



Regional (health board) variation in measles vaccine uptake across Scotland, 1986.

Horizontal axis is difference from mean (%). The fifteen health boards are, in descending order: Borders, Forth Valley, Fife, Highland, Dumfries and Galloway, Grampian, Orkney, and Tayside; and Greater Glasgow, Argyll and Clyde, Ayrshire and Arran, Lothian, Shetland, Lanarkshire, and Western Isles.

Source: Information and Statistics Division, Scottish Home and Health Department, 1987.

Scotland, 84% were administered to children between 13 and 24 months of age, suggesting successful implementation of policy:

Age when vaccine received (mo)	No
< 13	340 (5.7%)
13-24	5009 (83.7%)
25-60	520 (8.7%)
> 60	117 (1.9%)

Variation in vaccine uptake is far more serious. Nokes and Anderson illustrate this point with Department of Health statistics for England. The picture in Scotland is even more striking (figure). Although the mean uptake rate for measles vaccine in Scotland during 1986 is higher than that for England (76% vs 71%), regional variation in Scotland ranges from 53% to 92% and the uptake rate when calculated for general practice areas within the Grampian region, for example, varies from 30% to 100%. This emphasises the need to concentrate effort at the small-area level.

The key to achieving high uptake of immunisation is education of health professionals. Regular monitoring of uptake rate at small-area level should be done, and general practitioners and health visitors must be given feedback on their performance. Local vaccination coordinators will help, but they must be given the necessary authority and resources in order to be effective. This means giving a higher profile to the specialty of public health.

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TREATMENT OF DISSEMINATED PERITONEAL HYDATID DISEASE WITH PRAZIQUANTEL

SIR,—On Aug 5, 1987, a 13-year-old boy presented with a large pelvic mass, which he had felt for a year. Sonography showed a multiloculated cyst. Unfortunately needle biopsy of the cyst wall was done and the boy sent home. Histological examination showed hyaline in the cyst wall.

Within 7 weeks the boy returned with severe ascites. Laparotomy on Sept 24 revealed that the peritoneum was transformed into thick membranes covered by many small cysts. The large hydatid cyst was removed. Parts of the peritoneum were soaked with 0.5% cetrinide in an attempt to destroy some of the small cysts.¹ However, most of the peritoneum was inaccessible because of the changes.

Starting on the first postoperative day, the patient was given oral mebendazole 100 mg thrice daily. This drug has, however, a very poor effect on *Echinococcus granulosus*.² Praziquantel can be effective in hydatid disease,^{3,4} so we changed to use of this drug (1200 mg), on

day 7. From the next day he was given 600 mg thrice daily (54.4 mg/kg per day) for 28 days. Sonography before discharge revealed a hydatid cyst in the pelvis containing five daughter cysts with diameters of 2-4 cm. This cyst was covered by adherent intestinal loops and therefore not found during the operation.

The patient was readmitted on Feb 5, 1988, with suppuration from the operation wound. He was given local treatment as well as ampicillin orally until Feb 15. He was also given praziquantel 1500 mg daily 14 days before and after operation on March 6. The hydatid cyst was removed and found to contain a few scoleces, about half of which were alive. Otherwise the peritoneal serosa was normal.

The patient received 93.6 g praziquantel in total. On follow-up after 6 months, he was well. No further cysts were seen on sonography, and no side-effects of the drug were found.

Praziquantel is useful in managing small cysts while larger cysts, especially when daughter cysts are found, may still need surgical management.

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1. Macpherson CNL, Wood AM, French CM. The use of Cetrinide (R) as a scolocidal adjunct to hydatid surgery. In: Tukei PM, Njogu AR, eds. Current medical research in East Africa with emphasis on zoonoses and waterborne diseases 1982. 53-56.
2. Schantz PM, van den Bossche H, Eckert J. Chemotherapy for larval echinococcosis in animals and humans. report from a workshop. *Z Parasitenk* 1982; 25: 5-26
3. Yao Ping Li, Li Jun. Praziquantel in treatment, an investigation with abdominal hydatidosis: preliminary reports of animal experiments and evaluation of 101 clinical cases. 13th International Hydatidology Conference, Madrid, 1985. abstr 234.
4. Morris DL, Richards KS, Chinnery JB. Protoscolocidal effect of praziquantel: in-vitro and electron microscopical studies of *Echinococcus granulosus*. *J Antimicrob Chemother* 1986; 18: 1-6.

CARBON DIOXIDE BREATHING AND MOUNTAIN SICKNESS

SIR,—Harvey et al¹ found that 3% carbon dioxide (CO₂) breathing improved symptoms of acute mountain sickness (AMS). They claim that the effect of CO₂ was due to both an increase in arterial PO₂ (found in all eight subjects) and an increase in cerebral blood flow (measure in three), resulting in an increase in cerebral oxygenation. However, their claims that a cerebrovascular effect of CO₂ is critical in improving AMS, and that "man at altitude is gravely handicapped by the limiting effects of hypocapnia" are not supported by their data.

The improvement in AMS with 3% CO₂ breathing may simply be due to the large increase in arterial PO₂, which is expected on the basis of central chemoreceptor stimulation of ventilation and improvement in ventilation-perfusion matching.² Breathing oxygen-enriched air also rapidly improves high altitude headache, but constricts cerebral vessels, reducing cerebral blood flow. A direct comparison of 3% CO₂ breathing and oxygen breathing would have been informative. A proper study to assess the importance of cerebral blood flow (CBF), however, would manipulate arterial oxygen content of CBF independently. The only trial in which arterial oxygen was held constant while CO₂ (and, presumably, CBF) was increased caused greater symptoms of AMS.³ Without separating arterial oxygen content from flow, the suggestion that CO₂-induced vasodilatation improved AMS remains speculation.

A role for hypocapnic vasoconstriction in the pathophysiology of AMS is not supported by other published work. People with AMS have relative hypoventilation, lower PaO₂, and higher, not lower, PaCO₂ than normal.⁴ The CBF falls with improvement and reduced hypoxia.⁵ Increasing CBF without a concomitant increase in arterial oxygenation is probably more detrimental than beneficial.³ That inspiring a low concentration of CO₂ improves tolerance to acute hypoxia is well established but is irrelevant to AMS, which differs from acute hypoxia. Such observations are more relevant to aviators and climbers to extreme altitudes with very low PaCO₂, than to people with AMS at moderate altitudes. Nor does the fact that 3% CO₂, like oxygen, eliminates periodic

breathing have a bearing on the pathophysiology of AMS. Periodic breathing is related to high altitude, but not to development of AMS.

The work on Pike's Peak suggested a benefit of CO₂ breathing in AMS.⁶ Thirty tourists with various symptoms, mostly headache and dizziness, were given 1 litre/min CO₂ to breathe, and the effects were "in most cases, subjectively beneficial"; CO₂ stabilised irregular breathing patterns. Also, a recent study by my colleagues and I on Mount McKinley confirmed the results of Harvey et al that 3% CO₂ breathing improved symptoms nearly as much as oxygen breathing did. Estimated CBF by transcranial doppler did not, however, increase in those breathing 3% CO₂, while CBF fell sharply in those given oxygen. Increasing CBF with 7% CO₂ breathing negated the beneficial effects of increased oxygenation. The best combination for improving symptoms of AMS appeared to be a decrease or no change in CBF accompanied by an increase in arterial oxygen content. This concept is supported by the action of acetazolamide, which does not increase CBF, as Harvey et al claim, when given in the usual clinical doses.⁷ Because of metabolic acidosis, it does, however, maintain cerebral flow, despite a lower PCO₂, and increase arterial oxygenation because of its effect on ventilation. Since oxygenation is improved without an increase in CBF, the example of acetazolamide supports the greater importance of arterial oxygenation over CBF. Since Harvey et al increased both CBF and arterial oxygenation, their statement that vasodilatation helped to improve mountain sickness is unproven, and, based on other work, may be erroneous. Our data and those of Harvey et al, however, do point to a beneficial effect of increased PaO₂ which cannot be attributed to cerebral vasoconstriction and therefore casts doubt on the traditional explanation that the headache results from vasodilatation.

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1. Harvey TC, Raichle ME, Winterborn MH, et al. Effect of carbon dioxide in acute mountain sickness: a rediscovery. *Lancet* 1988; ii: 639-41.
2. Swenson ER, Robertson HT, Middaugh ME, Hlastala MP. Inspiration of CO₂ improved ventilation-perfusion matching in the dog. *FASEB J* 1988; 2: A924 (abstr).
3. Maher JT. Acute mountain sickness. increased severity in eucapnic hypoxia. *Aviation, Space Emur Med* 1975; 46: 826-29.
4. Hackett PH, Rennie D, Hofmeister SE, et al. Fluid retention and relative hypoventilation in acute mountain sickness. *Respiration* 1982; 43: 321-29.
5. Hackett PH, Roach RC. Cerebral blood velocity and high altitude illness. In Proceedings of 2nd International Symposium on Intracranial Hemodynamics: Transcranial Doppler and Cerebral Blood Flow, 1988 (abstr)
6. Childs SB, Hamlin H, Henderson Y. Possible value of inhalation of carbon dioxide in climbing great altitudes. *Nature* 1935; 135: 457-58.
7. Huang SY, McCullough RE, McCullough RG, et al. Usual clinical dose of acetazolamide does not alter cerebral blood velocity. *Resp Physiol* 1988; 72: 315-26.

MENTAL PROBLEMS AND FREQUENT USE OF ANALGESICS

SIR,—“Somatisation”¹ is common in both general and specialist medical practice, and such patients account for many consultations, laboratory investigations, and prescriptions. Frequent use of analgesics in people with mental problems may be an example of this behaviour. We have correlated the use of over-the-counter analgesics with reported symptoms of mental distress in a large cross-sectional population study.

During the second Tromsø Heart Study (1979-80) more than 13 000 men and women answered questions about symptoms and mental problems (depression, problems in coping with daily life, insomnia) and about how often they used some over-the-counter pain relievers, mainly containing salicylates. Details about the survey are given elsewhere.² We have compared the frequency of reports of mental problems in those reporting frequent and infrequent use of analgesics. The table gives the age-adjusted figures. Significant ($p < 0.001$) associations were observed, especially in men.

It is reasonable that pain should lead to both frequent use of over-the-counter analgesics and symptoms of mental distress. In a multiple regression analysis we adjusted the association between analgesic use and mental problems for the different painful

FREQUENCY (%) OF SELF-REPORTED MENTAL PROBLEMS ANALYSED BY FREQUENCY OF USE OF ANALGESICS

Frequency of use of analgesics	No	% reporting symptoms of mental problems			
		Depression	Problems with coping	Insomnia	One or more symptoms
1-3 times per week	251/483*	24/20	19/13	14/13	29/27
1-3 times per month	1048/2007	12/15	7/7	6/9	15/20
Seldom or never	5312/4191	8/10	5/5	4/7	11/14

*Men/women.

conditions reported in the same survey—eg, pain suggesting coronary heart disease, intermittent claudication, or rheumatoid arthritis, besides back pain, gnawing pains in the pit of the stomach, and cramping abdominal pain. In both sexes, the frequency of use of analgesics was independently associated with prevalence of the three symptoms of mental distress ($p \leq 0.001$), even when adjusted for physical conditions, but the strength of the association was reduced, by about 20% and 35% in men and women, respectively.

We do not think that frequent use of analgesics is causally linked to symptoms of mental strain. The probable explanation is that people use analgesics to try to fight the diverse bodily sensations that accompany minor psychiatric disorders.

Since we do not have information about all types of common pain (eg, headache) and since information on the severity of physical and mental symptoms is unavoidably restricted in a self-administered questionnaire, this study cannot settle the question whether people with mental distress use mild analgesics more than can be explained by their somatic problems. However, the strength of the relationships (table) and their persistence after adjustments do point in this direction.

The finding reported here is a spin-off from a study of risk factors for cardiovascular diseases, and there was no a priori hypothesis. We suggest that this hypothesis should be included in future epidemiological studies on the relation between mental and physical health.

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1. Lipowski ZL. Somatization: the concept and its clinical application. *Am J Psychiatry* 1988; 145: 1358-68.
2. Jacobsen BK, Thelle DS. The Tromsø Heart Study: responders and non-responders to a health questionnaire, do they differ? *Scand J Soc Med* 1988; 16: 101-04.

MOSAICISM AND SPORADIC HAEMOPHILIA: IMPLICATIONS FOR CARRIER DETERMINATION

SIR,—Haemophilia A and B frequently occur in families without any history of the disease. These “sporadic” cases reflect the introduction of new mutations into the population. When a mutation is identified in a family, the origin of the mutation can be traced and the carrier status of female relatives can be ascertained.^{1,2} We call attention to the possibility of mosaicism occurring after the mutagenic event and the implications for genetic prediction of haemophilia.

During analysis of haemophilia pedigrees in Finland, we encountered the case illustrated in the figure. The proband has severe haemophilia A due to a partial deletion of exons 5 and 6. A factor VIII probe³ containing exons 4-7 was hybridised to a Southern blot of *Sst*I-digested DNA obtained from peripheral blood leucocytes of the patient and family members interested in carrier diagnosis. An aberrant band was seen in the patient's sample and is diagnostic for the deletion. DNA from the patient's sister also shows this aberrant band, indicating that she is a carrier of severe haemophilia. In contrast, the mother's sample does not contain the mutation. Identical results were obtained by Southern blots with the restriction enzyme *Taq*I. The mother is heterozygous for three diagnostic DNA polymorphisms⁴ (*Xba*I, St14, and DX13), and her daughter and son inherited the same allele of each from her. Thus we conclude that the mother is likely to be mosaic for the mutation, in either her germline or somatic tissue.