Howell-Jolly bodies in idiopathic steatorrhoea

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SYNOPSIS Large numbers of Howell-Jolly bodies were found in the bone marrow and peripheral blood, both before and after corrective haematinic therapy, in three patients with idiopathic steatorrhoea with associated splenic atrophy, who presented with megaloblastic anaemia. The proportion of erythrocytes containing Howell-Jolly bodies was much higher in these patients when compared with the number found in post-splenectomy subjects. Red cell survival studies of patients' own red cells, sensitized with a potent anti-D serum, showed an abnormally prolonged survival in the three patients with splenic atrophy when compared with those in two splenectomized subjects, in four patients with coeliac disease, and in seven normal controls. There appears to be a relationship between atrophy of the reticuloendothelial system and Howell-Jolly body production in idiopathic steatorrhoea.

Howell-Jolly bodies are found in varying proportions of erythrocytes after splenectomy, in congenital absence of the spleen, and in splenic atrophy; they are also found in other conditions such as megaloblastic anaemias, severe haemolytic anaemias, and leukaemia. It is well established that megaloblastic anaemia may be a complication of idiopathic steatorrhoea and that certain cases of the disease develop splenic atrophy. Niewig and Arhends (1953) reported large numbers of Howell-Jolly bodies in the peripheral blood in cases of non-tropical sprue with associated splenic atrophy.

We have investigated five patients with idiopathic steatorrhoea, all of whom presented with a megaloblastic anaemia. In the course of the investigations large numbers of Howell-Jolly bodies were found in the peripheral blood of three patients and it was later shown that all three had splenic atrophy. We have also compared, in these five patients, the percentage of red cell precursors and peripheral blood erythrocytes that contained Howell-Jolly bodies, before and after corrective haematinic therapy. The peripheral blood was examined for the presence of Howell-Jolly bodies in 11 other patients with idiopathic steatorrhoea who had normal sized spleens and no evidence of megaloblastic haemopoiesis, in 29 children and four adults with coeliac disease, and in 50 patients who had undergone splenectomy. As a test of functioning splenic tissue, the erythrocytes of the three patients with splenic atrophy, seven normal

controls, two splenectomized patients, and four patients with coeliac disease, were sensitized with potent Rh antibodies, labelled with radioactive chromium and then injected back into the patients, and the cell survival measured.

MATERIAL AND METHODS

Iliac crest bone marrow aspirates, stained by May-Grünwald-Giemsa, were examined from five patients with idiopathic steatorrhoea before any haematinic treatment was started and then again five weeks after the completion of intensive intramuscular injections of vitamin B₁₂, folic acid, and iron. The proportion of red cell precursors containing Howell-Jolly bodies was assessed on each occasion. The peripheral blood was examined at monthly intervals up to nine months after the haematinic therapy was started. One marrow aspirate from a case of splenectomy was also examined.

Blood films were examined for the presence of Howell-Jolly bodies from the 16 patients with idiopathic steatorrhoea on numerous occasions, and single film examinations were carried out on each of 29 children and four adults with coeliac disease, and 50 splenectomized subjects. Ten thousand erythrocytes were examined on each occasion and the films were stained with May-Grünwald-Giemsa.

To determine the red cell survival of patients' own sensitized cells, 10 ml. of blood was collected into acid-citrate dextrose solution and the cells were then washed twice in sterile normal saline and incubated for one hour at 37°C. with an equal volume of sterile incomplete anti-D serum (titre at least 1/64). The cells were washed three times in normal saline and a direct antiglobulin test was performed to check that the cells were sensitized. The

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2.5 ml. of the cells was incubated with ^{51}Cr for one hour at room temperature. The cells were then washed three times in normal saline and injected into the patient. The survival of the tagged cells was then measured.

RESULTS

The results are summarized in Tables I to III.

TABLE I

PERCENTAGE OF RED CELL PRECURSORS CONTAINING HOWELL-JOLLY BODIES BEFORE AND AFTER CORRECTIVE HAEMATINIC THERAPY IN FIVE CASES OF IDIOPATHIC STEATORRHOEA PRESENTING WITH A MEGALOBlastic ANAEMIA

Case No.	Before Therapy (Megaloblastic Marrow)	After Therapy (Normoblastic Marrow)	Splenic Atrophy
1	6.4	5.4	Yes
2	7.3	6.1	Yes
3	7.1	5.7	Yes
4	1.8	None	No
5	1.6	None	No

TABLE II

NUMBER OF CASES EXAMINED FOR PRESENCE OF HOWELL-JOLLY BODIES IN PERIPHERAL BLOOD

Type of Case	No. Examined	No. in which Howell-Jolly Bodies Found	No. with Splenic Atrophy
		First Examina- tion	After Therapy
Idiopathic steatorrhoea			
With megaloblastic anaemia	5	5	3
Without megaloblastic anaemia	11	0	—
Coeliac disease			
Children	29	0	—
Adults	4	0	—
Splenectomy	50	50	—

TABLE IIb

HOWELL-JOLLY BODIES IN PERIPHERAL BLOOD IN THREE PATIENTS WITH SPLENIC ATROPHY

Case No.	Percentage of Howell-Jolly Bodies before Haematinic Therapy		Percentage of Howell-Jolly Bodies after Therapy	
	Range	Average	Range	Average
1	4.1-5.2	5.0	1.9-6.8	4.1
2	6.4-8.2	7.1%	2.9-7.3	5.3
3	3.9-5.0	4.3%	2.1-6.2	3.9

TABLE IIc

PERCENTAGE OF HOWELL-JOLLY BODIES FOUND IN 50 POST-SPLENECTOMY BLOOD EXAMINATIONS

Range	Average
0.0001-3.1	0.3

TABLE III

RED CELL SURVIVAL OF PATIENTS' OWN SENSITIZED CELLS

Type of Case	Number Tested	Time Taken to Remove Sensitized Cells from the Circulation
Normal controls	7	60 minutes
Coeliac disease	4	65 minutes
Post-splenectomy	2	4 hours
Splenic atrophy	Case 1	106 hours
	2	8½ hours
	3	148 hours

In the first marrows, of all five patients, the Howell-Jolly bodies that were present in the red cell precursors were nearly all multiple, but after haematinic therapy, in the three patients with splenic atrophy, they were nearly all single. Of the red cell precursors, 0.8% contained single Howell-Jolly bodies in one bone marrow examination from a post-splenectomy subject.

The individual red cell survival of each patient tested was plotted graphically and the values given above were obtained from the graphs. It is seen that the patients with splenic atrophy were unable to remove the sensitized cells from the circulation as quickly as the patients in the control and other groups tested.

DISCUSSION

Howell-Jolly bodies are Feulgen positive and represent true nuclear fragments which are formed by karyorrhexis of normoblast nuclei. In the megaloblastic anaemias, due to vitamin B₁₂ and folic acid deficiency, usually more than 1% of the late erythroid precursors contain Howell-Jolly bodies and the majority of these cells contain more than one Howell-Jolly body (Dawson and Bury, 1961). Dawson and Bury examined three post-splenectomy marrows and found only single Howell-Jolly bodies in less than 1% of the erythroid precursors; we corroborated this finding by our examination of one post-splenectomy marrow.

Of the five patients with idiopathic steatorrhoea who presented with megaloblastic anaemia, three had splenic atrophy. Multiple Howell-Jolly bodies were found in all five marrows initially but after corrective therapy none were found in the marrow or in the peripheral blood in the two cases without splenic atrophy, indicating that their presence was initially due to megaloblastic erythropoiesis. In the three patients with splenic atrophy erythropoiesis became normoblastic after intensive haematinic therapy. However, a high proportion of erythroid precursors still contained Howell-Jolly bodies but these were nearly all single. In these three cases the proportion of erythroid precursors containing

Howell-Jolly bodies was far higher than might have been expected when comparing them with simple post-splenectomy marrows. Niewig and Arhends (1953) reported large numbers of Howell-Jolly bodies in the blood of three patients with non-tropical sprue with associated splenic atrophy. Our peripheral blood studies (Tables IIa and b) confirm this observation, and it is interesting that even after corrective therapy the average percentage of erythrocytes containing Howell-Jolly bodies in the cases with splenic atrophy was 4.1, 3.9, and 5.3 respectively, whereas the average percentage found in 50 splenectomized subjects was only 0.3. No Howell-Jolly bodies were seen in 11 other cases of idiopathic steatorrhoea or in 29 children and four adults with coeliac disease.

If splenic atrophy develops in idiopathic steatorrhoea there may be atrophy of the rest of the reticuloendothelial system. In order to test for functioning splenic tissue and a competent reticuloendothelial system, the red cells of the patients with splenic atrophy were sensitized with a potent anti-D serum and their survival measured (Table 3). The seven normal controls and four patients with coeliac disease removed their sensitized cells within 65 minutes and the two splenectomized patients removed their cells within four hours. However, the three patients with splenic atrophy took a much longer time to remove their sensitized cells from the circulation, which must reflect a poorly functioning spleen and reticuloendothelial system. All patients tested were Rh positive and the same anti-D serum was used in each case.

The presence of increased numbers of Howell-Jolly bodies in the three patients with splenic atrophy does not appear to be due to a primary erythropoietic disorder as the bone marrows had reverted

from megaloblastic to normoblastic erythropoiesis after haematinic therapy. Their presence must be associated with splenic atrophy but it is odd that far more Howell-Jolly bodies were found in these patients compared with those who had had their spleens surgically removed.

It appears that in idiopathic steatorrhoea, if there is atrophy of the reticuloendothelial system, even in the presence of an apparently normal bone marrow, large numbers of Howell-Jolly bodies are produced. The follow-up, after correction to normoblastic erythropoiesis in the three patients with splenic atrophy, was long enough to eliminate circulating erythrocytes containing Howell-Jolly bodies that were present in the peripheral blood when the patients first presented with megaloblastic bone marrows. The exact role of the spleen and Howell-Jolly production is still not yet fully understood (Crosby, 1963), and it is difficult to determine whether the Howell-Jolly bodies in the three 'corrected' patients are normal ones which were not removed or whether they are due to an excess production. The latter seems more likely, but this is very difficult to explain as it seems to involve the production by the reticuloendothelial system of something necessary to stop Howell-Jolly body formation, *i.e.* to promote proper nuclear division.

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