complex relationship of thrombin action and ADP induced aggregation in plasma with platelets not subjected to alteration by isolation and washing. The more consistent enhancement of ADP action by fibrinogen with platelets resuspended in heated plasma rather than in buffer saline may imply the existence of additional factors or conditions for optimum aggregation.

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[1] Gaarder, A., Jonsen, J., Laland, S., Hellem, A., and Owren, P. A., *Nature*, **192**, 531 (1961).
[2] Born, G. V. R., and Cross, M. J., *J. Physiol.*, **168**, 41P (1963).
[3] Brinkhous, K. M., LeRoy, E. C., Cornell, W. P., Brown, R. C., Hazlehurst, J. L., and Vennart, G. P., *Proc. Soc. Exp. Biol. Med.*, **98**, 379 (1958).
[4] Born, G. V. R., and Cross, M. J., *J. Physiol.*, **168**, 178 (1963).
[5] Maxwell, R. E., Nickel, V. S., and Lewandowski, V., *Biochem. Biophys. Res. Comm.*, **7**, 50 (1962).
[6] Shermer, R. W., Mason, R. G., Wagner, R. H., and Brinkhous, K. M., *J. Exp. Med.*, **114**, 905 (1961).
[7] Ware, A. G., Fahey, J. L., and Seegers, W. H., *Amer. J. Physiol.*, **154**, 140 (1948).
[8] Schmid, H. J., Jackson, D. P., and Conley, C. L., *J. Clin. Invest.*, **41**, 543 (1962).
[9] Gokcen, M., and Yunis, E., *Nature*, **200**, 590 (1963).
[10] Kaser-Glanzmann, R., and Luscher, E., *Thromb. Diath. Haem.*, **7**, 480 (1962).

Close Association of I Blood Group and Disease

We recently had occasion to search for compatible red cell donors for an I-negative patient with anti-I. Since more than 99·9 per cent of adults are I-positive we found no I-negative donors. Then, to our surprise, we found many I-negative patients in our hospital population.

The I system was first recognized in 1956[1], but much information is at present being described which indicates that this is a unique blood-group[2]. Although most normal adults are I-positive, all cord blood red cells are I-negative, $i_{(cord)}$. The rare normal adults who can be called I-negative all actually have some trace of reactivity and can be graded as $I_{(int)}$, or i_2 or i_1, depending on the test reagent. Anti-I reagents react best at low temperatures and some discriminate within the ABO system.

The anti-I serum which we used in this investigation was a 'natural' agglutinin produced by an untransfused group A_2 I-negative patient with acquired heart disease. It strongly agglutinates I-positive red cells of group O and A_2 at 22° C and of group A_1 at 15° C. A_2 I-positive red cells were rapidly eliminated when transfused to this patient. The serum weakly agglutinated several samples from normal donors which were sent to us as I-negative. These cells probably represent *Ii* heterozygotes $I_{(int)}$. The results on the patient population are given in Table 1. There was no obvious correlation of these data with age, race or peripheral leucocyte count.

Table 1

Diagnosis	I-positive	I-negative	
	+ + +	Inter-mediate	Negative
Leukæmia			
Chronic myelogenous	16	3	4
Chronic lymphocytic	1	0	1
Acute myelogenous	1	1	2
Acute lymphocytic	7	1	3
Carcinoma, cervical	2	0	1
Neuroblastoma	1	1	0
Familial inclusion body anæmia	0	0	1
Lupus, systemic	2	0	1
Mitral stenosis	2	0	1
Other heart disease	21	0	0
Other blood dyscrasia	8	0	0
Other carcinoma, adenoma, brain tumour	22	0	0
Renal	4	0	0
Uveitis	3	0	0
Familial Mediterranean fever	2	0	0
Other	4	0	0
Total	96	6	14
Blood donors	333	0	0

Several published bits of information indicate a relationship between the I system and blood dyscrasia. Some cases of leukæmia in which the A antigen is weak show a depressed I reactivity[3]. A few anti-*i* sera have been described from patients with reticulosis or leukæmia. In one of these cases this was an auto-antibody and the patient had chronic myelogenous leukæmia[4]. Sixteen of our I-negative patients were tested for cold agglutinins at 2° C. Six patients had a low-titre panagglutinin, four had anti-I and none had anti-*i*. Blood from an I-negative patient collected into warm saline remained I-negative.

Although it is tempting to see this close relationship between mostly neoplastic disease and a rare blood group as indicative of genetic abnormality, it is more probably a less specific connexion. There does not seem to be any abnormal I in the few families of our patients investigated, nor is the absence of I associated with elevated fœtal hæmoglobin or the Ph′ chromosome.

The classical cold hæmagglutinin of primary atypical pneumonia is anti-I, and individual sera are known to show different levels of activity with a series of normal red cells. Despite the experience of other authors that red cells from patients with 'hæmatological disease' including leukæmia have an enhanced agglutinability with a cold antibody from the cold-hæmagglutinin syndrome[5], the cells of our patients seem to be on the low end of the I test spectrum. Although the reasons for this may be genetic it is more probable that there is some abnormality of the agglutinogen site on their red cells. This may be a non-specific blocking effect related to an infectious or neoplastic agent.

Note added in proof. Some increase in *i*-activity has been found in leukæmia and other diseases (Giblett, E. R., and Crookston, M. C., *Nature*, 201, 1138; 1964). The relationship between their anti-*i* (from donor We.) and our anti-I (from donor Fa.) was tested by Dr. Giblett. No correlation was found.

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[1] Wiener, A. S., Unger, L. J., Cohen, L., and Feldman, J., *Ann. Intern. Med.*, **44**, 221 (1956).
[2] Race, R. R., and Sanger, R., *Blood Groups in Man*, fourth ed. (Blackwell, Oxford, 1962).
[3] Jenkins, W. J., and Marsh, W. L. (unpublished observations quoted in ref. 2).
[4] van Loghem, J. J., van der Hart, M., Veenhoven-van Riesz, E., van der Veer, M., Engelfriet, C. P., and Pectoom, F., *Vox Sang.*, **7**, 214 (1962).
[5] Dacie, J. V., Lewis, S. M., and Tills, D., *Brit. J. Hæmat.*, **6**, 362 (1960).

Morphological Demonstration of Two Red Cell Populations in Human Females Heterozygous for Glucose-6-phosphate Dehydrogenase Deficiency

In 1961 Lyon[1] postulated that in the female one of the two *X*-chromosomes is inactivated. Though the exact timing of this occurrence is not known, two populations of cells will result, one carrying the paternal and the other carrying the maternal *X*-chromosome. In the heterozygous state for *X*-chromosomal diseases mosaicism of normal and pathological cells would be expected. Though this hypothesis is not applicable to all recessive traits, there is some evidence of its validity in favism. Several investigations have shown by indirect methods that two populations of red cells may occur in females heterozygous for glucose-6-phosphate dehydrogenase deficiency[2–4]. Nevertheless, it has not yet been possible to demonstrate visually different types of erythrocytes.