Age group (years)	Annual age specific incidence rate (×100 000)	1989		1990		1991		1992		1993†		Expected No of cases during 1989-93†
		No of treatment cycles /1000	Expected No of cases	No of treatment cycles /1000	Expected No of cases	No of treatment cycles /1000	Expected No of cases	No of treatment cycles /1000	Expected No of cases	No of treatment cycles /1000	Expected No of cases	
Incidence in Ferrara, Italy ¹												
0-39	0.58	725	0.35	756	0.37	520	0.25	384	0.19	66	0.03	1.19
40-59	1.82	1801	2.73	1874	2.84	1318	2.00	975	1.48	169	0.26	9.31
≥60	2.42	1842	3.71	1941	3.91	1498	3.02	1176	2.37	269	0.54	13.55
Total		4368	6.79	4571	7.12	3336	5.27	2535	4.04	504	0.83	24.05
Incidence in Olmsted County, Minnesota, United States ²												
0-39	1.07	725	0.65	756	0.67	520	0.46	384	0.34	66	0.06	2.18
40-59	2.84	1801	4.26	1874	4.44	1318	3.12	975	2.31	169	0.40	14.53
≥60	3.25	1842	4.99	1941	5.26	1498	4.06	1176	3.19	269	0.73	18.23
Total		4368	9.90	4571	10.37	3336	7.64	2535	5.84	504	1.19	34.94

*Expected number of cases was derived by applying age specific incidence to corresponding number of therapeutic cycles. As each subject was defined as being at risk for only one month after administration of drug, average annual incidence was divided by 12.

†Until November 1993.

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Science supports the use of gangliosides

EDITOR,—The possible correlation between the administration of gangliosides and the onset of a polyradiculoneuritis of Guillain-Barré type has been discussed for many years, but the pharmacological, clinical, and epidemiological evidence of such an association does not indicate a causal relation.

We are therefore surprised that Gianluca Landi and colleagues should resume the controversy.¹ They present—in a scanty and partial way—data that have been widely discussed and evaluated in many meetings of independent experts. This data has also been discussed by the Italian Health Council and during official hearings on the subject, both in Italy and in Spain. Moreover, this topic has been widely debated in several letters and publications in major scientific journals.^{2,3}

The cases are presented as being the result of an original study, thus representing something new. When the cases are analysed thoroughly most of them fall into one of several categories, since the Guillain-Barré syndrome is a multifactorial disease with an unknown aetiology and with different clinical manifestations.

Among the reported cases it is possible to distinguish patients who showed prodromal signs of a polyradiculopathy that in themselves could explain the therapeutic use of gangliosides (for example, facial paralysis, low back pain, sensory disturbances in the limbs); patients who already had clinical manifestations of a parietic condition (for example, multiple brain metastases, brain haemorrhage, head trauma); and patients who had pathological signs that could be identified as pathogenic features (for example, inflammatory, infective, or aspecific events such as flu or fever). When the subjects who do not belong to any of these groups are considered, the alleged responsibility of gangliosides is anecdotal.

Finally, the authors' opinion on the ratio of risk to benefit for gangliosides is a personal one. A huge number of clinical trials of these drugs over many years, not only in Italy, have supported the therapeutic use of gangliosides. In addition, the value of the research studies in neuroscience performed at Fidia's laboratories is internationally recognised.^{4,5}

MARINO MASSAROTTI

Medical Department, Fidia S.p.A.

RITA MATANO

Medical Department,
Fidia,
35031 Abano Terme,
Italy

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Variation in caesarean section rates

What difference does it make?

EDITOR,—The controversy over the optimal rate of caesarean section continues^{1,2} in the absence of clear evidence on the relative benefit of higher or lower rates. There is a large literature on the variation in rates, but this is mostly concerned with its determinants^{3,4} rather than the more fundamental question: what difference does it make?

Craig R Leitch and James J Walker state a commonly held view—that the focus of study should be the reasons or indications for caesarean section.² Yet, as they also state on the basis of their unit's experience over 30 years, a large difference in caesarean section rates (7% rising to 17%, judging from their figure) is compatible with the absence of change in the most common indications, failure to progress and fetal distress. Both these indications are continuous variables, so it is a question of degree: what is the threshold at which the clinician decides that a caesarean section would be the best course of action? This has clearly changed over time.

Given the increase in the caesarean section rate in recent decades, the large variation that exists internationally, and the variation among different units in the same country, there is scope for comparison of outcomes among units having differing rates and, therefore, differing thresholds. The variation among different units in the same country is much less likely to be confounded by other factors, which may have altered over time or may differ among different societies and health care systems.

An analysis of pregnancies in one English health region compared groups of obstetric units, categorised according to their caesarean section rates, to see what effect the rate had on a range of outcome variables.⁵ Care was taken to avoid confounding and selection effects. Among maternal variables, higher caesarean section rates were associated with an increased risk of postnatal blood transfusion—showing the sensitivity of the method. For fetal variables, including perinatal mortality, the results showed a clear difference in the balance of advantage of relatively high or low rates between very low birthweight infants and the other 97% of deliveries.

It is interesting that, although everyone is aware of the need for outcome studies, at least in theory, clinical journals declined to publish this study. The paper is to be published in an epidemiological journal, possibly as much for its innovative methodology as for its substantive content.

MICHAEL JOFFE

Academic Department of Public Health,
St Mary's Hospital Medical School,
London W2 1PG

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Maternal mortality higher after caesarean section

EDITOR,—The claim of Lawrence Mascarenhas and colleagues that maternal mortality after elective caesarean section is similar to that after vaginal delivery¹ is unfounded and certainly not supported by the references they quote.^{2,3} As previously reported, the confidential inquiry into maternal deaths in 1982-4 showed that elective caesarean section was associated with a risk of direct death 4.5 times greater than that associated with vaginal delivery.⁴ The confidential inquiry for 1985-7 could not provide any data on the number of caesarean sections in England and Wales, and hence no case fatality rate could be calculated.

The number of caesarean sections has been estimated for 1988-90,⁵ yielding an estimate of the direct case fatality rate of 0.21/1000. This compares with a case fatality rate of 0.017/1000 for vaginal delivery (the numerator (37) is calculated by subtracting the 57 direct deaths in cases of caesarean section from the 94 direct deaths of women delivering a baby (from table 1.3) and the denominator (2081809) by subtracting the 278500 caesarean sections (table 13.2) from the 2360309 maternities (table 1.2)). Unfortunately, there are no data on the overall proportions of elective and emergency caesarean sections, but if the proportion of elective caesarean sections was the same as that in 1982-4 (46%) there would have been 128110 elective caesarean sections in 1988-90, with 19 direct deaths and a case fatality rate of 0.148/1000 (8.7 times greater than the rate for vaginal delivery). Similarly, there would have been 38 direct deaths in 150390 emergency caesarean sections, with a case fatality rate of 0.25/1000 (1.7 times greater than the rate for elective caesarean sections).