

Table 1. DEHYDROGENASE ACTIVITIES OF L1210 CELLS

	Sensitive	Mercaptopurine-resistant	Amethopterin-resistant
Succinic dehydrogenase activity	++ or +	+ or 0	+ or 0
Lactic dehydrogenase activity	++++ or +++	+ or 0	+ or 0

few positively stained granules, whereas in the four-plus smears the majority of the cells showed many positive granules (Fig. 1). The sensitive cells were found to have a much greater lactic dehydrogenase activity than the resistant cells, a fact which lends support to the idea that they have a more active glycolytic metabolism. The former also had a greater succinic dehydrogenase activity, but the difference was less marked. The results suggest that sensitive cells may be generally more active in their respiration than the resistant cells.

The fact that sensitive and resistant L1210 cells have differences in respiratory metabolism which can be demonstrated cytochemically suggests that a similar examination of human leukæmic cells would be worth while. If cytochemical differences could be found between sensitive and resistant cells, they would be valuable for predicting the effect of therapeutic agents on human leukæmias.

I am grateful to Dr. L. Law for providing the resistant strains of L1210 cells, to Dr. S. R. M. Bushby and Miss M. Barnett for maintaining them and supplying me with inoculated mice, to Miss T. Minett for technical assistance and to the Lady Tata Trust for a grant-in-aid.

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Hæmoglobin 'Bart's' and the Sickling Phenomenon

WHILE examining the hæmoglobin of hydrops and erythroblastosis foetalis, in an attempt to correlate foetal disease with hæmoglobin 'Bart's', five consecutive cases (four in Indonesia and one in Malaya) were found in which foetal hydrops and erythroblastosis were associated with this type of hæmoglobin^{1,2}. Four of these cases were examined in detail, and the sickling phenomenon was noted in the abnormal erythrocytes; the amounts of the abnormal fast-moving hæmoglobin were very high, and formed by far the major component. A small amount of hæmoglobin *H* was detected in all four specimens; no hæmoglobin *S* was detected in any of them. Hæmoglobin 'Bart's' is now believed to be identical with the Fessas and Papaspyrou type of hæmoglobin³⁻⁵.

In order to eliminate the possibility of false sickling⁶, tests on the abnormal erythrocytes were carried out simultaneously with control tests of normal erythrocytes on the same slide. The abnormal erythrocytes, when left on a slide under a cover-glass, without sealing, or when left between two cover-glasses, were found to sickle in 1-1½ hr.; after 24 hr. most of these erythrocytes were sickled (Fig. 1). If the blood were stored under paraffin for 24 hr., sickling was not seen on immediate examination, but appeared after the slide had been left for about 1 hr.; thus it appears that de-oxygenation of the blood is not the cause of

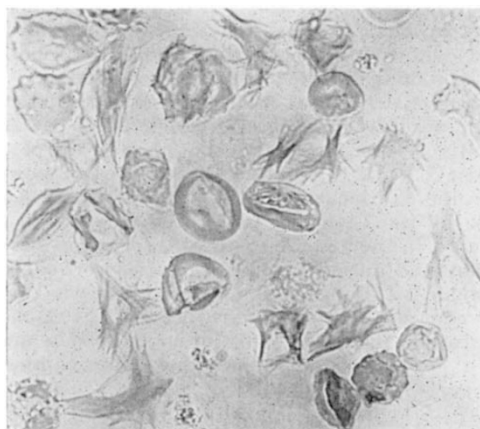


Fig. 1. Sickling of erythrocytes containing hæmoglobin 'Bart's' + *H*

the sickling. If oxygen, nitrogen, or carbon monoxide were bubbled through the blood, the erythrocytes were found not to sickle immediately; but, if left for 1 hr. or more on the slide, sickle cells appeared. Sickling was found to occur at any point over the pH-range studied, 6.4-7.8. Clear solutions of the hæmoglobin prepared from these erythrocytes, when left to stand, were found to develop a precipitate; on examination this was found to be composed of fine granules.

The easy sickling of these cells seems to be provoked by a peculiarity of the 'Bart's' (= *F* and *P*) hæmoglobin. The influence of hæmoglobin *H* cannot be entirely ruled out, but this hæmoglobin by itself has never been reported to be associated with sickling.

While these investigations were in progress, Atwater *et al.* reported the sickling of erythrocytes containing another fast-moving hæmoglobin (*I*) in high concentration⁷.

Since the completion of this communication, three further cases of severe hydrops foetalis associated with a large amount of hæmoglobin 'Bart's' have been found. Careful examination of the red blood cells again revealed the sickling phenomenon in all three of them, while control studies were negative.

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PATHOLOGY

Energy Pathways of Hepatoma No. 5123

SINCE the original experiments of Warburg with slices of tumour there has been intense investigation of, and discussion about, a specific tumour energy metabolism^{1,2}. This concept, originally characterized by high rates of aerobic and anaerobic glycolysis, has been extended to include certain ancillary features: a moderate respiratory rate with minimal increase in respiration following the addition of