow up)
9c*	11.6.88	14.4.89	Left talipes equinovarus (surgery required)

\*Infants with defects for which timing of exposure to aluminium sulphate could be an explanation.

talipes rate, and the four infants with talipes had been exposed at different times during gestation (one during the first trimester, two during the second, and one during the third). Deformations such as talipes could arise if during pregnancy there was a period of gross reduction in amniotic fluid or with reduced fetal movements. It is conceivable that maternal ingestion of the strongly acidic aluminium loaded water after the Lower Moor incident could have resulted in a loss of amniotic fluid. There was no indication of this loss in the clinical obstetric records, but a transient loss is unlikely to have been noted. Alternatively, the incident may have affected fetal motor development, with consequently reduced fetal movements. Animal experiments have shown both skeletal malformations<sup>4</sup> and neuromotor defects<sup>5,6</sup> so either explanation is feasible, but it should not be forgotten that the association with talipes may be a statistical artefact.

After an incident in pregnancy paediatricians may be more likely to identify or document minor defects.

Many of the more common minor defects might be recorded, but we found no evidence of any increase in recording other than of talipes. There may, however, have been a difference in defect ascertainment in the different hospitals where these infants were delivered. Although there was some overlap, the Lower Moor and Bastreet women delivered in two different hospitals. There was only one deformation in 65 deliveries before the incident in women from Lower Moor compared with five deformations in 88 deliveries after the incident, but this change could be due to a change in staff or perception of talipes in the hospital, rather than an increase in incidence.

Problems of interpretation can arise in any study of teratogenicity if the exposure to chemicals results in defects incompatible with intrauterine life. Thus exposure in early pregnancy resulting in early pregnancy loss is unlikely to show up in these data. The study was able to identify only those miscarriages resulting in admission to hospital, which is more likely relatively late in pregnancy.

The lack of an association with frank congenital malformations (as opposed to deformations) should not be construed as meaning that aluminium sulphate has no teratogenic effect in humans. Firstly, only 39 mothers were exposed in the first trimester of pregnancy (two of these had infants with minor defects). Secondly, this study has considered only defects apparent at birth or shortly after birth. It is well known that only a proportion of defects is identified in this way. It is therefore essential that these children are followed up to ascertain the rates of internal malformations that become apparent later and also any problems in either motor or mental development or in behaviour and temperament. Such a study is currently underway.

In conclusion, this study has shown a lack of major problems associated with fetal exposure to high doses of aluminium. Indeed the pregnancies in the area had, if anything, a better outcome with fewer preterm deliveries. Although we looked for many specific outcomes, only one possible deleterious association was found, and that (an excess of talipes) did not seem to be associated with long term problems for the child.

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- 1 Oliver JMT, Garcia MC, Galiana JR, et al. Spanish toxic oil and congenital malformations. *Lancet* 1983;i:181.
- 2 Matsumoto H, Koya G, Takeuchi T. Fetal minamata disease. *J Neuropathol Exp Neurol* 1965;24:563-74.
- 3 Akar N, Ata Y, Aytekin AF. Neural tube defects and Chernobyl? *Paediatr Perinatal Epidemiol* 1989;3:102-3.
- 4 Lappe M. Trace elements and the unborn: review and preliminary implications for policy. In: Rose J, ed. *Trace elements in health: a review of current issues*. London: Butterworths, 1988.
- 5 Bernuzzi V, Desor D, Lehr PR. Developmental alterations in offspring of female rats orally intoxicated by aluminium chloride or lactate during gestation. *Teratology* 1989;40:21-7.
- 6 Marlow M, Stellern J, Errera J, Moon C. Main and interaction effects of metal pollutants on visual-motor performance. *Arch Environ Health* 1985;40:221-5.
- 7 Morton MS, Elwood PC, Abernethy M. Trace elements in water and congenital malformations of the central nervous system in south Wales. *Br J Prev Soc Med* 1976;30:36-9.
- 8 Golding J, Butler NR. The socioeconomic factor. In: Falkner F, ed. *Prevention of perinatal mortality and morbidity*. Basel: Karger, 1984:31-46. (Child Health and Development Vol 3.)

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