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Do Cervical Smears Save Lives?

SIR,—We wish to correct the statement which was made in the leading article entitled "Do Cervical Smears Save Lives?" (7 June, p. 585).

At no time have we offered the interpretation that the apparent disparity in incidence rates of in situ carcinoma and invasive carcinoma of the cervix are evidence that over 50% of cases undergo spontaneous regression. In 1962 we observed that a comparison of the incidence rates of in situ and invasive lesions suggested that about 60% of in situ carcinoma cases may go on to become invasive cancer, but also noted that many more in situ incidence cases must be observed before the figure would be statistically reliable.¹ In 1968 we published results on a much larger series of cases,² and, using the same formula, this suggested that 43% would become invasive if untreated. We have never stated that the remainder actually regress. Our understanding of the natural history of in situ carcinoma is still incomplete. While we are of the opinion that a few cases undergo spontaneous regression, it would appear more likely that most of those that do not

invade persist as in situ carcinoma for many years. Unfortunately it is not possible to predetermine those cases that will remain in situ.

Speculations based upon incidence data of in situ carcinoma are biased by a number of factors, of which an important one is the increased frequency of screening women with atypical smears reflecting varying degrees of dysplasia. The difficulties of determining the time of onset of in situ carcinoma and of following constantly expanding and changing groups in the population make an analysis based on incidence data unreliable.—We are,

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Maternal Rh Immunization

SIR,—In their article "Incidence of Maternal Rh Immunization by ABO Compatible and Incompatible Mating" Dr. W. A. Ascari and colleagues (15 February, p. 399) raise the question of the frequency of immunization during pregnancy, and, *pari passu*, the possible need—or, as they see it, lack of need—of prophylactic treatment during pregnancy. They write that if "immunization can occur during the course of pregnancy, it must do so very infrequently, and may result from the extraordinary circumstances where large foetal-maternal haemorrhages occur 'intra-partum.' Nevanlinna and Vainio found only four examples of maternal immunization in 4,153 Rh-negative primiparae. . . ."

Translating "intra-partum" to mean during pregnancy, and looking first at the possible circumstances of immunization, we note that Woodrow and Finn¹ showed a relatively large bleed *not* to be an extraordinary event in pregnancy, and that Zipursky *et al.* have reported² that two injections of 0.1 ml. of foetal cells immunized two of 11 volunteers, while Zipursky has also observed³ that a single such injection can immunize. A foetal-maternal bleed of this size would not be called large; it is not an extraordinary circumstance.²

As to frequency of immunization, Dr. Ascari and his colleagues did not give too detailed consideration to Nevanlinna and Vainio's study.⁴ In it the authors state that

the last maternal serum specimens were drawn "approximately one month before the expected time of birth"; in our experience, "in 60% of the cases in which antibodies develop in a first pregnancy they do so after this time. Further, in a series collected from 1953 to 1958 it is unlikely that Nevanlinna and Vainio used an enzyme method of antibody detection; again, in our experience of first-pregnancy immunizations recognizable by 36 weeks' gestation, only 20% are detected by the indirect Coombs method, whereas all are detected by a sensitive enzyme method. Combining these two factors, it is probable that about 90% of the examples of immunization in Nevanlinna and Vainio's series were missed, and that the true frequency was more like 40 per 4,000 or 1%.

One may carry this calculation farther. Dr. Nevanlinna⁴ has written us that he did not know the ABO or Rh types of most of the babies. So we may look upon the 4,153 as a random sample of Rh-negative primigravidae. In a Manitoba population⁵ 65% of the babies would be Rh-positive, and about 80% of these would be ABO compatible with their mothers. So in the sample 80% of 65%, or 52% of the women, would be "at risk." The immunization rate would then be of the order of 2% of those at risk, which is in agreement with current figures for the frequency of formation of anti-D during the first pregnancies of Rh-positive women carrying an ABO-compatible Rh-positive foetus. These figures are:

Population	No. of Women	No. Immunized
Winnipeg, 1967-8 ⁵ ..	210	5
Winnipeg, 1968-9 ⁶ ..	265	5
Vancouver ⁹ ..	144	3
Edmonton ⁹ 10 ..	179	10
Liverpool ¹¹ ..	1,502	16
† Total ..	2,300	39

The probability that a primipara who has borne an ABO-compatible Rh-positive baby will develop anti-D in the ensuing six months is about 8 or 9% (8.5 for the Liverpool study (19 October 1968, p. 139) and 8.9 for the Western Canadian).⁶ The frequency with which she will develop anti-D in her next Rh-positive