a high proliferation rate and low self-renewal[4,5]. Recently, experimental data have been reported suggesting that only the proliferating stem cells are able to respond to the stimulus for differentiation and that this stimulus is part of the feedback controlling the number of stem cells[6]. The heterogeneity of stem cells can be explained on the basis of this hypothesis by postulating that stem cells which have divided recently are more likely to do so again and are more sensitive to the stimulus for differentiation. Accordingly, the rapidly proliferating stem cells with high sensitivity to the stimulus for differentiation and therefore low self-renewal capacity, could supply most of the cells for differentiation; while the slowly proliferating stem cells will be unlikely to differentiate and therefore provide a reserve population. In the event of a shortage of stem cells, however, the stimulus for differentiation must decrease so that many stem cells no longer differentiate and thus can no longer be considered to be lacking in self-renewal capacity. The extent to which stem cells are called upon to self-renew will therefore depend on the level of homeostatic control operating and this will alter the distribution of stem cells with differing proliferation and self-renewal capacity. Thus the composition of cells within developing or vanishing spleen colonies would appear to be as much due to the exigencies of the spleen colony assay as to any stem cell inadequacy.

To conclude, therefore, it is an oversimplification to suggest that stem cells scored at less than 11 days do not measure cells with extensive proliferative capacity. Furthermore these cells may well have a major role in the maintenance of haematopoiesis, even though some of them are not capable of long-term haematopoiesis. A more comprehensive view is needed of the 'nature' of stem cells and their 'nurture' as a result of the homeostatic control, together with experimental data demonstrating whether the differentiation and self-renewal observed in the spleens of the assay mice reflects what they do in the tissue from which they were taken. Until such information is available it is premature to question the validity of much of the work done in this field over the past 20 years, and restrict the counting of colonies until later than 11 days, with the attendant problems of reduced mouse survival and reduced number of colonies that can be counted on each spleen.

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ISCOVE *ET AL.* REPLY—Our experiments confirmed previous work in showing that day 7–8 spleen colonies are mainly erythroid and lack primitive precursors, whereas most 11–12 day-old colonies are multilineal and do contain primitive precursors. Because similar numbers of macroscopic colonies are found at early and late time points, it was assumed in the earlier literature that early and late colonies were the same colonies, and that their differing compositions reflected changes in local regulatory influences with time. If the assumption of identity between early and late colonies was correct, then properties of pluripotentiality and renewal capacity had to be ascribed to the cells originating colonies scored at earlier time points as well as to those forming the later colonies. Hence the widespread acceptance of the view that spleen colonies are a measure of pluripotential precursors with some renewal capacity regardless of when they are scored.

The significant point made by our study was that early macroscopic colonies are transient and are not the forerunners of the later colonies. We are left then with the observations that the early colonies are not multilineal and do not contain primitive precursors. There is therefore no positive indication that they originate from pluripotential cells with renewal capacity.

There is now a 20-year tradition of clonal analysis in experimental haematology. The basic approach is to ascribe potentials to precursor cells on the basis of the character of the clones they ultimately produce. We also subscribe to the converse, namely, not to attribute capacities that are not observed in the resulting clones. Blackett raises a legitimate question, namely, that the behaviour of colony-forming cells observed in the conditions of their assay could differ from their behaviour in steady-state marrow. This problem is inherent in the nature of colony assays whether performed *in vivo* or in culture. The way out will involve methods for specific and direct identification of 'stem' cells which have yet to be devised.

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Tiltmeter recordings re-analysed for earthquake precursors

HERE I aim to qualify the conclusions of a paper by Gerard[1] which appeared to give good evidence for precursory earth tilt preceding earthquakes near Wellington, New Zealand.

Gerard was very conscious of the need to allow the equipment to settle long enough before attempting to interpret the tiltmeter recordings. He also used statistical procedures to assess and allow for the tilts induced by rainfall and other meteorological factors. The long-term trend was removed and the resulting tilt departures in the north–south and east–west directions were displayed on a polar plot. Two groups of points lay well outside the 1-μrad diameter circle, preceding and around the times of earthquakes having magnitudes of 5.5 and 6.2.

In this laboratory, we have continued Gerard's tiltmeter programme and the records taken at Wellington have been analysed up to November 1981. With the much longer run of data, it has been possible to re-examine the validity of the earlier analysis[2]. It now seems that neither of the previously reported precursors is likely to be significant, as they can be attributed to a nonlinear response to rainfall combining with the statistical techniques used.

For example, there was a period of very heavy rain, causing local flooding, in December 1976. Much of the water ran off instead of soaking into the ground around the tiltmeter site, so the departure in tilt was not proportional to the total rainfall. When the data were corrected statistically for the effects of rain, this month was therefore over-corrected. The spurious signal thus generated was spread by the five months of lag correlation allowed. It was further shaped by the 24-month running mean, trailing the data points by four months, which was used to remove residual seasonal effects and trend. It then appeared to be a precursor to the magnitude 6.2 earthquake in January 1977.

We hesitate to express confidence in any of the results from this tiltmeter programme, as it has not been possible to correct adequately for rainfall. It seems essential to minimize the meteorological effects by site selection, and we suggest the use of bore holes several hundred metres deep from level terrain. Correlation with ground water level may then correct more appropriately for the effects of rain.

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