Protection of the Pulmonary Microvasculature by Fine Screen Blood Filtration*

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Particulate matter accumulates in stored blood and may be directly infused into the pulmonary microvasculature by blood transfusion, causing the respiratory distress syndrome (RDS). The protective effect of fine screen filtration by a 40-μ filter in massive blood transfusion was studied prospectively in 54 patients with trauma. Seventeen patients (control) received from 10 to 40 units (mean 18.8 units) of blood through the standard 170-μ blood filter and were compared to 27 patients (filter) who received from 10 to 63 units (mean 17.9 units) of blood through the 40-μ filter. Seven of the 17 control patients developed the clinical picture of RDS following treatment of their trauma. Despite the similarity in source of injury, anatomic area injured and surgical treatment, only two of the 27 patients with a filter developed the clinical signs of RDS. Three of the seven patients with RDS in the control group and both of the patients with RDS in the group in whom the filter was used had significant chest injury. Three patients in the control group without chest trauma died of intractable hypoxemia. Open lung biopsies and needle biopsies were performed in ten additional patients. Particulate matter in the precapillary arterioles was present in four patients receiving massive blood transfusion without the fine screen filter and in no patients with the fine screen filter. The fine screen filter is recommended to protect the pulmonary microvasculature in transfusions of stored blood.

The increase in severe trauma, complex surgical procedures, frequent use of cardiopulmonary bypass and better organ support systems has been accompanied by an increased frequency of the respiratory distress syndrome (RDS).¹ The etiologic factors involved are as multiple as the factors causing shock, low perfusion states and eventual system failure. Some of these factors such as oxygen toxicity, infection, over-hydration, hypoventilation, atelectasis, improper ventilatory assistance, congestive heart failure, hypovolemia, fatty emboli and multiple pulmonary emboli can be controlled to decrease the incidence and mortality of RDS. Another factor, massive blood transfusion (MBT) has been recently implicated as a possible etiologic agent.²⁻⁴ Fibrin, platelet and leukocyte aggregates, denatured protein, fat and cellular stroma accumulate in stored blood.⁷⁻⁸⁻¹² Direct infusion of the microvasculature results in dosage-related pulmonary damage. Elevated screen filtration pressure in trauma victims and the presence of particulate matter emboli in the capillaries and arterioles were demonstrated.⁶⁻¹⁰ The standard blood filter of approximately 170-μ pore size, allows the introduction of these substances. Efforts to prevent dissemination of microaggregates in stored blood have resulted in the design of finer filters ranging from 25 to 40 μ in pore size.⁴⁻⁸⁻¹¹⁻¹³⁻¹⁵ Varying success has been demonstrated in the filtration of blood during cardiopulmonary bypass in the venous line, coronary suction line and/or the arterial line.¹⁷⁻²¹ The presence of aggregates and microemboli has been directly or indirectly demonstrated and related to neurologic and pulmonary complications.²²⁻²⁵

Recognizing the high incidence of pulmonary insufficiency followed by RDS in trauma patients, a prospective study was designed to evaluate the effect of finer filtration of homologous blood transfusions in patients with trauma. This investigation is an extension of a previously reported study² and further emphasizes the use of a finer filter in massive blood transfusion to prevent the RDS.

CLINICAL MATERIAL

From January through October, 1972, 18 patients received massive blood transfusion through a standard 170-μ filter (Fenwall Laboratories). In the first study, this group was compared to 13 patients who received all blood transfusions through the Ultipor fine screen 40-μ filter (Ultipor, Pall

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Table 1—Clinical Material

<table>
<thead>
<tr>
<th>Patients</th>
<th>Control</th>
<th>with Filter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>17</td>
<td>27</td>
</tr>
<tr>
<td>Male/female</td>
<td>14:3</td>
<td>24:3</td>
</tr>
<tr>
<td>Age (yrs.)</td>
<td>23-55</td>
<td>9-64</td>
</tr>
<tr>
<td>Range/mean</td>
<td>31</td>
<td>36</td>
</tr>
<tr>
<td>Blood administered during operation</td>
<td>10-40</td>
<td>10-63</td>
</tr>
<tr>
<td>Range/mean</td>
<td>18.8</td>
<td>17.9</td>
</tr>
<tr>
<td>Mortality</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

Corporation). Because of the results of the original pilot study, the 40-μ filter was adapted for all massive blood transfusions following that period. From October, 1972 to July, 1973, 14 patients were studied and received all of their blood transfusions through the 40-μ fine screen filter (Table 1). One additional patient, transferred from another hospital, received all blood transfusions through the standard filter during that period. Thus, the control group of 17 patients who received all blood transfusions through the standard 170-μ filter (control group) was compared to the 17 patients who received all blood transfusions through the 40-μ filter (group with filter).

In the control group, the age range was from 23 to 55 years, with a mean of 31 years. In the group with a filter, the age range was from 9 to 63 years, with an average of 36 years. Only patients who received ten or more units of blood (approximating an entire blood volume) were considered candidates for the study. The mean amount of blood received by the control group was 19 units as opposed to 17.9 units in the group with filter. The range was from 10 to 40 units in the control group and 10 to 63 units in the group with fine screen filter. Eight of 17 patients died in the control group and 4 of 27 in the group with filter.

Penetrating trauma was the most common type of injury (Table 2). Gunshot wounds accounted for 11 patients in the control group and 18 in the group with filter. Blunt trauma resulted in three injuries in the control group and five in the group with filter. The remaining injuries were caused by shotgun and stab wounds.

Table 2—Cause of Injury

<table>
<thead>
<tr>
<th>Patients</th>
<th>Control</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Gunshot wound</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>Shotgun wound</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Stab wound</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Blunt</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 3—Primary Site of Injury

<table>
<thead>
<tr>
<th>Patients</th>
<th>Control</th>
<th>with Filter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdomen</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Chest</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Multiple</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Extremity</td>
<td>—</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>27</td>
</tr>
</tbody>
</table>

The primary sites of injury were relatively the same in both groups (Table 3). The abdomen was the most frequently involved area. The chest was primarily injured in 3 of 17 patients in the standard and in 4 of 27 patients in the group with filter, although there was chest involvement to a minor degree in most of the patients. Most patients with blunt trauma had flail chest associated with their injuries. All patients underwent surgical treatment for their injuries. Standard surgical repair was accomplished, with efforts directed toward control of hemorrhage. Vascular repairs, abdominal laparotomy and thoracotomy were accomplished shortly after admission.

In order to assess the presence of the respiratory distress syndrome, a chest x-ray film was taken daily for four days following injury. Arterial oxygen tension (PaO₂) arterial carbon dioxide (PaCO₂), arterial pH and oxygen saturation were obtained immediately after operation and for the four days following. Inspired oxygen concentration (FiO₂) at the time of arterial blood gas level procurement was likewise recorded, with tidal volume and respiratory rate if the patient was on a respirator. In addition to the usual required laboratory studies on the severely injured patient, most patients had sequential studies immediately after operation and for the four days following. The studies were determinations of hemoglobin, prothrombin time, partial thromboplastin time, bilirubin, cholesterol, total protein and albumin.

Criteria for extubation following operation were similar to those described by others. If the patient was to remain in intubation for more than 48 hours or if a significantly flail chest was present, a tracheostomy was performed. Either the Bennett MA-1 volume respirator or Emerson volume respirator was utilized in all patients with flail chest or prolonged intubation. When atelectasis occurred, bronchocopy was performed. Frequent endotracheal suctioning was maintained to assure cleared airways. Oxygen concentrations were always maintained below 60 percent FiO₂ and positive end expiratory pressure were utilized early when oxygen concentration fell to low levels. Serum albumin and furosemide were utilized in the treatment of hypoxemia. Both groups were treated similarly in the period after operation. Over hydration was avoided by the use of a central venous catheter and in some cases monitoring of the pulmonary artery wedge pressure, as described, by use of a direct flow balloon catheter (Swan-Ganz catheter, Edwards Labs).

In most instances, the blood was administered under external pressure by a pressure bag pump, with the fine screen filter used until the filter clogged. The filter generally could accommodate from five to ten units of blood without difficulty, depending on the age of the blood. Every unit of blood in the group with filters was given through the 40-μ filter. In the control group it was administered through the standard 170-μ filter.

Open lung biopsies were taken at the time of operation in ten additional patients who received ten or more units of filter or control blood, most of whom died in the operating room because of failure to control the hemorrhage. Five
patients received all of their blood transfusions through the standard filter, and five received transfusions through the fine screen filter. All lung biopsy specimens were examined by light microscopy and electronmicroscopy when possible. Tissue for light microscopy was fixed in 10 percent formaldehyde solution; specimens for electronmicroscopy were preserved in 2.4 percent gluteraldehyde. Patients who died during the course of the study likewise had either open lung biopsy or needle biopsy shortly before death.

Criteria for the RDS are shown in Table 4. Chest x-ray film changes were similar to those described by others; that is, "white" fluffy infiltrates were noted bilaterally. These chest x-ray film changes usually occurred 24 to 48 hours following injury. In both groups, prolonged ventilatory assistance was necessary when the previously described criteria for extubation were not present. The presence of hypoxemia to the degree listed in any one blood gas analysis was considered significant.

Pathologic Findings

Previous documentation of microemboli in the pulmonary precapillary arterioles was shown in our earlier study. Particulate matter emboli, however, were not found in any of the added patients who received blood through the 40-µ fine screen filter. The overall lung architecture appeared to be better preserved in the patients receiving blood through the fine screen filter, in that fewer free alveolar macrophages and less intraalveolar hemorrhage were noted. Fibrin deposits, cell membranes and platelet aggregates were demonstrated in the pulmonary precapillary arterioles of open lung biopsy specimens following use of unfiltered blood both in the acute situation during massive blood transfusion (Fig 1, 2) and when death occurred or repeated operation was performed in the last period after operation (Fig 3). Unfortunately, needle biopsy specimens did not disclose the large amount of lung architecture necessary for adequate sampling of the pulmonary arterioles. Electronmicroscopy of these sections demonstrated the classic changes of respiratory distress syndrome in the patients who died with acute pulmonary insufficiency. Light microscopy also demonstrated these changes in the control group (Fig 4).

Results

The previous report detailed the RDS in the control group. With the added patient in this study, seven patients had severe hypoxemia occurring immediately after operation and MBT, according to the previously described criteria (Table 5). One patient with severe hypoxemia died with both bleeding diathesis and multiple system failure within 12 hours following operation. Three other patients, with abdominal injuries only, died of intractable hypoxemia on the 4th, 5th and 24th days after operation. Pulmonary insufficiency contributed to death in the remaining two patients. Thus, marked pulmonary insufficiency with the full picture of RDS occurred in 6 of 17 patients receiving massive blood

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Figure 1. Photomicrograph of lung biopsy showing a pulmonary arteriole "free floating" fibrin embolus. Note intra-alveolar hemorrhage and numerous free alveolar macrophages in alveolar spaces of surrounding lung. Specimen is from open lung biopsy during massive blood transfusion of 12 units of blood during operation to control hemorrhage.

Figure 2. Photomicrograph of lung showing occlusion of precapillary vessel with platelet aggregates, cell membranes and debris. Tissue section is from the specimen as in Figure 1.

Figure 3. Photomicrograph of "shock lung" showing small muscular pulmonary artery. Note that lumen is partially filled by embolus composed of fibrin, platelets and fragments of cellular debris. This patient received 12 units of blood following abdominal injury and died on day after operation of intractable hypoxemia. (hematoxylin and eosin stain x 315)
transfusion through the standard blood filter, excluding the patient with severe hypoxemia who died within 12 hours of operation. Another two patients had moderate to slight hypoxemia only. Chest injury was present in 3 of the 17 patients with severe RDS (Table 6).

In the patients who received all blood transfusions through the 40-μ filter, the three patients who had some degree of pulmonary insufficiency were previously described. Two patient died within 27 hours. The other had severe flail chest, with pulmonary contusion and lung injury. The third patient had chronic emphysema and did not have the x-ray film changes of RDS. Of the 14 additional patients in the extended study who received all fine screen-filtered blood, only one patient had moderate hypoxemia, and none had the clinical picture of RDS. He was a 63-year-old man who had congestive heart failure and other difficulties following flail chest and blunt chest trauma. He died with pulmonary insufficiency and severe bronchopneumonia on the 38th day after operation. Of the remaining patients with

Table 6—Comparison of Severe RDS with or without Chest Injury

<table>
<thead>
<tr>
<th></th>
<th>Group Control</th>
<th>with Filter</th>
</tr>
</thead>
<tbody>
<tr>
<td>With chest injury</td>
<td>3/17</td>
<td>2**/27</td>
</tr>
<tr>
<td>No chest injury</td>
<td>4*/17</td>
<td>0/27</td>
</tr>
<tr>
<td>Total</td>
<td>7/17</td>
<td>2/27</td>
</tr>
</tbody>
</table>

*Three patients died of intractable hypoxemia.  **Both patients had flail chest and multiple trauma.

filter, five had evidence of slight hypoxemia, i.e., at least one PaO₂ value was below 100 mm/Hg, while maintaining ventilation on the equivalent of 40 percent inspired oxygen content. An additional patient had moderate hypoxemia (PaO₂ below 70 mm/Hg). Other than the previously mentioned patient who died in the added group and the three previously described patients in the first report, none of the 23 remaining patients required prolonged ventilatory assistance beyond 12-24 hours or a tracheostomy for respiratory support. Chest x-ray film changes indicative of RDS did not occur in any of the remaining patients, and they survived despite severe injuries and the administration of massive amounts of blood.

**COMMENTS**

Since our first report of the prevention of post-traumatic pulmonary insufficiency by fine screen filter, five had evidence of slight hypoxemia, i.e., at least one PaO₂ value was below 100 mm/Hg, while maintaining ventilation on the equivalent of 40 percent inspired oxygen content. An additional patient had moderate hypoxemia (PaO₂ below 70 mm/Hg). Other than the previously mentioned patient who died in the added group and the three previously described patients in the first report, none of the 23 remaining patients required prolonged ventilatory assistance beyond 12-24 hours or a tracheostomy for respiratory support. Chest x-ray film changes indicative of RDS did not occur in any of the remaining patients, and they survived despite severe injuries and the administration of massive amounts of blood.

**Table 5—Respiratory Distress Syndrome in the Control Group and those with Filter**

<table>
<thead>
<tr>
<th></th>
<th>Group Control</th>
<th>with Filter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest x-ray film findings abnormal</td>
<td>8/17</td>
<td>2/27</td>
</tr>
<tr>
<td>Ventilatory assist † 4 days</td>
<td>6/15*</td>
<td>2/26*</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>8/15*</td>
<td>3/26*</td>
</tr>
<tr>
<td>Severe hypoxemia</td>
<td>7/17</td>
<td>2/27</td>
</tr>
<tr>
<td>Died from pulmonary failure</td>
<td>3/17</td>
<td>0/27</td>
</tr>
</tbody>
</table>

*Two control and one patient with filter died before 4 days after operation.

**POST TRAUMATIC PULMONARY INSUFFICIENCY**

Figure 5. Mechanism responsible for production of respiratory distress syndrome or posttraumatic pulmonary insufficiency following massive blood transfusion of stored blood is shown. Standard filters 170 μ allows particulate matter to plug precapillary arterioles causing clinical picture similar to multiple small pulmonary emboli.

**PROTECTION OF PULMONARY MICROVASCULATURE**
tation, we have additional support for the argument for fine screen filtration in massive blood transfusion. This report consists of a series of the most critically ill patients treated in civilian practice. The incidence of pulmonary insufficiency in the control group is not surprising, since this correlates well with the experience of others.1,3,5,8 The second part of this report was not a randomized study, although most injuries were paired earlier in the experience. After the original results, the danger of massive blood transfusion without the fine screen filter was considered to be great enough to discontinue the control group.

This potential mechanism of post traumatic pulmonary insufficiency following massive blood transfusion accounts for only one factor in the etiology of the respiratory distress syndrome (Fig 5). Intravascular coagulation, emboli from sources other than banked blood, fat emboli and foreign material emboli may cause the pathologic and clinical findings of RDS.9,10-14 Slight hypoxemia occurred in a significant number of patients, and the pulmonary insufficiency following chest injury was also present in both groups. On the other hand, there was a marked difference in the clinical course of the patients receiving blood through the fine screen filter, especially as noted in the past year.

The presence of particulate matter in only the pulmonary precapillary arterioles would seem to indicate that the source was of a mechanical nature rather than widespread intravascular coagulation, which usually occurs at the capillary level. The type of debris seen in the precapillary arterioles was similar to that obtained on the filter surfaces. In some tissue sections, the materials were not lodged firmly in the precapillary arterioles, but appeared to be free floating (Fig 1). At present, this type of precapillary arteriole embolus has not been demonstrated in the patients receiving blood through the fine screen filter during the acute episodes of MBT or in the period at the time of the patient's death after operation. Nevertheless, more clinical studies should be directed at least toward the pathologic changes found in open lung biopsy specimens in the patient with trauma at the time of operation for repair of chest injuries.

The safety of the use of the fine screen filter on the formed elements of blood was demonstrated in our original report.8 There were no differences between the studies after filtration in both groups.

Because of the absence of a significant amount of particulate matter in fresh blood (24 hours old or less), we have not used the fine screen filter in its administration. Methods of blood component therapy such as packed cells with cell washing also eliminate the problem of particulate matter infusion. This technique is possible in the period after opera-

tion when blood transfusions are not deemed urgent.
45 Tackett LR: Brain tissue in pulmonary emboli. Arch Pathol 78:292, 1964

Beginnings of the Chinese and their Civilization

The earliest traces of Homo thus far discovered in China are what geologists call the Pleistocene epoch of the Cenozoic era, which is said to have been about a million years ago. The most striking discovery was that of the Peking Man (Sinanthropus Pekinesis). Southwest of Peking extensive excavations brought to light remains of a number of individuals who dwelt in caves, who had crude stone tools, who may have had articulate speech, and who are said to have possessed mongoloid features. Beginning in 1954, somewhat similar findings were made in several localities in Shansi. Later while the loss was deepening, but before it attained its eventual dimensions, what was undoubtedly Homo sapiens existed. Some of his representatives were cave dwellers, like the Peking man. The cave dwellers hunted and fished, decorated themselves with necklaces, imported luxuries, buried their dead, and probably had clothes.

Latourette, K S: The Chinese—Their History and Culture (eighth printing), New York, Macmillan, 1971