

Patient	Age (yr)	Employment in air spraying (mo, mo/yr)	Reported start of symptoms (mo/yr)	Clinical condition	Chest X-ray	Arterial pH, PO <sub>2</sub> (mm Hg), PCO <sub>2</sub> (mm Hg)	Spirometry, 1993 (FVC [L], FEV <sub>1</sub> [% pred])	Spirometry, 1994 (FVC [L], FEV <sub>1</sub> [% pred])
A	19	9 (2/92-11/92)	11/92	Respiratory distress	Bilateral alveolar-interstitial infiltrates	7.56, 25, 29	ND	..*
B	22	16 (9/91-1/93)	9/92	Respiratory distress	Bilateral alveolar-interstitial infiltrates	7.45, 70, 40	0.68 (19) 0.64 (20)	1.00 (27) 0.89 (28)
C	22	10 (9/91-6/92)	6/92	Respiratory distress	Bilateral alveolar-interstitial infiltrates	7.50, 27, 46	0.71 (22) 0.57 (20)	0.73 (23) 0.68 (24)
D	23	1 (7/92)	9/92	Weight loss, occasional chest tightness	Bilateral basal reticular markings	ND	2.87 (80) 2.08 (67)	2.66 (75) 1.84 (59)
E	26	Occasionally (11/91-11/92)	9/92 9/92	Asthenia, mild dyspnoea on exercise	Normal	7.45, 78, 32	3.10 (87) 2.69 (86)	3.14 (91) 2.73 (91)

Pred=predicted, ND=not done. \*Deceased.

Table: **Characteristics of textile workers on admission (February/March, 1993) and 1 year later**

table) were painters who used hand-held spray guns to spray paint onto lace cloth; subject D worked in another room, but she had replaced her sister (C) for one month; subject E was an aid doing occasional spray-painting. Spray-painting had started in the middle of 1991, with products originating from Spain, reportedly from January, 1992, onwards.

Subjects A, B, and C were admitted in respiratory distress. Their symptoms had begun between June and November, 1992, with work-related eye, nose, and throat irritation, dry cough, and fever; after a few weeks, they had dyspnoea on exercise, weight loss, and asthenia. On admission they had tachypnoea and cyanosis, diminished lung sounds, severe hypoxaemia (in two subjects) and, where measurable, severe reductions in forced vital capacity (FVC) and in forced expiratory volume in one second (FEV<sub>1</sub>). Chest radiography showed bilateral, mainly basal alveolar-interstitial infiltrates. Other conventional investigations (including tuberculosis) did not contribute. The patients were given oxygen, corticosteroids, and antibiotics. Patient A died in respiratory distress 20 days after admission; no necropsy was done. The two other patients improved while in hospital, but were still dyspnoeic when discharged after 7 and 5 days. Subjects D and E had had similar symptoms but they were much less severely affected.

The four surviving women were re-evaluated in February, 1994. The two more affected women (B, C) still complained of severe dyspnoea, dry cough, and bronchial hyper-reactivity; both had peripheral cyanosis, and one (C) had clubbing of the fingers. In general, chest radiographic appearances and pulmonary function had not improved. Fibreoptic bronchoscopy showed, in all four, an inflamed bronchial mucosa, with haemorrhagic areas and bleeding on contact. Biopsy was done in only one subject (C), and showed a columnar secretory epithelium resting on a very thin chorion. Patch tests carried out with the incriminated formulation (left over in the factory, found 1 year after closure of the workshop) led to severe irritation within 2 h of application (open test) and beginning of skin necrosis after 72 h (occlusive test).

Although we have no pathological evidence that the pulmonary disease in our patients was similar to that described in the Spanish patients, the features of this outbreak make it highly probable that the same agent or agents, caused the disease in both locations. The owner of the factory in Tlemcen acknowledged that the paint ingredients had been obtained from a supplier from Spain. Most of the evidence points to Acramin FWN as the causal agent, but the mechanisms for this very severe and hitherto unreported type of occupational pulmonary toxicity are still unknown. Another possibility, on the grounds of circumstantial evidence only, is that other compounds, such as polyfunctional aziridine cross-linking agents, were perhaps responsible.<sup>1</sup> It is very important for the prevention of similar occurrences that these and other possible toxic mechanisms

should be investigated experimentally. In the meantime, the outbreak in Algeria shows that hazardous substances or work-processes banned from one country can be exported and cause disaster in another (developing) country.<sup>2</sup>

F Ould Kadi, B Mohammed-Brahim, A Fyad, S Lellou, B Nemery  
Centre Hospitalo-Universitaire d'Oran, Service de Médecine du Travail, Oran, Algeria; and K U Leuven Laboratorium voor Pneumologie (Longtoxicologie) and Afdeling Arbeids- en Verzekeringsgeneeskunde, B 3000 Leuven, Belgium

- 1 Sanz P, Prat A. Toxicity in textile air-brushing in Spain. *Lancet* 1993; **342**: 240.
- 2 Castleman BI, Navarro V. International mobility of hazardous products, industries, and wastes. *Annu Rev Publ Health* 1987; **8**: 1-19.

### Saturated fat intake in Minsk (Belarus), a high-risk area for heart disease

SIR—Mortality from coronary heart disease (CHD) has gone up in Eastern European countries since 1970.<sup>1,2</sup> It has been suggested that this is related to increased intake of saturated fatty acids.<sup>2</sup> A low intake of linoleic acid may contribute also.<sup>3</sup> Reliable data on food intake in the former Soviet Union are difficult to come by, so we assessed dietary fatty acid intake from fatty acid composition in subcutaneous fat aspirates.<sup>4</sup> Adipose-tissue fatty acid composition correlates with CHD in European whites.<sup>3</sup> Fat aspiration<sup>4</sup> was done in patients admitted to Hospital 10, Minsk, Belarus, for elective surgery for endemic goitre (women, n=21; courtesy of Dr N W Andreev, department of endocrinology) or evaluation of gastric complaints (men, n=22; courtesy of Dr L A Baranova, department of gastroenterology). The aspirates were frozen at -20°C and analysed in the Netherlands.<sup>4</sup>

Values of saturated, monounsaturated, and n-6 and n-3 polyunsaturated fatty acids, and omega-3 fatty acids were in the range found in Western Europe<sup>3,5</sup> (table). We found no

Fatty acid* (%)	Men (n=22)†	Women (n=21)†
SFA	28.6 (0.4)	26.4 (0.4)
MUFA	51.9 (0.5)	52.1 (0.6)
PUFA	13.5 (0.5)	15.5 (0.4)
P/S ratio	0.48 (0.02)	0.59 (0.02)
Linoleic acid	10.9 (0.5)	12.4 (0.4)
20:5n-3 (EPA)	0.1 (0.0)	0.1 (0.0)
22:6n-3 (DHA)	0.2 (0.0)	0.2 (0.0)

\*Mean (SE): SFA=saturated (C10; C12; C14; C15; C16; C17; C18, and C20); MUFA=monounsaturated (C16.1; C18.1; C20.1; C22.1, and C24.1); PUFA=polyunsaturated (C18:2n-6; C18:3n-3; C18:4n-3; C20:2n-6; C20:3n-3; C20:4n-6; C20:5n-3; C22:2n-6; C22:4n-6; C22:4n-3; C22:5n-3, and C22:6n-3); total made up by about 6% unidentified fatty acids; P/S ratio, polyunsaturated/saturated ratio, EPA=eicosapentaenoic acid; DHA=docosahexaenoic acid.  
†Average age for men and women 32.9 and 45.8 years, respectively; body mass index 24.5 and 26.8; blood pressure 121.6/78.9 and 127.6/77.4; 18 and 4 were smokers.

Table: **Fatty acid composition of adipose tissue in Belarussian men and women**

indication that Belarussian fat consumption is unusually low in linoleic acid and fish oils or is characterised by a profile that is associated with increased CHD. The assumed high intake of saturated fatty acids could not be confirmed by saturated fatty acid levels in adipose tissue. Dietary fat may not be a major determinant of high mortality from CHD in Belarus.

J A Bijlsma, T W A de Bruin, D W Erkelens, M B Katan

Department of Internal Medicine, University Hospital Utrecht, 3508 GA, Netherlands; Department of Human Nutrition, Agricultural University, Wageningen

- 1 Deev AD, Oganov RG. Trends and determinants of cardiovascular mortality in the Soviet Union. *Int J Epidemiol* 1989; **18** (suppl 1): S137-44.
- 2 Kesteloot H. Nutrition and health. *Eur Heart J* 1992; **13**: 120-28.
- 3 Wood DA, Riemersma RA, Butler S, Thomson M, Macintyre C, Elton RA. Linoleic and eicosapentaenoic acids in adipose tissue and platelets and risk of coronary heart disease. *Lancet* 1987; *i*: 177-82.
- 4 Katan MB, Van de Bovenkamp P. Eicopentaenoic acid in fat. *Lancet* 1987; *i*: 862-63.
- 5 Riemersma RA, Wood DA, Butler S, et al. Linoleic acid content in adipose tissue and coronary heart disease. *BMJ* 1986; **292**: 1423-27.

### Risk of recurrent spontaneous abortion for pregnancies discovered in the fifth week of gestation

SIR—Spontaneous abortion rates are influenced by previous pregnancy history, maternal age, and other confounding factors.<sup>1,2</sup> Most of these data were derived when a diagnosis of pregnancy loss was made after eight or nine weeks' gestation. Recent cohort studies have reported the outcome of pregnancies identified by ultrasound, but still most were recognised only by 8 weeks' gestation. By contrast, pregnancies are now widely diagnosed earlier because of sensitive human chorionic gonadotropin (hCG) assays and transvaginal ultrasound. A relevant clinical question is whether extant estimates of recurrence risks are appropriate for counselling women after losses detected this early in gestation. Specifically, we are unaware of recurrence risk data for women whose pregnancy losses were discovered in the fifth gestational week, perhaps the most common time at which pregnancy loss is now recognised.

We are conducting a cohort study that provides such data.<sup>3</sup> The purpose of our study is to assess the potential deleterious effects of fertilisation involving ageing gametes. We are analysing women who became pregnant while practising natural family planning (NFP), a contraceptive method that entails periodic abstinence and charting of both signs of fertility and specific days of sexual intercourse. Between January, 1987, and March, 1993, we identified pregnancies occurring among NFP users in six skilled NFP centres: two in Santiago, Chile; Bogota and Mendellin, Colombia; Milan, Italy; and Washington, DC. Study volunteers provided interview information on socio-demographic characteristics and previous reproductive history. Using standard NFP charts, subjects prospectively recorded their basal body temperature (BBT) and physical signs, which allowed day of ovulation to be determined on the basis of peak mucous day (defined as the last day of vulvar lubrication and/or stretchable mucous present at the vulva). Given the calculated day of ovulation, menses would be predicted to occur 14 days later. If menses did not occur, women would, of course, recognise pregnancies in the 5th week after the last menstrual period.

Updating our preliminary data,<sup>4</sup> 951 pregnancies ascertained in this way resulted in 98 spontaneous abortions (10.1%) and 8 additional stillbirths. The well-established

Women	Pregnancies	Losses	Relative risk (95% CI)
No previous pregnancy	360	31 (8.6%)	0.92 (0.59-1.45)
Previous pregnancies:			
No previous loss	407	39 (9.6%)	1 (1-36)
1 loss	138	18 (13.0%)	2.24 (0.81-2.30)
2 losses	42	9 (21.4%)	2.86 (1.17-1.29)
3 losses	4	1 (25.0%)	286 (0.51-16.02)
	951	98 (10.1%)	

Table: Loss rates for women whose pregnancies were ascertained in the fifth gestational week

maternal age effect was confirmed for pregnancies ascertained in the 5th week of gestation. Loss rates were 15.2% for women with a history of previous losses compared with 9.2% for those without such losses (age-adjusted relative risk, 1.52; 95% CI 1.09-2.42). Loss rates increased with increasing number of previous losses (table); this trend was highly significant ( $\chi^2=6.2$ ;  $p=0.013$ ). The magnitude of this increase is similar to that previously reported for pregnancies determined in traditional fashion.<sup>1,2</sup> Loss rates neither varied further as a reflection of alcohol consumption or smoking nor increased with gravidity, except in the small group of 24 women who had had 5 or more pregnancies (loss rate 33.3%).

Our data offer reassurance that recurrence risk figures used to counsel women whose pregnancies are recognised at 8 weeks or beyond can now be generalised to women whose pregnancies are recognised as early as the 5th gestational week. Like Regan and colleagues,<sup>5</sup> we found lowest loss rates among women with no previous losses, irrespective of whether the pregnancy was or was not the first. Recurrence risks after two losses still do not exceed 25%, although our data are too limited to allow precise comments about women who have three or more previous losses.

J L Simpson, R H Gray, J T Queenan, M Barbato, A Perez, P Mena, W S Stevenson, F Pardo, R T Kambic

Baylor College of Medicine, Houston, TX, USA; Johns Hopkins University, Baltimore, MD; Georgetown University and the Institute for Reproductive Health, Washington, DC; Centro Ambrosiano Metodi Naturali, Milan, Italy; Pontificia Universidad Catolica de Chile, Santiago, Chile; Universidad de Chile, Santiago; Maryland and District of Columbia NFP Providers Association, Washington, DC; Javeriana Universidad, Bogota, Columbia

- 1 Stein Z, Kline J, Susser E, Shrouf P, Warburton D, Susser M. Maternal age and spontaneous abortion. In: Porter IH, Hood EB, eds. Human embryonic and fetal death. New York: Academic Press, 1980: 107-27.
- 2 Warburton D, Fraser FC. Spontaneous abortion risks in man: data from reproductive histories collected in a medical genetics unit. *Am J Hum Gen* 1974; **16**: 1-25.
- 3 Simpson JL, Gray RH, Queenan JT, et al. Pregnancy outcome associated with natural family planning (NFP): scientific basis and experimental design for an international cohort study. *Adv Contracept* 1988; **4**: 247-64.
- 4 Simpson JL, Gray RH, Queenan JT, et al. Fetal outcome among pregnancies in natural family planning acceptors: an international cohort study. *Am J Obstet Gynecol* 1992; **165**: 1981-82.
- 5 Regan L, Braude PR, Trembath PL. Influence of past reproductive performance on risk of spontaneous abortion. *BMJ* 1989; **299**: 541-45.

### Central nervous system pathways mediating angina pectoris

SIR—In their report of positron emission tomography in patients during angina provoked by intravenous dobutamine, Rosen and colleagues (July 16, p 147) infer that changes in regional cerebral blood flow relate to neurological activation in the same areas and that this provides evidence for