students and not therefore classed. This is an exceptionally skewed population and not appropriate as a basis for drawing general conclusions.

The authors' selective quotation from the world literature is unfortunate. They could have quoted papers from countries where there has been no decline in semen quality. Their reference to Carlsen *et al*'s paper is also selective.² Most serious reanalyses of the data in that paper suggest that no decline has occurred in the past 30 years. What is in dispute is why figures in the 20 years before that seem to have been higher.

The factors that influence sperm quality are numerous, and the variability of specimens is considerable. Unless authors base their results on large studies and control for the many confounding variables then their contribution to our understanding of the problem is likely to be modest at best and in some cases misleading.

STEPHEN FARROW
Professor

Barnet Health Authority,
Colindale Hospital,
London NW9 5HB

- 1 Irvine S, Cawood E, Richardson D, MacDonald E, Aitken J. Evidence of deteriorating semen quality in the United Kingdom: birth cohort study in 577 men in Scotland over 11 years. *BMJ* 1996;312:467-71. (24 February.)
- 2 Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;305:609-13.

Rise in semen quality between 1970 and 1990 in meta-analysis was non-significant

EDITOR,—The much discussed meta-analysis by Carlsen and Giwercman and ourselves, which showed a decrease in semen quality during 1940-90,¹ is repeatedly misquoted as having shown a significant increase during 1970-90.^{2,3} The slight rise during this period was non-significant ($P = 0.36$); the dramatic significance reported by Brake and Krause² rests on an erroneous calculation.

NIELS KEIDING
Professor

Department of Biostatistics,
University of Copenhagen,
DK-2200 Copenhagen N,
Denmark

NIELS E SKAKKEBAEK
Professor

Department of Growth and Reproduction,
National University Hospital,
DK-2100 Copenhagen Ø,
Denmark

- 1 Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence of decreasing quality of semen during past 50 years. *BMJ* 1992;305:609-13.
- 2 Brake A, Krause W. Decreasing quality of semen. *BMJ* 1992;305:1498.
- 3 Vine MF. Worldwide decline in semen quality might be due to smoking. *BMJ* 1996;312:506. (24 February.)

Recent decline may be relatively late stage of long term process

EDITOR,—The hypothesis that semen quality has declined is not new, but the current widespread interest dates from the meta-analysis of worldwide studies by Carlsen *et al*.¹ This met with numerous methodological criticisms, which implied that more reliable evidence was required before the merits of the hypothesis could be judged. It is important to look at other measurements, such as sperm motility and morphology, and functional measures of biological fertility (notably time to pregnancy) and to consider general methodological issues such as publication bias. I will focus here on the need for clarity about time and place.

In the meta-analysis the apparent decline was primarily between the early studies (before the mid-1960s) and the later ones; this was compatible with a stepwise drop, possibly due to a

shorter duration of abstinence.² The subsequent papers have necessarily focused on a more recent timescale as they originate from laboratories with continuously available data. Thus data from Paris, which showed a decline in semen quality,³ covered the years 1973-92, a period during which the meta-analysis showed a stable or even increasing trend. Although both papers did suggest a decline, they are incompatible if there has been a simultaneous worldwide decline; the same is true in relation to the data from Edinburgh in 1984-95.⁴

In contrast, data from Toulouse show no decline during 1977-92.⁵ In contrasting their findings with those from Paris the authors were forced to question the hitherto widespread assumption that any decline has been world wide and simultaneous everywhere. The Toulouse findings are not incompatible with the original meta-analysis¹ because the mean sperm counts in Toulouse were comparable to those reported world wide after the mid-1960s: a decline could already have occurred in Toulouse before 1977.

An intriguing feature of the Toulouse data is that older men tended to have a higher sperm concentration (3.3% annually). This could represent the type of cohort effect that was shown in the Edinburgh data⁴; alternatively, it could just be that older men tended to have longer periods of abstinence, and it is a pity that this information is not available. Was semen volume recorded?

A further question is, if there has indeed been a decline, could it have started before the earliest studies were performed? As men have poor semen quality compared with other mammalian species we may be looking at a relatively late stage of a long term process.

MICHAEL JOFFE
Senior lecturer

Imperial College School of Medicine at St Mary's,
London W2 1PG

- 1 Carlsen E, Giwercman A, Keiding N, Skakkebaek NE. Evidence for decreasing quality of semen during past 50 years. *BMJ* 1992;305:609-13.
- 2 Olsen J. Is human fecundity declining—and does occupational exposure play a role in such a decline if it exists? *Scand J Work Environ Health* 1994;20(special issue):72-7.
- 3 Auger J, Kunstmann JM, Czyglik F, Jouannet P. Decline in semen quality among fertile men in Paris during the past 20 years. *N Engl J Med* 1995;332:281-5.
- 4 Irvine S, Cawood E, Richardson D, MacDonald E, Aitken J. Evidence of deteriorating semen quality in the United Kingdom: birth cohort study in 577 men in Scotland over 11 years. *BMJ* 1996;312:467-71. (24 February.)
- 5 Bujan L, Mansat A, Pontonnier F, Mieuisset R. Time series analysis of sperm concentration in fertile men in Toulouse, France, between 1977 and 1992. *BMJ* 1996;312:471-2. (24 February.)

Results of Scottish study may be due to confounding with age

EDITOR,—In their paper analysing the sperm quality of a sample of Scottish men Stewart Irvine and colleagues show an association between birth cohort and sperm numbers and concentrations.¹ This univariate association is interpreted as a deterioration of semen quality with later year of birth. The authors also present data to show that their results could equally be explained by a rise in sperm numbers with the age of the subjects and that the relation with birth cohort is no longer evident after adjustment for age. The authors dismiss the explanation based on the age of the subjects as biologically implausible, citing other studies.

L Bujan and colleagues, analysing similar data from men in Toulouse, also found a rise in sperm concentrations with the age of their subjects.² They suggest that this is probably the result of reduced frequency of ejaculation in older men and show that after adjustment for this factor there is no evidence of an effect of birth cohort on sperm concentration.

D M de Kretser's editorial suggests that the difference between the two studies may be explained by different environmental conditions in the two areas.³ There is an easier explanation in terms of the statistical analyses presented in the two papers. The Scottish authors have ignored the fact that their results may be due to confounding with age, whereas the French study has accepted this highly plausible explanation.

GILLIAN RAAB
Professor

Applied Statistics Research Group,
Mathematics Department,
Napier University,
Edinburgh EH11 4BN

- 1 Irvine S, Cawood E, Richardson D, MacDonald E, Aitken J. Evidence of deteriorating semen quality in the United Kingdom: birth cohort study in 577 men in Scotland over 11 years. *BMJ* 1996;312:467-71. (24 February.)
- 2 Bujan L, Mansat A, Pontonnier F, Mieuisset R. Time series analysis of sperm concentration in fertile men in Toulouse, France, between 1977 and 1992. *BMJ* 1996;312:471-2. (24 February.)
- 3 De Kretser DM. Declining sperm counts. *BMJ* 1996;312:457-8. (24 February.)

Increasing evidence that Young's syndrome is associated with mercury

EDITOR,—In the editorial on declining sperm counts¹ D M de Kretser refers to our observation that Young's syndrome (obstructive azoospermia with sinusitis, bronchitis, or bronchiectasis) has virtually disappeared in men born since 1955, when mercury in the form of calomel was removed from teething powders.² Further evidence for the connection of this syndrome with mercury may be derived from the pronounced fall in death rates from pink disease (acrodynia) in 1940-6, while the second world war was in progress.³ This coincides with a fall in the incidence of mercury poisoning in hatters in the United States.⁴ At that time mercury was required for the manufacture of detonators rather than for its more innocent uses, in which it nevertheless resulted in its fair share of damage, not only in reproductive but also in cerebral function.

We agree with de Kretser's plea for regulatory and research agencies to continue to assess the action of toxic agents on the reproductive system and that there should be no delay that may compromise the fertility of future generations.

ANN DALLY
Research fellow

Wellcome Institute for the History of Medicine,
London NW1 2BE

BILL HENDRY
Consultant urologist

149 Harley Street,
London W1N 2DE

- 1 De Kretser DM. Declining sperm counts. *BMJ* 1996;312:457-8. (24 February.)
- 2 Hendry WR, A'Hern RP, Cole PJ. Was Young's syndrome caused by mercury exposure in childhood? *BMJ* 1993;307:1579-82.
- 3 Clements PW. The rise and decline of pink disease. *Med J Australia* 1960;ii:922-5.
- 4 Wedeen RP. Were the hatters of New Jersey "mad"? *Am J Ind Med* 1989;16:225-33.

Authors' reply

EDITOR,—Jacques de Mouzon and colleagues' data represent the largest series of retrospective data addressing the question of secular changes in semen quality. They suggest a decline in semen quality with later year of birth, approximating to a 15% fall in sperm concentration when men born in the late 1940s are compared with those born after 1965.

A J P Eccersley and Stephen Farrow are concerned that we combined data from men of proved fertility with data from younger men of unproved fertility. We did so because previous