from the syndrome.[5] Further work is needed on the physiological and behavioural aspects of the parent-infant interaction that occurs among groups in whom bed sharing is common before this practice is implicated in the pathogenesis of the sudden infant death syndrome.

I SADAF FAROOQI
GREGORY Y H LIP
D GARETH BEEVERS

Department of Medicine,
Dudley Road Hospital,
Birmingham B18 7QH

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Helping women with premenstrual syndrome

EDITOR,—P M S O'Brien's review of the premenstrual syndrome is misleading in its discussion of late luteal phase dysphoric disorder.[1] O'Brien is incorrect in stating that this diagnosis "refers only to the mood disturbance of premenstrual syndrome"; the diagnostic criteria for the disorder listed in the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised include physical and behavioural symptoms as well,[2] giving a category essentially identical with what O'Brien terms "primary premenstrual syndrome."

T H LEIGH

Tavistock Clinic,
Tavistock Centre,
London NW3 5BA

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Concurrent infection with hepatitis B and C viruses

EDITOR,—Larry Mimms and colleagues report an interaction between hepatitis B and C virus in patients who received both viruses through contaminated blood transfusions: coinfection with hepatitis C virus reduced the multiplication of hepatitis B virus.[1] Our experience with patients coinfected with these viruses is different.[2]

We tested serum samples from a cohort of 60 haemophilic subjects for markers of hepatitis C virus infection by second generation enzyme linked immunosorbent assay (ELISA) and recombinant immunoblot assay and for presence of hepatitis C virus RNA by reverse transcriptase polymerase chain reaction. Forty two of the serum samples tested were positive for antibodies to hepatitis C virus by ELISA, of which 35 were positive and seven were indeterminate (c22 band only) by recombinant immunoblot assay. RNA from hepatitis C virus was detected by the polymerase chain reaction in 33 of these 42 samples, including four of those that were indeterminate by recombinant immunoblot assay. Five of the cohort were known to be chronic carriers of hepatitis B virus: all were positive for antibodies to hepatitis C virus but none was positive for hepatitis C virus RNA. Only four of the 37 patients who were not carriers of hepatitis B virus were negative for hepatitis C virus RNA. This difference was significant ($P < 0.001$, Fisher's exact test).

Our data suggest that replication of hepatitis B virus inhibits replication of hepatitis C virus in coinfected chronic carriers of hepatitis B virus. This raises the possibility that inhibiting hepatitis B virus replication by treating such patients with interferon may result in reactivation of hepatitis C virus infection once the treatment is stopped. In conclusion, the virological outcome of coinfection with hepatitis B virus and hepatitis C virus may not be as straightforward as Mimms and colleagues suggest. It may depend on which virus infects a patient first as well as the relative doses of infection.

WILLIAM L IRVING
G DOLAN

University Hospital,
Queen's Medical Centre,
Nottingham NG7 2UH

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Clusters of anophthalmia

No link with benomyl in Italy . . .

EDITOR,—Since the *Observer* reported a possible link between apparent clusters of anophthalmia and microphthalmia in England and Wales and the pesticide benomyl,[1] several articles have commented on possible strategies to manage public and media concern, the methodology to identify clusters, the difficulty in assessing disease clusters with unreliable data, and the weakness of retrospective studies.[2-5] Analysis of cases routinely reported to the national congenital malformation surveillance scheme (CMSS) in England and Wales and to the European congenital malformations registries (EUROCAT) suggested that pesticides based on benomyl are unlikely to be major causes of anophthalmia and microphthalmia.[4,5]

In Italy the National Committee of the Congenital Malformations Registries also made a descriptive analysis of cases of anophthalmia and microphthalmia collected during 1986-90 and presented the results to the Ministry of Health. After exclusion of malformations associated with chromosomal and other genetic syndromes, 33 cases of anophthalmia and 78 cases of microphthalmia were reported in 940 615 births, giving prevalences of 0·35 and 0·83 per 10 000 births respectively; results similar to those of the European registries.[4] The prevalance of the two malformations, separately and together, was evaluated for 18 regions: interregional distribution was not significantly heterogeneous ($\chi^2 = 18{\cdot}61$, df = 17, $P = 0{\cdot}3$), and in no region was the prevalence significantly different from the mean prevalence.

A correlation analysis by region was then made between the prevalence of the malformations and use of benomyl based pesticides (derived from reports of the National Statistical Institute (ISTAT)). There was no significant correlation by region, nor when the regions were grouped by four levels of pesticide consumption. An analysis by parental occupation was performed on a subset of the data (768 005 births) with babies with preauricular tags acting as controls. Of the 95 parents of babies with anophthalmia and microphthalmia, 4·2% (two fathers and two mothers) had agricultural occupations compared with 4·7% (48/1032) of the control parents (odds ratio = 0·9 (95% confidence interval 0·23 to 2·55)).

On the basis of these results, the association between use of benomyl and anophthalmia and microphthalmia seems unlikely.

FABRIZIO BIANCHI

Istituto Fisiologia Clinica del CNR,
Dipartimento Epidemiologia e Biostatistica,
56124 Pisa, Italy

ANNA CALABRO

Clinica Pediatrica, Università,
Perugia, Italy

ELISA CALZOLARI

Istituto Genetica Medica, Università,
Ferrara, Italy

PIER PAOLO MASTROIACOVO

Clinica Pediatrica, Università Cattolica,
Rome, Italy

GRAZIA PETRELLI
AMEDEO SPAGNOLO

Istituto Superiore di Sanità,
Laboratorio Epidemiologia e Biostatistica,
Rome, Italy

ROMANO TENCONI

Dipartimento Pediatria, Università,
Padua, Italy

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. . . or in Norway

EDITOR,—The relation between parental exposure to the fungicide benomyl and anophthalmia in children has received attention.[1] We have investigated the hypothesis that a maternal occupational activity that could result in exposure to benomyl during the first trimester is a risk factor for anophthalmia or microphthalmia. A Norwegian multiregister study offered the opportunity to explore this association.

A national cohort of farming families has been established from all five agricultural or horticultural censuses during 1969-89. All 157 360 personal farm holders born later than 1924 have been identified, and information concerning the activity at the farm at the time of the censuses has been gathered for the individual holding. By means of their national personal identification number, the spouse and children of the holders were identified in the central person register. The linking procedures have identified 248 696 farmers and spouses born during 1925-74 and 323 359 children born during 1952-91. Linkage with the medical birth registry of Norway gave information on the perinatal outcome of 192 416 pregnancies during 1967-91.

Benomyl was introduced in Norway in 1971. It is mainly used as a fungicide in greenhouses and orchards; it is also used to a limited extent during the spring in fields of vegetables and, since the mid-1970s, in the late autumn in grain fields. Its use has been limited in Norway: the maximum sale was 1682 kg active compound in 1980. We considered farm activities after 1970 that might result in exposure to benomyl at a relevant time: work in greenhouses throughout the year; in orchards for children conceived in April-June; with vegetables grown in fields for children conceived in January-April; or cultivating grain for children conceived in August-November. Eleven per cent (n = 21 843) of the entire cohort of infants born in 1967-91 had potentially been exposed to benomyl according to these criteria. Four of the 192 416 children had been diagnosed as having anophthalmia or microphthalmia (*International Classification of Diseases*, eighth revision, codes 744.0-744.1), yielding a crude prevalence of 0·21/10 000 new-