**Table 1**

| Maternal smoking habit | CHD *A* | | CHD *B* | | Control week minus *A* | |
|---|---|---|---|---|---|---|
| Smoker | 34 | (39.5%) | 81 | (39.7%) | 4,626 | (29.4%) |
| Non-smoker | 52 | (60.5%) | 127 | (60.3%) | 11,093 | (70.6%) |
| Total | 86 | (100%) | 204 | (100%) | 15,719 | (100%) |

$A \times (\text{control} - A)$; $\chi_1^2 = 4.2$, $P < 0.05$.
$B \times (\text{control} - A)$; $\chi_1^2 = 10.2$, $P < 0.005$.
$(A+B) \times (\text{control} - A)$: $\chi_1^2 = 14.3$, $P < 0.001$.

nated as "smokers" if they had smoked at least one cigarette a day after the fourth month of pregnancy, and had not reported a change in the average number they smoked. They were coded as non-smokers if they had not smoked at all after the fourth month. Those with changeable or unknown habits were excluded.

Table 1 shows that in both groups (*A*) and (*B*) there was a significant increase in the proportion of mothers who smoked, compared with the mothers of singletons in the control week who did not have infants with congenital heart disease. The incidence of congenital heart disease in singleton babies of mothers who smoked was 7.3 per 1,000 births, compared with the 4.7 per 1,000 of babies of non-smokers (that is, a 50% increase). Because some of this effect could have been explained by maternal age, parity and social class, an analysis of variance was carried out allowing for these factors.

For this analysis we used relevant information on the control week population and on all deaths. The cases were grouped according to whether the mother was younger than 30 or 30+; of parity less than 2 or parity 2+; of social classes[6] I, II, III, or social classes IV, V; and whether a smoker or non-smoker. The model $\frac{1}{2} \log \frac{x_t}{n_t - x_t} = \alpha + \beta_t$ was used, where $x_t$ was the number of cases with congenital heart disease (CHD), $n_t - x_t$, the number of cases without CHD in a given cell, and $\beta_t$ a linear function of the independent variables[7].

The results (Table 2) indicate that the smoking effect is independent of maternal age, parity and social class, and is highly significant ($P < 0.001$).

The small number of cases in any particular category made it difficult to ascertain definitely whether any specific types of CHD were particularly associated with maternal smoking, but it seems that this may be true of patent ductus arteriosus and Fallot's tetralogy. (This finding will be discussed in a further communication.)

As far as we know, there has been only one previous study of maternal smoking habits in relation to CHD[8], in which the maternal histories of 100 cases of CHD were compared with an equal number of controls and no significant difference was demonstrated. But an effect of the same order as we have demonstrated here is unlikely to have been statistically significant in a comparison of two samples of this size.

We think the present results sufficiently interesting to warrant further epidemiological and experimental investigations into a possible relationship between smoking and congenital heart disease.

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**Table 2** Analysis of Variance

| Source | $\chi_1^2$ | |
|---|---|---|
| Smoking | 11.7 | ($P < 0.001$) |
| Parity | 6.3 | ($P < 0.01$) |
| Social class | 0.6 | ($P < 0.05$) |
| Maternal age | 0.2 | ($P < 0.05$) |

Test for "goodness of fit" of model; $\chi^2$ (11 d.f.) = 4.1 ($P > 0.05$).

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# Reverse Transcriptases and Ageing

REVERSE transcriptases introduce new possibilities not only in tumour research but in theoretical models of ageing. It would be of immediate interest to know whether finite clones lack, and virus-transformed "immortal" clones possess, enzymes of this sort.

Ageing may be due to noise or to masking of information in the genome, or (with slightly greater experimental backing[1,2]) to error and mis-specification at the synthetase level. Reverse transcriptases present a new feedback path to complicate such models. A reverse transcriptase would have "rejuvenatory" potential if it could restore lost or masked primary information from secondary copies. It could do this in the presence of mis-specification if it could combine information, or if it were primed only by correct RNA. If epigenetic masking plays the part suggested by Medvedev[3], the price of clonal immortality in mammalian cells might be malignancy. There is also the possibility that a reverse transcriptase might be itself a mis-specified synthetase as postulated by Orgel[1]. In these cases it could generate malignancy using only the cell's own genetic repertoire, appear spontaneously, but in other respects resemble a virus without viral products (other than more synthetase). Further work on the cytoplasmic transmissibility of clonal senescence and non-senescence[2,4,5] might conceivably indicate whether any of these speculations are relevant. At the moment it appears that it is clonal senescence which is transmissible cytoplasmically and non-senescence, plus malignancy, which is virally inducible.

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