

ing absence of placentals from Australia (7), but this is a problem on which discussion is still at the speculative stage (2, 3, 32), where it will remain until relevant fossils are discovered.

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- J. R. Griffiths [*Aust. Petrol. Explor. Ass. J.* **11**, 75 (1971)] has suggested that those dolerites "are probably related to the onset of tension within the plate." K. M. Creer [*Earth Sci. Rev.* **6**, 369 (1970)] and M. W. McElhinny [*Nature* **228**, 977 (1970)] have pointed to a major problem: land-based studies of paleomagnetic pole positions indicate that Australia and Antarctica were apart in the Triassic to mid-Jurassic and together during the later Mesozoic, whereas sea-floor magnetic observations indicate that separation began during the early Cenozoic. I know of no geological evidence from southern Australia to support this concept of continental bouncing.
- H. Wopfner, *Proc. Pap. 2nd Gondwana Symp. South Africa 1970* (1971), p. 273.
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- Adapted from Tectonic map of Australia and New Guinea (1:5,000,000) (Geological Society of Australia, Sydney, 1971).
- N. H. Ludbrook, *Trans. Roy. Soc. S. Aust.* **91**, 65 (1967); *Geol. Soc. Aust. Spec. Publ.* **2**, 39 (1969); W. K. Harris and B. McGowran, *Quart. Geol. Notes Geol. Surv. S. Aust.* **40**, 5 (1971); *S. Aust. Dep. Mines Rep. Invest.*, in press. The Permian at Bacchus Marsh in western Victoria probably is part of the same system, but the small assemblage of shelly fossils there [G. A. Thomas, *J. Paleontol.* **43**, 1283 (1969); M. J. Garrett, *Aust. J. Sci.* **32**, 108 (1969)] might suggest also that the structural trends discussed here broke through to the Pacific margin of Gondwanaland.
- For example, P. M. Hurlley (9); D. A. Brown, K. S. W. Campbell, K. A. W. Crook, *The Geological Evolution of Australia and New Zealand* (Pergamon, Oxford, 1968); J. J. Veivers, *J. Geol. Soc. Aust.* **18**, 87 (1971). Furthermore, R. E. Wass [discussion in (11)] has recorded a fenestellid bryozoan from the Cooper Basin, in which no foraminifera or organic-walled phytoplankton have been found as yet. That record invites further paleogeographic speculation but does not negate the model proposed here.
- F. Ahmad, *Proc. Pap. 2nd Gondwana Symp. South Africa 1970* (1971), p. 179; H. Martin and N. Wilczewski, *ibid.*, p. 225.
- The geology of the Otway Basin is summarized in *The Otway Basin of Southeastern Australia*, H. Wopfner and J. G. Douglas, Eds. (Special Bulletin of the Geological Surveys of South Australia and Victoria, Adelaide, 1972).
- W. P. Sproll and R. S. Dietz [*Nature* **222**, 345 (1969)] have shown how the Otway Basin might have formed by block faulting as a result of rifting. According to H. Wopfner (12), "the Jurassic-Cretaceous history of the Otway Basin is thus a classical example of transformation of an intracratonic basin into a pericratonic basin by progressive collapse (or removal) of the southern cratonic rim." Wopfner has also noted the contrast between Australian basins in which marine Early Cretaceous sedimentation is succeeded by nonmarine conditions and the marginal Otway Basin in which the reverse succession is observed.
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- N. H. Ludbrook, *J. Geol. Soc. Aust.* **5**, 127 (1958); D. Lowry, *Geol. Surv. West. Aust. Bull.* **122**, 1 (1970).
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- R. H. Tedford, *Geol. Soc. Amer. Abstr. Programs* 3 (part 7), 730 (1971).
- S. V. Margolis and J. P. Kennett, *Science* **170**, 1085 (1970); *Amer. J. Sci.* **271**, 1 (1971). Inferred ice-rafting in the Pacific, into present-day subantarctic latitudes, implies that an ice cap would have interfered with the most likely migration route, that is, from the region of Victoria Land and the Ross Sea via Tasmania. Using planktonic foraminiferal evidence from California, P. L. Steineck [*Lethaia* **4**, 125 (1971)] has suggested independently a Middle Eocene "refrigeration." W. E. Le Masurier [*Antarct. J.* **5**, 154 (1970)] has dated basaltic rocks in Marie Byrd Land identified as hyaloclastics (formed by eruption under an ice cover) at  $42 \pm 9 \times 10^6$  years.
- There is no direct evidence that I know of in Australia for the Eocene ice cap on Antarctica. Berggren (27) has suggested that the cherts of Horizon A in the Atlantic Ocean reflect an influx of cold north polar water admitted by spreading on the Reykjanes Ridge. Ramsay (28) has pointed to a link in time between those cherts and the postulated Antarctic ice cap. Y. Herman [*Nature* **238**, 392 (1972)] has suggested that the genesis of the cherts of Horizon A and similar rocks requires the coincidence of sea-floor spreading (continental breakup) and temperature zonation, that is, cooling. The cherts in Horizon A in the Middle Eocene carbonates of the Eucla Basin overlie a planktonic foraminiferal assemblage [B. McGowran and J. M. Lindsay, *Quart. Geol. Notes Geol. Surv. S. Aust.* **30**, 2 (1969)] which are part of a short-lived

influx into New Zealand and southern Australia of species adapted to relatively warmer water (B. McGowran, *S. Aust. Dep. Mines Mineral Resour. Rev.*, in press). Again, a rich assemblage of land plant remains in southern Australia has the character of a wet forest [R. T. Lange, *Neues Jahrb. Geol. Palaeontol. Monatsh.* **1970**, 486 (1970); R. V. Southcott and R. T. Lange, *Rec. S. Aust. Mus.* **16**, 1 (1971)]; that flora is of latest Early Eocene age and thus is intermediate in age between the finds of possible ice-rafted sediment in the South Pacific (33). It can be expected that the formation and decay of any southern ice cap, and the consequent changes in the temperature and distribution of oceanic waters occurred more than once and perhaps more rapidly than can be resolved by current biostratigraphic methods. For a brief summary of contrasting but not necessarily conflicting lines of evidence on antarctic climate in the Early Tertiary, see Y. T. Mandra, *Antarct. J.* **5**, 178 (1970).

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McGowran is to be congratulated for his clear and careful analysis of geological evidence concerning the date of separation of Australia and Antarctica. However, this date is not directly relevant to my interpretation (1) of the prototherian-metatherian fauna of Australia and New Guinea. According to my hypothesis, this fauna is a relict sample of the mammalian fauna that inhabited Pangaea before detachment of East Gondwana (Antarctica-India-Australia-New Guinea) [table 1 and figure 1, A and B, in (1)]. I attribute the survival of this relict fauna to isolation that dates from the separation of West Gondwana and East Gondwana (more specifically, South America and Antarctica), which McGowran excludes from his discussion, not from the subsequent separation of Antarctica and Australia [figure 1D in (1)].

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## Myeloid Leukemia: Does Blood Loss

### Increase the Incidence in X-irradiated Rats?

Myeloid leukemia rarely occurs in the rat, and even after substantial irradiation the incidence is usually low (1). For example, Moloney *et al.* (2) found only six granulocytic leukemias among 161 Wistar rats x-irradiated with 450 r. Recently, however, Gong (3) reported a considerably greater incidence, with 44 myeloid leukemias

among 199 Sprague-Dawley rats exposed to doses of 25 to 350 r. Significantly, the frequency rose to 100 percent when the animals were subjected to acute blood loss at either 1, 2, or 3 months after irradiation. It was suggested that x-irradiation, even with doses less than 25 r, induces a proneness to leukemia which tends to persist

Table 1. Mortality/morbidity 9 to 10 months after total-body or hind-leg (HL) x-irradiation of rats with or without subsequent bleeding.

Group	Rats (No.)	Dead (%)	Killed* (%)	Body weight†	Leukocyte count† ( $\times 10^{-3}$ )	Hematocrit†
50 r	42	0	4.8	303 $\pm$ 9	5.3 $\pm$ 0.3	45.3 $\pm$ 0.4
50 r, bled	26	7.7	0	299 $\pm$ 7	5.9 $\pm$ 0.4	45.7 $\pm$ 0.3
350 r	36	0	5.6	291 $\pm$ 11	5.5 $\pm$ 0.3	44.2 $\pm$ 0.4
350 r, bled	24	0	8.3	279 $\pm$ 5	6.3 $\pm$ 0.4	44.5 $\pm$ 0.4
50 or 350 r (HL)	82	1.2	0			
50 or 350 r (HL), bled	62	1.6	0			
Unirradiated	16	0	0	293 $\pm$ 12	5.6 $\pm$ 0.4	45.9 $\pm$ 0.4

\* Killed because of evident pathology. † Mean  $\pm$  standard deviation determined 8 months after x-irradiation on at least 22 rats in each irradiated group and on all 16 rats in the unirradiated group.

and which can be uncovered or activated by anemic stress. We examined this intriguing and potentially important finding but were unable to detect a leukemia-triggering effect of blood loss in irradiated rats.

Our experiments were performed with 11- to 12-week-old Sprague-Dawley rats obtained at one time from a single supplier. Rats were caged singly with food and water freely available and were assigned randomly to the various experimental groups for predetermined killing and duration-of-life study. Animals were irradiated with either 50 or 350 r, some over the entire body and others only over the hind legs. Partial-body irradiation was included because of the anticipated profound effect of acute blood loss with whole-body irradiation. The x-ray source was a G.E. Maxitron operated at 300 kv (peak), 20 ma, half value layer 1.65 mm Cu, target-to-skin distance 70 cm, and dose rate 90 r/min. Lithium fluoride dosimeters were used to monitor the exposure and the effectiveness of body shielding. Because of the shielding requirement, all animals were irradiated under light Nembutal anesthesia with appropriate rotation for a uniform exposure. Rats were bled by cardiac puncture 1 month after irradiation; about two-thirds of the blood volume (6.4 percent of body weight) was removed in two sessions 24 hours apart.

Very little mortality or morbidity occurred during the 9- to 10-month observation period (Table 1). There were four deaths: one nonbled rat partially irradiated with 350 r died at 1 month; one bled rat partially irradiated with 350 r died at 7 months, and two bled rats totally irradiated with 50 r died at 7 and 10 months. In addition, six animals were killed because of evident pathology, for example, tumor mass,

severe anemia, or inanition. These animals were distributed equally among the nonbled 50-r, nonbled 350-r, and bled 350-r total-body-irradiated groups. Myeloid leukemia was not found in any of these cases, which included two animals with a presumptive *Hemobartonella muris* infection. There were no significant differences in mortality/morbidity incidence or in body weight, total and differential leukocyte count, and hematocrit among the various experimental groups. The last three parameters were evaluated in bled and nonbled total-body-irradiated animals at 4 and 8 months.

The absence of myeloid leukemias within 9 to 10 months of irradiation is consistent with the experience of Moloney (2), who found a long latent period for the few leukemias that occurred. However, the finding of only 4 percent mortality among the 50- and 350-r bled animals by 10 months after total-body irradiation contrasts sharply with Gong's results. He observed 50 percent mortality at 5 weeks and 100 percent mortality by 35 weeks for 15 Sprague-Dawley rats bled 1 month after 50 r, and 50 percent mortality at 29 weeks and 80 percent by 40 weeks in 17 rats given 350 r and similarly bled. It should be noted that in our study about one-third of the rats died of shock within a few hours of bleeding, whereas apparently none died when bled from the exposed jugular vein in Gong's experiments. However, even if this acute attrition tended to eliminate irradiated animals with a greater proclivity for leukemia, which is unlikely, it could not account for the absence of myeloid leukemia and the very low subsequent mortality in view of the reported 100 percent incidence in bled irradiated animals. Moreover, there was a significant difference ( $P < .05$ )

in mortality of the nonbled irradiated groups in the two investigations. Six percent of 199 nonbled rats exposed to 25 to 350 r succumbed in Gong's experiments but no deaths occurred among 78 similarly treated animals in our study.

Leukemoid reactions are not uncommon after x-irradiation, and their differentiation from myeloid leukemia is often difficult (2). One of our rats was considered to have a possible leukemia, but there was no evidence of leukemic infiltration on autopsy and further study revealed red cell inclusions characteristic of *Bartonella* infection. Another questionable diagnosis was resolved by the failure to transmit leukemia via a marrow transplant in newborn rats. Perhaps many of the leukemias Gong reported were actually leukemoid reactions in response to pulmonary infections, necrotic tumors, and so forth.

It may be significant that our animals were caged singly, a condition which would lessen the probability of cross-infection. If infectious processes were indeed involved, it is necessary to assume their potentiation by the extensive blood loss in irradiated rats. Appropos of this is a recent report, also by Gong (4), that bleeding per se markedly reduced the long-term survival of RF mice, presumably because of myeloid leukemia. It would be important to know whether a similar effect occurs in strains other than the RF, which has a 2 to 3 percent incidence of spontaneous myeloid leukemia (5). In any event, we must conclude that the concept of a leukemia-triggering effect of blood loss is not supported by our findings in irradiated rats.

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6. We thank R. Lamela and G. Dunn for their assistance. Work was performed under the auspices of the Atomic Energy Commission.

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