Comment

The presence of HIV in semen has been well documented,[2 3] but the relation between the viral load in semen and peripheral blood CD4 counts is not a simple one.[3] No studies have looked at the serial viral load of genital fluids during treatment for other sexually transmitted diseases, although a single case report has suggested that chlamydial urethritis may increase shedding of HIV-1 in the semen.[4] Our results help explain how transmission of HIV may be facilitated by concomitant sexually transmitted diseases and add further support for an aggressive approach to treating sexually transmitted diseases in HIV infected patients, as a means of reducing transmission of HIV and for reinforcing the benefits of using condoms.[5]

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Use of the capture-recapture technique to evaluate the completeness of systematic literature searches

Pat Spoor, Mark Airey, Cathy Bennett, Julie Greensill, Rhys Williams

Capture-recapture methods were pioneered in ecology and derive their name from censuses of wildlife in which several animals are captured, marked, released, and subject to recapture. In epidemiology the technique examines the degree of overlap between two (or more) methods of ascertainment and uses a simple formula to estimate the total size of the population. When the number already identified is subtracted from this estimate the number of cases not ascertained by either (or any) of the methods can then be calculated. It has been suggested that studies which attempt to ascertain all cases of a given disease in a population should use this method to estimate the number of missing cases.[1 2]

There are direct parallels between epidemiological studies which attempt to ascertain all available cases and systematic literature searches which attempt to identify all publications on a given topic: both should incorporate estimates of the number of cases or publications they fail to identify. Our study compared, for one journal, the results of searching an electronic literature database with those of hand searching, both carried out for the Cochrane collaborative review group on diabetes.[3]

Methods and results

The Medline database was searched from January 1984 to October 1994 for articles in *Diabetic Medicine* likely to be describing randomised controlled trials, as defined by Dickersin *et al* and using their search strategy.[4] Independently, a handsearch of the journal for the same period was carried out, with the same aim.

The maximum likelihood estimator, $N = M(n/m)$, was used to estimate the total population size,[2] where M is the number of publications identified by Medline, n the number identified by hand searching, and m the number identified by both sources. The estimated number unidentified by either method was calculated by subtraction. The maximum likelihood estimator is biased for small samples, for which Chapman's method is more appropriate.[5] This estimates the total population size as $N = (M + 1)(n + 1)/(m + 1) - 1$. The variance of N is estimated as $\mathrm{Var}(N) = (M + 1)(n + 1)(M - m)(n - m)/((m + 1)2(m + 2))$, from which 95% confidence intervals can be constructed.

Table 1—*Extent of overlap in the number of publications found by Medline search of "Diabetic Medicine" (January 1984 to October 1994) and by hand searching*

		Medline search	
		Found	Not found
Hand search	Found	115	35
	Not found	8	2*

*Estimated by capture-recapture technique, rounded to the nearest whole number.

Table 1 shows the number of publications identified by each method and the overlap. The articles missed by the hand search are attributed to human error; those not identified by the Medline search were improperly indexed, either because until recently no appropriate methodological subject heading existed or because the abstract failed to describe the study design. For our data both the maximum likelihood estimator and Chapman's method gave the same estimate of total population size (160, 95% confidence interval 158 to 164) rounded to the nearest whole number. The number of articles "missed" was 2 (0 to 6).

Comment

A caveat to the application of these methods is that if there is positive dependency between the two sources—that is, if an article identified by hand searching is more likely to be ascertained in Medline than one not so identified—then the estimates will underestimate the true population. If, however, Medline and the hand search are negatively dependent then the estimates will overestimate the true population.[2] Log-linear modelling offers an alternative approach to modelling dependency among data, where it is present.

The term capture-recapture is not so appropriate for the technique's use in epidemiology or literature searches since, while cases and publications may be said to be "captured," nothing is being "recaptured." As applied in epidemiology the method has been termed "ascertainment intersection."[2] However, we suggest the more informative descriptor "comparison of multiple methods of ascertainment" (or COMMA) for this useful technique, which we advocate for all systematic literature searches.

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Iron deficiency anaemia and febrile convulsions: case-control study in children under 2 years

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Febrile convulsions are the most common type of seizure and occur in 2-4% of all children.[1] A family history of convulsions; maternal smoking; and alcohol consumption during pregnancy have been associated with febrile seizures,[2 3] but the risk factors remain largely unknown.

Iron is involved in the metabolism of several neurotransmitters, and monoamine and aldehyde oxidase are reduced in iron deficiency anaemia[4], which is common during the second and the third year of life and has been associated with behavioural and development disturbances.[5] Thus we investigated the association between iron deficiency anaemia and febrile seizures by a case-control study.

Patients, methods, and results

All 156 children aged 6-24 months admitted to Castellammare di Stabia Hospital, Naples, between 1 January 1993 and 30 June 1995 with diagnosis of febrile convulsions were enrolled in the study. They were healthy children without previous afebrile seizures or central nervous system disease. A febrile convulsion was defined as a seizure that occurred while the child had a rectal temperature of at least 38.3°C or an axillary temperature of at least 37.8°C documented either in the emergency department or in the history. Two groups of controls were selected: a random sample of children admitted to the same ward with diagnosis of respiratory and gastrointestinal infection during that period, and a group of healthy children randomly selected from the provincial birth register for an iron deficiency survey in Greater Naples during 1994.

Routine haematological investigations were performed for hospitalised patients at hospital admission and for population controls at the Department of Paediatrics of Naples. Data were collected from clinical records by two medical students unaware of the study hypothesis.

Iron deficiency anaemia was defined as the presence of haemoglobin concentration <105 g/l, mean corpuscular volume <70 fl, and serum iron concentration of <5.4 μmol/l. In our population of this age group the prevalence of anaemia is about 10%; we assumed that a prevalence of 20-25% among cases would be clinically relevant. Relative risk was calculated by odds ratio and 95% confidence interval by Cornfield's method.

No differences in distribution of gender, maternal age and education, birth weight and type of birth were found among study groups. Mean age was 15 (SD 5.6) months for cases, 12.4 (5) months for hospital controls, and 13 (2) months for population controls. Anaemia was significantly more common in cases (30%) than hospital (14%) and population (12%) controls (table 1).

Comment

The association between iron deficiency anaemia and febrile seizures has not been described before, and chance or unknown confounding are possible explanations. None the less, selection bias as well as confounding by social class do not seem likely in this study.

Fever can worsen the negative effects of anaemia or of iron deficiency on the brain and a seizure can occur as a consequence. Alternatively, anaemia can be associated with the severity of a febrile illness, and more severe cases could be more likely to get seizures. None the less, febrile seizures usually occur early in the illness, before haemoglobin concentration has a chance to drop as a result of infection.

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Table 1—*Haemoglobin concentrations in children with febrile seizures and controls. Values are numbers (percentages)*

Haemoglobin concentration (g/l)	No (%) of cases (n = 146)	Hospital controls: No (%) (n = 146)	Hospital controls: Odds ratio (95% confidence interval)	Population controls: No (%) (n = 147)	Population controls: Odds ratio (95% confidence interval)
≥105	102 (70)	125 (86)	1	130 (88.4)	1
<105	44 (30)	21 (14)	2.6 (1.4 to 4.8)	17 (11.6)	3.3 (1.7 to 6.5)