CORRESPONDENCE

Smoking and Pregnancy

SIR,—Some of us decline to accept Dr Goldstein's own evaluation of his criticisms[1–3]. He states[3], as an "undisputed" fact, that ". . . the distribution of birthweights for babies of smokers is the same as that for non-smokers except that it is shifted downwards by about 170 g". (This is known as the 'displacement hypothesis'.) It follows that the mean birthweight of infants born to smoking mothers should also be "about 170 g" less than that for babies born to non-smoking mothers. In Yerushalmy's study[4], the observed differences in the mean birthweights were 209.1 g for "whites" and 204.8 g for "blacks". By suitably stretching our imaginations we can, perhaps, regard these as being "about 170 g". However, Yerushalmy[5] also tested the hypothesis that the distributions of low birthweights, allowing a displacement of 200 g between the smoking and non-smoking series, are the same. He found that the distributions differ significantly ($0.005<P<0.01$). The 'displacement hypothesis' is therefore rendered improbable by Yerushalmy's[5] findings.

So much for "undisputed" facts. Apart from raising doubts about Goldstein's most confident assertions, they do not affect Yerushalmy's arguments. To quote Yerushalmy[5], ". . . the major conclusions in the paper (ref. 4) do not rest on the results of the displacement hypothesis". In particular, contrasts between the findings for infants of smoking mothers and smoking fathers cannot easily be reconciled to a cause-effect hypothesis[4]. Although smoking mothers, and especially smoking fathers, had a higher incidence of low-birthweight babies than corresponding non-smokers, prognosis (death and congenital anomalies) for the low-birthweight babies of smoking fathers was much worse than for low-birthweight babies of smoking mothers[4]. By far the best prognosis was given for infants of matings in which the mother smoked and the father did not. This finding applied both to "whites" and "blacks". Furthermore, the general unsoundness of arguing from simple association to cause was emphasised by the large biological and mode-of-life differences demonstrated between smoking and non-smoking gravidas.

Now to answer Goldstein's second point[3]. Yerushalmy[6] found that women who began to smoke after the birth of their baby had a much higher incidence ($\times 1.8$) of low-birthweight babies than those who did not take up smoking. His investigation was confined to all births that occurred in women aged twenty-five or less, and in women who started to smoke in this age-range. Goldstein[3] argues that the observed difference in the incidence of low-birthweight babies arises because mothers who started smoking before twenty-five years of age would have had their babies at an earlier age than those who did not take up smoking: younger mothers, he claims, have lighter babies. Yerushalmy[7] has previously shown that his findings do not support this objection: ". . . within the limited range of ages under twenty-five years the variation in the proportion of low-birthweight infants is very small and could not account for the large differences found." He supported his argument with a table showing the mothers' age, total live births, and the numbers and incidence of low-birthweight infants[7]. We can split the age-range conveniently into two groups to give equal numbers (164) of low-birthweight infants: for mothers in the age-range fifteen to twenty-one years, the incidence of low-birthweight babies was 6.2% (164/2639); and for those in the age-range twenty-two to twenty-five it was 5.6% (164/2906). The small difference does not approach significance (χ^2 with Yates correction $=0.71$; $0.3<P<0.5$). By contrast, the differences in the incidence of low-birthweight babies born to mothers in different smoking categories were large and significant. For "white" non-smokers, the incidence was 5.3%, but for "white" mothers who took up smoking after the birth of their baby it was 9.5% ($P<0.01$)[6]. The corresponding incidence[6] for mothers who smoked during pregnancy was 8.9%; and for those who gave up smoking after the birth of their baby it was 6.0%, similar to that for non-smokers. Trends for "blacks" resembled those for "whites", but because of smaller numbers, the only statistically significant difference was between those mothers who gave up smoking after the birth of their baby—with an incidence of low-birthweight babies of 13.4%—and those who smoked both during pregnancy and afterwards—with an incidence of 19.9% ($P<0.02$). This collective evidence[6] therefore fails to corroborate the causal hypothesis. Each of its features is remarkably consistent with the view that the smoker, rather than the smoking, is responsible for the high incidence of low-birthweight infants[6,7].

Finally, I return to the questions raised in your editorial of September 14. A news story based on an accurate report of an article by Goldstein opened with the statement that cigarette smoking during pregnancy "caused the deaths of 1,500 babies in Britain last year". Under pressure from your leading article, Goldstein conceded in these columns, on October 5, ". . . the scientific evidence for a causal relationship may not be very conclusive". These dual standards raise important issues.

The public should be able to trust definitive statements made by scientists in their own field of expertise. If subsequently this trust proves to be unfounded, the credibility of scientists will be undermined, not only to their detriment, but to that of society at large.

Yours faithfully,

P. R. J. BURCH

Department of Medical Physics,
University of Leeds,
The General Infirmary,
Leeds LS1 3EX

1 Goldstein, H., *Am. J. Epidemiol.*, **95**, 1 (1972).
2 Goldstein, H., *Am. J. Obstet. Gynec.*, **114**, 570 (1972).
3 Goldstein, H., *Nature*, **245**, 467 (1973).
4 Yerushalmy, J., *Am. J. Epidemiol.*, **93**, 443 (1971).
5 Yerushalmy, J., *Am. J. Epidemiol.*, **95**, 2 (1972).
6 Yerushalmy, J., *Am. J. Obstet. Gynec.*, **112**, 277 (1972).
7 Yerushalmy, J., *Am. J. Obstet. Gynec.*, **114**, 571 (1972).

SIR,—We join Professor Burch[1] in welcoming your leading editorial[2] on "smoking, pregnancy and publicity", and for noting that the elementary fallacy of inferring causality from statistical association is present in some reports that have received publicity.

In response to your editorial, Goldstein[3] cites a *British Medical Journal* editorial[4] that he states "suggests" validity of the smoking-causality hypothesis as an explanation for the statistical association between smoking behaviour of women and birth weights of their children. An alternative hypothesis, set forth by Professor Yerushalmy, is that the smoker rather than smoking influences birth weight[5]. Another expression of this hypothesis is that "smoking behaviour of women and birth weights of their children are influenced by a common cause . . . the individual genotype or constitution"[6]. The *British Medical Journal* editorial[4] does not merely suggest, but asserts that "no reasonable doubt now remains that smoking in pregnancy has adverse effects on the developing foetus". As we have noted[6], the editorial overlooked

several reports that disagree, especially those of Yerushalmy.

Ross and colleagues[7], and Goldstein[3], deny having inferred causality from correlation. To the causal quotation cited in the *Nature* editorial[2] may be added their own assertion[8], based on statistics, that "cigarette smoking during pregnancy increased the foetal plus neonatal mortality rate by 28% and reduced birth weight by 170 g. . . ." They also assert[7] that the constitutional hypothesis as evaluated by Yerushalmy[5] "suffers from severe methodological shortcomings, making it clearly untenable", citing a critique by Goldstein[9]. However, they neglect to mention Yerushalmy's rejoinder[10] which, in effect, demolished this critique[9].

Goldstein expressed his opinion that it would be "unethical" not to advise and encourage "pregnant women, especially 'high risk' ones, to stop smoking"[3]. In response to similar statements by Goldstein[9], Yerushalmy[10] commented, following a data analysis, that it would be unfortunate "to recommend a course of action based on conjectures, subjective notions, and easy explanations not supported by available data." The smoking-causality hypothesis to explain the association between smoking by women and birth weights of their children is incompatible with observed data[5,6]. Such incompatibility, if confirmed independently, requires rejection of this hypothesis.

A problem arises since human smoking behavioural subgroups, for example, smokers, non-smokers and ex-smokers, are self-selected rather than randomly selected, and thus are biased samples. This introduces special problems for statistical testing of hypotheses[5,6]. It is quite possible that for a subgroup of all smokers, tobacco use may be symptomatic of underlying needs, perhaps arising in part from variations in biogenic amine physiology, that tend to be alleviated by nicotine[6,11]. Cigarette smokers tend to adjust their smoking behaviours according to the nicotine content of cigarettes[12]. Accordingly, ethological homoeostatic mechanisms may be involved[6,13].

Goldstein cites animal studies in support of his position[3]. In addition to the usual caveat concerning inferences from experimental animal studies to man, based on interspecific physiological differences, there is a further problem. If habituated human smokers are on the average physiologically different from non-smokers, this difference may not be reflected in the physiology of experimental animals used in tests. Moreover, biogenic amine release in non-deficient test animals above homoeostatic optimal ranges may be harmful[14]. The fallacy of typology[15] may well be involved.

Consider the following observations: the negative association of carboxyhaemoglobin (COHb) levels of women with birthweights of their children[16]; the low COHb levels of some smokers[16,17], and the limited data for angina patients showing that high COHb levels of smokers are sustained during a non-smoking period[18]. These are compatible with a constitutional rather than a smoking-causality hypothesis. Such observations suggest caution regarding rejection of constitutional hypotheses and allegations that smoking-causality hypotheses concerning birth weight are in fact true. In this complex problem, available objective evidence for testing alternative hypotheses must be considered fairly, without overlooking critical reports that are detrimental to the smoking-causality hypothesis[4], or to any other hypothesis. It is to be hoped that in any scientific problem all available objective evidence may be utilised, thus minimising the need for subjective judgment and opinion.

Yours faithfully,

RICHARD J. HICKEY
Management and Behavioral Science Center

DAVID E. BOYCE
Regional Science Department

RICHARD C. CLELLAND
Department of Statistics and Operations Research,
The Wharton School

EVELYN B. HARNER
Anthropology Department,
College of Arts and Sciences,
University of Pennsylvania,
Philadelphia, Pennsylvania 19174

1 Burch, P. R. J., *Nature*, **245**, 277 (1973).
2 *Nature*, **245**, 61 (1973).
3 Goldstein, H., *Nature*, **245**, 277 (1973).
4 *Br. med. J.*, **1**, 369 (1973).
5 Yerushalmy, J., *Am. J. Obstet. Gynec.*, **112**, 277 (1972).
6 Hickey, R. J., Harner, E. B., Clelland, R. C., and Boyce, D. E., *Br. med. J.*, **3**, 501, 522 (1973).
7 Ross, E. M., Butler, N. R., and Goldstein, H., *Br. med. J.*, **4**, 51 (1973).
8 Butler, N. R., Goldstein, H., and Ross, E. M., *Br. med. J.*, **2**, 127 (1972).
9 Goldstein, H., *Am. J. Obstet. Gynec.*, **114**, 570 (1972).
10 Yerushalmy, J., *Am. J. Obstet. Gynec.*, **114**, 571 (1972).
11 Hickey, R. J., Clelland, R. C., and Harner, E. B., *Lancet*, i, 270 (1973).
12 Frith, C. D., *Psychopharmacologia*, **19**, 188 (1971).
13 Hickey, R. J., Harner, E. B., Clelland, R. C., and Boyce, D. E., *Naturwissenschaften*, **60**, 206 (1973).
14 Fuller, R. W., *Fedn Proc. Am. Socs exp. Biol.*, **32**, 1772 (1973).
15 Mayr, E., *Animal Species and Evolution* (Belknap Press of Harvard University Press, Cambridge, Massachusetts, 1963).
16 Astrup, P., Trolle, D., Olsen, H. M., and Kjeldsen, K., *Lancet*, ii, 1220 (1972).
17 Wald, N., Howard, S., Smith, P. G., and Kjeldsen, K., *Br. med. J.*, **1**, 761 (1973).
18 Hickey, R. J., Clelland, R. C., and Boyce, D. E., *Lancet*, ii, 571 (1973).

Editorial Department
MACMILLAN JOURNALS LIMITED
4 LITTLE ESSEX STREET, LONDON WC2R 3LF
Telephone Number: 01-836 6633. Telegrams: Phusis London WC2R 3LF
Telex 262024

MACMILLAN JOURNALS LIMITED
711 NATIONAL PRESS BUILDING
WASHINGTON DC 20004
Telephone Number: 202–737 2355. Telex 64280

Subscription Department
MACMILLAN JOURNALS LIMITED
BRUNEL ROAD, BASINGSTOKE, HANTS RG21 2XS
Telephone Number: Basingstoke 29242

Display Advertisement Department
MACMILLAN JOURNALS LIMITED
4 LITTLE ESSEX STREET, LONDON WC2R 3LF
Telephone Numbers: UK 01-836 6633. USA 202–737 2355

Classified advertisements
T. G. SCOTT & SON, LIMITED
1 CLEMENT'S INN, LONDON WC2A 2ED
Telephone Number: 01–242 6264/01–405 4743
Telegrams: Textualist London WC2A 2ED

Registered as a newspaper at the Post Office