HÆMATOLOGY

Paradoxical Effect of Magnesium Ions on Blood Coagulation

We have recently reported on the delay of whole-blood thrombin generation *in vitro* and *in vivo* which occurs when the concentration of magnesium is raised[1,2]. These results might have been thought to contradict the fact that addition of magnesium is known to enhance clotting of blood of which the calcium content has been lowered by previous passage through a suitable ion exchange column[3].

The inhibitory effect of magnesium on untreated blood has been explained on the basis of a competition between magnesium and calcium in processes where calcium is the more efficient catalyst[4]. We want to suggest that the present apparent contradiction can also be explained on similar lines because the outcome of the competition will depend on the concentration of either ion.

In decalcified plasma, magnesium alone will not restore coagulability. However, when sub-optimal amounts of calcium are added, magnesium will then enhance clotting. This can be understood if one assumes that some part or parts of the clotting mechanism can be activated by calcium alone, and that others can utilize magnesium though as a less efficient catalyst. Thus, if the amount of calcium is sub-optimal magnesium will be calcium-sparing; but if enough calcium is available to serve all clotting processes, added magnesium can then only displace the more efficient catalyst, and its effect will therefore be to retard clotting. Hence, the effect of a given concentration of magnesium on clotting will depend on the calcium concentration. Table 1 shows that with a calcium concentration of 5 m.equiv. per l., 10 m.equiv. per l. of magnesium is inhibitory, and with 2 m.equiv. per l. of calcium, 10 m.equiv. per l. of magnesium activates.

Table 1. Clotting Times (min.) of De-ionized Plasma diluted 10 : 1 with Additive

Ca^{++} (m.equiv. per litre)	Mg^{++} (m.equiv. per litre)			
	–	2	4	10
2	>60	11	12	32·5
3	15			
4	8·5			
5	7·5	7	8	11
6	7			
8	7			
10	7			
15	7	7	8	10
20	7·5			
30	9·5			
40	15			
50	>60			

Blood was taken into an ion exchange blood pack (Fenwall Laboratories, U.S.A.). Plasma was prepared by centrifuging at 1,500 r.p.m. for 20 min. 1 ml. of plasma added to 1 ml. additive in 8 × 75 ml. glass tubes incubated in a 37° C. water-bath. Clotting end-point was taken as the time when tubes could first be inverted without spilling (checked at ½-min. intervals).

As one might expect, with increasing quantities of magnesium the activating effect becomes less, and the inhibitory effect more pronounced. 2 m.equiv. per l. of magnesium will restore the clotting time of a calcium-poor plasma (2 m.equiv. calcium per l.) almost to normal, but will not inhibit the clotting of plasma containing normal amounts of calcium. On the other hand, 10 m.equiv. per l. of magnesium shows only little activation of the calcium-poor plasma, but marked inhibition at physiological levels. Furthermore, with the larger amount of magnesium the inhibition is diminished when calcium is present in high concentrations—bordering on those where calcium itself starts to become an inhibitor. This again illustrates the competition which exists between calcium and magnesium for clotting factors.

(This self-inhibitory effect of high calcium concentration is well-known, and has been explained[4] on a mechanical basis. The divalent calcium ion supposed to link two protein molecules will fail to form this bridge when it is in excess because too many of these molecules will have a calcium atom of their own.)

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[1] Anstall, H. B., Huntsman, R. G., Lehmann, H., Hayward, G. W., and Weitzman, D., *Lancet*, i, 814 (1959).
[2] Huntsman, R. G., Hurn, B. A. L., and Lehmann, H., *J. Clin. Path.*, **13**, 88 (1960).
[3] Soulier, J.-P., Proc. Seventh European Congress of Hæmatology, 1959 (in the press).
[4] Greville, G. D., and Lehmann, H., *J. Physiol.*, **103**, 175 (1943).

Electrophoretic Patterns of Haptoglobins in Apes

The haptoglobin serum groups are Mendelian characteristics of normal people as are blood groups. Two common genes, Hp^1 and Hp^2, have been found and their frequencies in all white peoples studied have been about 0·4 and 0·6 respectively[1-7]. Gene Hp^2 seems to be much rarer in Negroes than in Whites[1,5].

The sera of most mammalian species seem to contain haptoglobin, but the only electrophoretic pattern that we have found in domestic and laboratory animals studied resembles closely that of Hp^1Hp^1 (*Hp* 1–1) people. On account of this observation we have studied blood samples of different primates listed below with the starch gel electrophoresis method described earlier[6].

Macacus rhesus	17	specimens
Macacus radiata	10	,,
Papio hamadryas	1	,,
Cercopithecus aethiops	1	,,
Pan traglotydes	2	,,

Sera of all apes studied gave the pattern *C* of Fig. 1, which closely resembles the pattern *D* (human *Hp* 1–1).

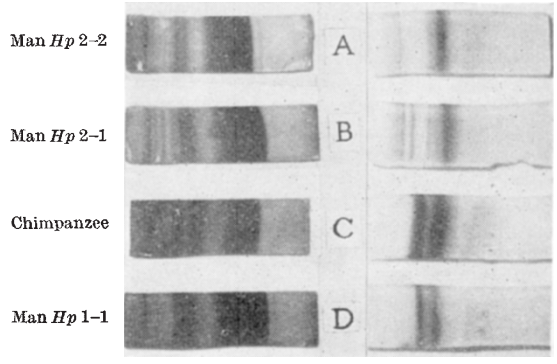

Fig. 1