Platelet Levels in Infectious Mononucleosis

By R. L. Carter

Acute thrombocytopenia is a rare but fairly well-documented complication of infectious mononucleosis.\textsuperscript{1,8} There is, however, little information on platelets in uncomplicated cases. In most accounts of the disease, platelet levels are either ignored or stated to be normal, and actual counts have been found in only two reports.\textsuperscript{2,3} Limarzi et al.\textsuperscript{2} investigated 25 cases and found that platelet levels were normal or occasionally increased: low levels were not encountered. Unfortunately, the method of counting was not described, the phase of the disease was not mentioned, and the Paul-Bunnell test was omitted or negative in 12 of the patients concerned. Serial estimations in 7 cases were reported by Angle and Alt.\textsuperscript{3} Using an indirect counting method, these authors found low levels in the early stages, returning to normal by the end of the third week; slightly elevated levels were occasionally seen in the second week.

In the course of recent work on infectious mononucleosis, platelet levels have been estimated in a large random group of patients.

\textbf{Methods}

Fifty-seven cases were studied, all of whom showed clinical, hematologic and serologic evidence of infectious mononucleosis. Clinical histories were taken in all cases to establish the phase of the disease. Platelet levels in venous blood samples were determined by the direct counting method of Brecher and Cronkite.\textsuperscript{4} The lower limit of normal by this technic is 140,000/cu. mm. Serial counts were not made. All results were recorded according to the phase of the disease, measured in weeks.

\textbf{Results}

The results are summarized in figure 1. The overall range is from 63,000–256,000/cu.mm.; the distribution of 47 counts from the first 4 weeks of the disease is shown in table 1. Five of the subnormal counts are <100,000/cu. mm. These are shown in table 2. Subsequent counts during convalescence are all within normal limits.

\textbf{Discussion}

The present study shows a moderate but fairly consistent reduction in platelet levels during the first 4 weeks of the disease. With one exception, the counts are well above the critical range at which spontaneous bleeding may occur and no patients with thrombocytopenic symptoms were encountered. In many cases, the reduction in platelets is too small to be detected in stained smears and is only shown up by direct counts. Raised levels of platelets were never seen.

Platelet levels in cases with overt thrombocytopenia show similar patterns:

\textit{Submitted July 31, 1964; accepted for publication Sept. 29, 1964.}
in 21 of the 29 thrombocytopenic patients reviewed by Radel and Schorr, purpura developed during the first week, and it was the presenting symptom in nine instances. No cases have been found in which thrombocytopenic purpura developed after the third week, and available accounts suggest that this is an early complication of infectious mononucleosis, even allowing for the difficulty in timing the precise onset of the disease. Since about 50 percent of uncomplicated cases also have lowered platelet counts at this time, it may be that patients with severe thrombocytopenia are merely extreme examples of the same pathologic process.

Comparable episodes of thrombocytopenia have been described in a number of acute infections, particularly in viral conditions. Rubella is the best documented of these since there is some information on platelet levels in patients
TABLE 1.—Platelet Counts during the Acute Phase of the Disease

<table>
<thead>
<tr>
<th>Normal</th>
<th>23 (48.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subnormal</td>
<td>24 (51.1%)</td>
</tr>
</tbody>
</table>

Table 2.—Platelet Counts < 100,000/cu. mm.

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 2</td>
<td>99,000</td>
</tr>
<tr>
<td></td>
<td>97,000</td>
</tr>
<tr>
<td></td>
<td>80,000</td>
</tr>
<tr>
<td></td>
<td>63,000</td>
</tr>
<tr>
<td>Week 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>98,000</td>
</tr>
</tbody>
</table>

without purpura, but other examples include measles and vaccinia. It seems likely that infectious mononucleosis can be included in this category. In many reports, the thrombocytopenia appears to be independent of the severity of the original infection, and may appear at any stage of the disease. In the viral group, however, it occurs almost entirely during the first 3 weeks, unlike the thrombocytopenia complicating diphtheria or scarlet fever which may appear for the first time at the fourth week, or even later.

The causal association between acute infections and thrombocytopenia is obscure and the mechanisms involved are largely speculative. In the case of infectious mononucleosis, the few relevant observations can be considered in three groups.

1. In three accounts, megakaryocytes have been reduced in numbers. In other reports they are said to be normal or increased in numbers, but often showing defective platelet formation.

2. One account mentions a platelet agglutinin which was shown to be independent of the Paul-Bunnell antibody, and Smith et al. record a positive indirect platelet antiglobulin consumption test.

3. Maupin and Monteil invoke hypersplenism and stress the remarkable beneficial effects of splenectomy in the patient described by Dameshek and Grassi, (this case, however, was complicated still further by an obscure pre-existing bleeding tendency).

The true significance of platelet agglutinins and platelet antiglobulin consumption tests is still disputed, and the role of hypersplenism is equally controversial. But it is certain that at least some types of thrombocytopenia are the consequence of immune responses to platelets whose antigenic nature has been modified, for example by certain drugs such as Sedormid and Quinidine. Evidence for an analogous state of affairs in the thrombocytopenias complicating acute infections is scanty. Viruses have been demonstrated on and within platelets in vitro, but similar findings have not been described in vivo. Kirstner and Stefanini immunized rabbits with their own platelets which had previously been incubated with Newcastle virus, and then challenged them with suspensions of the virus, but no thrombocytopenia was produced. A fall in platelet levels was, however, observed when certain bacterial filtrates were used. These findings may provide a basis for the purpura.
occasionally complicating recurrent infections by common organisms such as streptococci; they are difficult to apply to the viral group where repeated attacks of rubella and measles, (and infectious mononucleosis\textsuperscript{14}), are rare. In all cases which have been traced, the thrombocytopenic episode has been transient and recovery has been full and apparently permanent. In rare complications of this nature, enhanced individual susceptibility is often postulated. This seems unlikely, at least in infectious mononucleosis, where 50 per cent of cases appear to be mildly thrombocytopenic during the acute phase of the disease.

**Summary**

Platelet levels in 57 patients with infectious mononucleosis are recorded. Approximately 50 per cent of cases show some degree of thrombocytopenia during the first 4 weeks of the disease. Possible mechanisms for the change are reviewed and other acute infections complicated by thrombocytopenia briefly discussed.

**Summario in Interlingua**

Le nivellos del plachettas esseva determinate in 57 patientes con mononucleosis infectiose. Approximativemente 50 pro cento del casos mostra un certo grado de thrombocytopenia durante le prime quatro septimanas del maladia. Es discutite le possibile mechanismos responsabile pro le alteration. Un breve revista es presentate de altere acute infectiones complicate per thrombocytopenia.

**Acknowledgments**

I would like to thank Dr. A. A. Sharp and Dr. F. G. Bolton for help in preparing this manuscript, and Mrs. D. Hovard and Miss S. J. Crouch for technical assistance.

**References**

9. Freeman, T., and Wakefield, G. S.: Platelet-agglutinating factor in gland-
PLATELET LEVELS IN INFECTIOUS MONONUCLEOSIS

10. Maupin, B., and Monteil, R.: Les plaquettes dans la mononucléose infec-
11. Dameshek, W., and Grassi, H. A.: Infectious lymphadenosis (mononucleo-

R. L. Carter, M.A., B.M., B.Ch., Department of Pathology,
Platelet Levels in Infectious Mononucleosis

R. L. Carter