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ACUTE ARTERIAL INJURIES IN THE KOREAN WAR
A STATISTICAL STUDY*

LT. COL. H. HASKELL ZIPERMAN, M. C., U. S. A., F.A.C.S.

The surgery of acute arterial injuries has made tremendous advances since World War II. During the last war it was exceptional for an attempt at vascular repair to be made, as witness the fact that of 2,471 acute wounds of the arteries reported by DeBakey and Simeone, only 135 were repaired. Of these, 40 were repaired by non-suture vein graft, 14 by tube anastomosis and 81 by suture repair. Since 1946 when this statistical survey of World War II arterial injuries was published, great strides have been made in the field of vascular surgery and the attention and interest of large numbers of surgeons has been focused upon it. As a result of these factors, plus the development of rapid casualty evacuation by helicopter to surgical hospitals close to the battle line, more acute arterial injuries have been repaired by suture in 9 months of the Korean War than in this World War II sample series.

This survey was conceived as a means of analyzing the results of arterial injuries now rather than waiting for a year or two after the war is over to collect and analyze all available statistics. This is an important consideration in a continuing war where analysis can result in immediate improvement in technics, skills, and other surgical factors as a means of saving life and limb. It is recognized that there are certain shortcomings in the field collection of data needed for such a survey but, within limitations to be mentioned, this has proved to be a surprisingly accurate analysis of results.

Because of the rapid turn-over of medical personnel in this combat zone, the time limit for this study was set as January 1, 1952 to September 30, 1952, thereby having available for interview those doctors who in most instances had done the major portion of this arterial surgery. All cases were taken from operating room records and were then traced through the evacuation channels to their destination in Japan. It is realized that one shortcoming of this method is that an occasional patient might have developed further complications after leaving Japan for the Zone of the Interior.

It is further realized that the ultimate method for determining the success of arterial repair is by arteriography with radiopaque substances. Since all of these patients had already been evacuated from the combat zone at the time this study was undertaken (November, 1952), and since there is no practical need for such refined technics in a combat zone, this was not attempted. Such a survey has been conducted at Walter Reed Army Medical Center on a small number of these casualties, and is being reported separately by Major Edward J. Jahneke, Jr., USAF (MC).

As may be seen in Figure 1, the incidence of arterial wounds among American battle casualties of World War II was 0.96 per cent. The incidence of arterial injuries among wounded admitted to U. S. Army hospitals during the first nine months of
1952 was 2.4 per cent. (This figure includes all U. N. wounded admitted to U. S. Army hospitals.) It is felt that the latter figure is a more accurate reflection of the actual incidence of arterial wounds among the wounded admitted to hospitals, because all medical officers in this theater are acutely conscious of vascular injuries and invariably record them in their operative notes, even though other notes may not be as complete. That the use of the armored vest has had some influence on this increased incidence is probably true, but the extent of that influence is problematical, since this armor was available in limited quantities, as a research project only, from February to July, 1952.

In August, 1952, these vests became available in large enough quantities so that most combat personnel in the line had them for use. According to the report of the team conducting the body armor research, the use of the armored vest was associated with an increase in the incidence of wounds of the upper extremities from 38 per cent to 43 per cent of all wounds studied, and of the lower extremities from 44 per cent to 53 per cent of all wounds studied. Obviously this is a proportional and not an absolute increase. Associated with this increase in extremity wounds, it is logical to assume an increase in vascular injuries of the extremities. No explanation can be offered for the exact correspondence of this figure of 2.4 per cent with that of the Russo-Japanese War.

Since the most complete statistical report of the results of acute arterial injuries presented in the American literature was reported in 1946 by DeBakey and Simeone, a deliberate attempt has been made in this analysis to duplicate their method of reporting. This duplication will serve to give a fair and accurate comparison of the DeBakey and Simeone World War II sample study with Korean War results. In both surveys, only acute arterial trauma has been studied. There have been approximately 10 per cent as many arterial wounds in the nine month period of this war as is

---

**INCIDENCE OF ARTERIAL WOUNDS AMONG BATTLE CASUALTIES**

![Incidence Chart]

---

**Fig. 1**
reported in the World War II sample study. (It must be remembered that whereas the 234 arterial wounds reported in the Korean series represents the total nine months experience with U. N. wounded admitted to U. S. Army hospitals, the DeBakey and Simeone series represents a sample study of 2,471 arterial wounds among 163,980 U. S. Army battle casualties of World War II. Since the total U. S. Army wounded for World War II is 598,528 [a tentative fig-

ACUTE ARTERIAL INJURIES IN THE KOREAN WAR

LOCATION OF WAR WOUNDS OF ARTERIES

![Diagram showing location of war wounds of arteries]

A study of the incidence of these arterial injuries in the Korean War reveals that 218 of the 234 injuries, or 93.2 per cent, involved arteries of the extremities. Of these, 162 involved the "critical arteries" of the extremities (brachial, axillary, femoral, popliteal). This represents 69.2 per cent of the total arterial wounds in this series. An analysis of the relative frequency of arterial wounds in combat casualties (Fig. 2) reveals that the brachial, tibial, femoral and popliteal arteries are involved more frequently than any others. These arteries were involved in 84.2 per cent of the extremity arterial wounds in the Korean War as compared with 86.5 per cent of the extremity arterial wounds in World War II. As may be noted, the incidence of involvement of each of the vessels is approximately the same as that for World War II, with the exception of popliteal arteries. Since this total experience with vascular injuries is only 10 per cent of that in this World War II sample study, it is entirely possible that a larger group would yield a wound distribution exactly like that of the last war.

In an attempt to compare more closely the outcome of arterial injuries in the two wars, the same breakdown of wounds and results as used by DeBakey and Simeone was done. Table I shows these side-by-side, with no attempt made to compare
results by method of treatment. The most outstanding feature to be noted is the total percent of extremities lost—17.9 per cent in this series and 40.3 per cent in the earlier one. It is recognized that this difference could easily have been caused by a high percentage of injury to noncritical arteries in the former, as compared with the latter. That this is not true and that the two series do compare may be noted by comparison of per cent involvement of arteries such as the axillary, brachial, popliteal and femoral. (A small difference in the method of reporting of two items in this table should be noted. In the World War II sample study, the figures after brachial and femoral represent the total experience with these vessels and include injuries both above and below the profunda. In the portion of the table devoted to the Korean War, the figures after brachial and femoral represent those wounds of these vessels in which the portion of the artery injured was not specified. The total experience with these vessels is the sum of the unspecified group and the group above and below the profunda. This was done in order to make the totals coincide with the itemized figures.) As may be seen, the axillary artery injuries represented 3.0 per cent of the World War II series, and 5.68 per cent of the Korean War series. The brachial injuries in the two wars are respectively 24.3 per cent and 28.39 per cent of each series. It should be noted that the only significant difference in incidence in the two series is in wounds of the popliteal artery. In comparing the percentage of failures, note especially the differences listed for the critical arteries (axillary, brachial, femoral and popliteal). It may be noted that in each instance, a significant improvement in result is shown in the Korean series as compared with the DeBakey and Simeone World War II series.

Of the total number of arterial wounds, 132 (56.4 per cent) were repaired (Table II). One hundred and two arteries were ligated. Of these 102 arteries, only 42 were critical vessels whose ligation might lead to either gangrene of an extremity or death. Because of the increased consciousness on the part of all Eighth Army Surgeons of the importance of attempting to repair all injuries of critical vessels, it may be stated unequivocally that failure to repair a critical vessel was usually due to associated injuries which would have led to death if the vessel, rather than the other injury, had been operated on. In other words, surgical judgment and the decision to save a life rather than a limb was involved. In an unknown number of cases, both the associated injury and the arterial repair were accomplished in the same patient.

Of the total of 132 arterial repairs, 26 (19.7 per cent) resulted in gangrene of the extremity with necessary amputation. Since we were interested in the total number of arteries which remain patent after repair, indicating complete success of the procedure, a search was made through all available reports for deaths, postoperative hemorrhage, and postoperative sympathetic blocks which occurred in these 132 casualties. Where death occurred and the extremity was viable and dissection showed no evidence of thrombosis at the repair site, the repair was counted as successful. It was felt that delayed postoperative hemorrhage indicated failure, since a procedure designed to repair the leak frequently led to thrombosis. Since in this Combat Zone, postoperative sympathetic block is not routine, but was reserved instead for extremities of questionable viability, it was felt that employment of this procedure indicated an admission on the part of the surgeon that some impairment of vascular
**Table I. American World War II.**

<table>
<thead>
<tr>
<th>Artery</th>
<th>Total No.</th>
<th>% Total</th>
<th>No. Cases</th>
<th>% Per Cent</th>
<th>Total No.</th>
<th>% Total</th>
<th>No. Cases</th>
<th>% Per Cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>3</td>
<td>0.12</td>
<td>2</td>
<td>66.6</td>
<td>2</td>
<td>0.87</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Innominate carotid</td>
<td>10</td>
<td>0.04</td>
<td>3</td>
<td>30.0</td>
<td>1</td>
<td>0.44</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>External carotid</td>
<td>3</td>
<td>0.12</td>
<td>0</td>
<td>0.00</td>
<td>2</td>
<td>0.87</td>
<td>1</td>
<td>0.00</td>
</tr>
<tr>
<td>Internal carotid</td>
<td>2</td>
<td>0.10</td>
<td>2</td>
<td>100.0</td>
<td>2</td>
<td>0.87</td>
<td>1</td>
<td>25.0</td>
</tr>
<tr>
<td>Common carotid</td>
<td>2</td>
<td>0.10</td>
<td>2</td>
<td>100.0</td>
<td>2</td>
<td>0.87</td>
<td>1</td>
<td>25.0</td>
</tr>
<tr>
<td>Vertebral carotid</td>
<td>2</td>
<td>0.10</td>
<td>2</td>
<td>100.0</td>
<td>2</td>
<td>0.87</td>
<td>1</td>
<td>25.0</td>
</tr>
<tr>
<td>Subclavian</td>
<td>21</td>
<td>0.85</td>
<td>6</td>
<td>28.6</td>
<td>2</td>
<td>0.87</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Axillary</td>
<td>21</td>
<td>0.85</td>
<td>6</td>
<td>28.6</td>
<td>2</td>
<td>0.87</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Brachial</td>
<td>199</td>
<td>7.38</td>
<td>119</td>
<td>59.9</td>
<td>13</td>
<td>5.68</td>
<td>1</td>
<td>7.7</td>
</tr>
<tr>
<td>Above profunda</td>
<td>29</td>
<td>1.13</td>
<td>26</td>
<td>89.7</td>
<td>4</td>
<td>1.75</td>
<td>2</td>
<td>9.5</td>
</tr>
<tr>
<td>Below profunda</td>
<td>29</td>
<td>1.13</td>
<td>26</td>
<td>89.7</td>
<td>4</td>
<td>1.75</td>
<td>2</td>
<td>9.5</td>
</tr>
<tr>
<td>Radial</td>
<td>99</td>
<td>3.75</td>
<td>4</td>
<td>41.4</td>
<td>4</td>
<td>1.75</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Ulnar</td>
<td>69</td>
<td>2.65</td>
<td>1</td>
<td>1.5</td>
<td>6</td>
<td>2.62</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Radial and ulnar</td>
<td>28</td>
<td>1.09</td>
<td>11</td>
<td>39.3</td>
<td>2</td>
<td>0.87</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Common iliac</td>
<td>13</td>
<td>0.50</td>
<td>7</td>
<td>53.8</td>
<td>3</td>
<td>1.31</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>External iliac</td>
<td>30</td>
<td>1.20</td>
<td>14</td>
<td>46.7</td>
<td>1</td>
<td>0.44</td>
<td>0</td>
<td>9.0</td>
</tr>
<tr>
<td>Internal iliac</td>
<td>1</td>
<td>0.04</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Femoral</td>
<td>517</td>
<td>20.83</td>
<td>275</td>
<td>53.2</td>
<td>20</td>
<td>8.73</td>
<td>7</td>
<td>35.0</td>
</tr>
<tr>
<td>Above profunda</td>
<td>106</td>
<td>4.22</td>
<td>86</td>
<td>81.1</td>
<td>7</td>
<td>3.06</td>
<td>3</td>
<td>18.2</td>
</tr>
<tr>
<td>Below profunda</td>
<td>177</td>
<td>7.18</td>
<td>97</td>
<td>54.8</td>
<td>24</td>
<td>10.48</td>
<td>6</td>
<td>25.0</td>
</tr>
<tr>
<td>Profunda</td>
<td>27</td>
<td>1.07</td>
<td>0</td>
<td>0.00</td>
<td>5</td>
<td>2.18</td>
<td>1</td>
<td>40.0</td>
</tr>
<tr>
<td>Popliteal</td>
<td>502</td>
<td>20.10</td>
<td>154</td>
<td>72.2</td>
<td>29</td>
<td>12.66</td>
<td>11</td>
<td>37.9</td>
</tr>
<tr>
<td>Anterior tibial</td>
<td>129</td>
<td>5.23</td>
<td>11</td>
<td>8.8</td>
<td>9</td>
<td>3.93</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>265</td>
<td>10.76</td>
<td>36</td>
<td>13.6</td>
<td>22</td>
<td>9.61</td>
<td>4</td>
<td>18.2</td>
</tr>
<tr>
<td>Ant. and Post. tibial</td>
<td>91</td>
<td>3.75</td>
<td>63</td>
<td>69.2</td>
<td>4*</td>
<td>1.75</td>
<td>2</td>
<td>50.0</td>
</tr>
<tr>
<td>Peroneal</td>
<td>7</td>
<td>0.28</td>
<td>1</td>
<td>14.3</td>
<td>1</td>
<td>0.44</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Ant. tibial and peroneal</td>
<td>5</td>
<td>0.20</td>
<td>2</td>
<td>40.0</td>
<td>1</td>
<td>0.44</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Post. tibial and peroneal</td>
<td>1</td>
<td>0.05</td>
<td>1</td>
<td>100.0</td>
<td>1</td>
<td>0.44</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Both tibials and peroneal</td>
<td>1</td>
<td>0.05</td>
<td>1</td>
<td>100.0</td>
<td>1</td>
<td>0.44</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Volar arch</td>
<td>1</td>
<td>0.04</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
</tr>
</tbody>
</table>

*There were actually 234 separate arterial wounds but 5 cases had involvement either of both tibials or of the tibial and the peroneal and are simultaneously rather than separately recorded.

Of great interest is the method by which arterial repair was accomplished and the percent failure of each. Table III shows that 71, or 53.8 per cent, were repaired by end-to-end anastomosis, 43, or 32.6 per cent, by arteriotomy of a laceration through only part of the vessel wall, and 18, or 13.6 per cent, by interposition of a vein graft. All vascular suture was by evertting, either continuous or interrupted 5-0 black arterial silk. Vein grafts in all cases were taken from adjacent veins whose internal diameter approximated that of the injured vessel. In no instance was the concomitant vein utilized. As is to be expected, the largest percent of failures occurred in the group which required vein grafting. Since the insertion of vein grafts is technically the most difficult of the three procedures utilized, and since in most instances the most severe extremity wounds were associated with those cases requiring a graft, this is to
Table II.

<table>
<thead>
<tr>
<th>Description</th>
<th>Cases</th>
<th>% Cases</th>
<th>% Amputations</th>
<th>% Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. arterial injuries</td>
<td>234</td>
<td>100.0</td>
<td>31.0</td>
<td>19.7</td>
</tr>
<tr>
<td>Total no. arterial injuries ligated</td>
<td>132</td>
<td>100.0</td>
<td>26.0</td>
<td>23.5</td>
</tr>
<tr>
<td>Total no. arterial injuries repaired</td>
<td>102</td>
<td>100.0</td>
<td>26.0</td>
<td>23.5</td>
</tr>
</tbody>
</table>

Amputations after repair: 2%
Failures after repair: 19.7%

Table III. Types of Repair.

<table>
<thead>
<tr>
<th>Type of Repair</th>
<th>Cases</th>
<th>% Cases</th>
<th>Amputations</th>
<th>% Amputations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arteriorrhaphy</td>
<td>43</td>
<td>32.6</td>
<td>6</td>
<td>(18.6) 14.0</td>
</tr>
<tr>
<td>End to end anastomosis</td>
<td>71</td>
<td>53.8</td>
<td>14</td>
<td>(23.9) 19.7</td>
</tr>
<tr>
<td>Vein graft</td>
<td>18</td>
<td>13.6</td>
<td>6</td>
<td>(33.3) 33.3</td>
</tr>
<tr>
<td>Total</td>
<td>132</td>
<td>100.0</td>
<td>26</td>
<td>(23.5) 19.7</td>
</tr>
</tbody>
</table>

Figures in parenthesis ( ) represent failures as evidenced by death, hemorrhage, sympathectomy, or amputation.

be expected. As is further to be expected, the best results were obtained in the arteriorrhaphies, since these represented the most minor of the arterial wounds and technically were the easiest to repair. The last column in Table III shows the percent of amputations in each type of repair, while the figures in parenthesis represent the total failure rate of each.

The best means for critically analyzing the results of repair as compared with ligation is by eliminating those injured vessels whose sacrifice would not normally result either in death or amputation. Toward this end, Tables IV and V analyze the results of repair and ligation in these major vessels. As may be noted, a total of 169 major artery injuries (largely consisting of the axillary, brachial, femoral, and popliteal arteries, but also including the iliac, carotid and aorta) are found in this series, of which 127, or 75.1 per cent, were repaired, and 42, or 24.9 per cent, were ligated. Curiously enough, 20.5 per cent failures are noted in the repaired vessels as compared with 19.0 per cent failures after ligation. It must be noted, however, that the two series show discrepancies for several reasons. Among these are:

1. The total number of cases in the two groups is completely dissimilar, so that comparison is difficult.
2. Since either ligation or repair of brachial arteries result in a small percent of amputations, the ligations series is favorably weighted by the larger number of brachial arteries in that group. Fifty-four and eight-tenths (54.8 per cent) per cent of the ligations group is composed of brachial arteries, while only 33.1 per cent of the repair group consists of brachial arteries.
3. Again, only six of 29 popliteal arteries were ligated, whereas 23 of 29 popliteals were repaired. Although the amputation rate is lower after repair than ligation, notice there were eight amputations after repair, and three after ligation.
4. In this series, the results have been poorest in those repairs of the femoral artery above the bifurcation of the profunda and yet, as can be noted, no femorals above the profunda were ligated, because all had been repaired.

Note that in comparing the percent of amputations in the two groups that the results of repair are better than those for ligation, except in brachial arteries where the location of the injury is unspecified, in femoral arteries above the profunda, and in axillary arteries. Obviously, in the femoral artery above the profunda group (Table V) no valid comparison exists, since none were ligated and therefore, the percentage of amputations cannot be calculated.

The ideal in traumatic vascular surgery is the re-establishment of circulation to the part as quickly as possible. Unfortunately, under combat conditions, there is an unavoidable time lag between wounding and operation dependent on the tactical situation and other conditions beyond medical control. In addition to these military factors causing a time lag, many of these casualties have suffered other wounds such as penetrating wounds of the abdomen or
ACUTE ARTERIAL INJURIES IN THE KOREAN WAR

During the period for traumatic vascular surgery is 0-10 hours after wounding, actually many other factors influence these results, and some of these may be as important within certain limits as the time factor itself. Among these are the following:

1. There is a definite correlation between lack of vascular surgical experience of the operating surgeon and amputation rate. This is so noticeable that a continuing course in experimental vascular surgery under the direction of an experienced surgeon was conducted in one of the surgical hospitals.

2. Exposure of the casualty to inclement weather, especially cold, prior to being evacuated from the battlefield, likewise affects the amputation rate.

3. As was pointed out in Table III, the type of arterial repair necessary to re-establish continuity of the vessel affects the amputation rate.

Because it was felt that associated orthopedic injury might have some relation to outcome, the January, 1952, to September, 1952, series was broken down into two groups: those with, and those without, associated fracture of the long bones of the involved extremities. Of a total of 33 vascular wounds which were ligated, nine were associated with fractures of adjacent long bones, and 24 were not. Of the nine

<table>
<thead>
<tr>
<th>Table IV. Results of Repair—Critical Arteries.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No.</td>
</tr>
<tr>
<td>Brachial artery</td>
</tr>
<tr>
<td>Above profunda</td>
</tr>
<tr>
<td>Below profunda</td>
</tr>
<tr>
<td>Femoral artery</td>
</tr>
<tr>
<td>Above profunda</td>
</tr>
<tr>
<td>Below profunda</td>
</tr>
<tr>
<td>Axillary artery</td>
</tr>
<tr>
<td>Popliteal artery</td>
</tr>
<tr>
<td>Common iliac</td>
</tr>
<tr>
<td>Common carotid</td>
</tr>
<tr>
<td>Internal carotid</td>
</tr>
<tr>
<td>Aorta</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

*Represents death of casualty.
†One arteriorrhaphy failed after secondary closure of wound and probably due to infection.
TABLE V. Results of Ligation—Critical Arteries.

<table>
<thead>
<tr>
<th>Artery</th>
<th>Total No.</th>
<th>No. Ligated</th>
<th>% Ligated</th>
<th>No. Amputations</th>
<th>% Amputations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial artery</td>
<td>40</td>
<td>10</td>
<td>25.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Above profunda</td>
<td>4</td>
<td>1</td>
<td>25.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Below profunda</td>
<td>21</td>
<td>4</td>
<td>19.0</td>
<td>2</td>
<td>16.7</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>20</td>
<td>4</td>
<td>20.0</td>
<td>2</td>
<td>10.0</td>
</tr>
<tr>
<td>Above profunda</td>
<td>7</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Below profunda</td>
<td>24</td>
<td>4</td>
<td>16.7</td>
<td>1</td>
<td>25.0</td>
</tr>
<tr>
<td>Axillary artery</td>
<td>13</td>
<td>4</td>
<td>30.8</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Popliteal artery</td>
<td>29</td>
<td>6</td>
<td>20.7</td>
<td>3</td>
<td>50.0</td>
</tr>
<tr>
<td>Common iliac</td>
<td>3</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Common carotid</td>
<td>4</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Internal carotid</td>
<td>2</td>
<td>1</td>
<td>50.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Aorta</td>
<td>2</td>
<td>0</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Total</td>
<td>169</td>
<td>42</td>
<td>24.9</td>
<td>8</td>
<td>19.0</td>
</tr>
</tbody>
</table>

Extremities with fractures and vascular injuries, three, or 33.3 per cent, were amputated. Of the 24 extremities with vascular injuries which had no associated fractures, three, or 12.5 per cent, were amputated. Seventy-one (71) vascular wounds were repaired, of which 26 were associated with fractures of the adjacent long bone, and 45 had no associated fracture. The amputation rate for those with fractures was seven, or 26.9 per cent, and the rate for those without fractures was 11, or 24.4 per cent. The results are obviously inconclusive, and definite conclusions will have to await wider experience.

The problem of ligation of the concomitant vein has come to the fore once again in this war as it did in World Wars I and II. It assumes a new and different importance this time, however, since more of the critical arteries are now being repaired rather than ligated. All observers in this Theater agree that where the concomitant vein of an extremity is ligated because of injury to both artery and vein at the time of wounding, there is a slower return of that extremity to normal after arterial repair. This is true even with elevation of the extremity and the application of an elastic bandage. That this is due to interference with venous return and edema is unquestioned. On at least two occasions within the author’s experience, this has resulted in gangrene and amputation of an extremity, which on dissection showed a patent anastomosis. It has been felt necessary on this basis to caution all surgeons to avoid destruction of venous channels in dissection and to repair those concomitant veins in which only a small laceration exists in the lateral wall. Because of the fear that thrombosis with pulmonary embolization might occur, complete transections of the concomitant vein have not been repaired. Further study of this interesting phase of vascular repair is to be continued.

CONCLUSIONS

1. Arterial repair by the suture method has been used successfully in the repair of arterial wounds among combat casualties in the Korean War. By this method, the amputation rate has been reduced from 40.3 per cent of World War II to 17.9 per cent.

2. Statistics show that there is an increased incidence of arterial wounds among combat casualties and that this type of wound is of increasing importance among casualties of the Korean War.

3. The effect on the amputation rate of orthopedic injury associated with arterial wounds is questionable.

BIBLIOGRAPHY

Carcinoma of the Breast and Pregnancy

Analysis of 920 Cases Collected from the Literature and 22 New Cases*

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There is a general belief among surgeons today that pregnancy has an unfavorable influence on carcinoma of the breast. This belief is so strong that some surgeons call the combination a hopeless one. A study of 22 patients with coincident pregnancy and carcinoma of the breast from Bellevue, University, and Roosevelt Hospitals of New York creates a more optimistic attitude. A review of 132 pertinent published articles on this subject in the world literature was made in which 920 case reports were collected. These reports also strengthened a more optimistic view.

Coincidental occurrence of carcinoma of the breast and pregnancy is uncommon. In a report of 25,159 cases of carcinoma of the breast by 22 authors, 737 (2.9 per cent) were pregnant or lactating at some time during the course of disease (Table I). Three large obstetrical services reported that only 13 patients with new or previously treated carcinoma of the breast were found in 123,884 pregnancies observed (Table II).

Since so few patients were available for study, either in our group or in the literature, all reported cases were analyzed. Again, because of the variability of the reports, this series was studied from only three points of view:

1. Follow-up of patients in whom carcinoma developed during pregnancy or lactation.

2. Follow-up of patients in whom pregnancy followed treatment of a breast carcinoma.

3. Effect of abortion on the survival rate in patients with carcinoma treated before or during pregnancy.

Carcinoma Developing During Pregnancy or Lactation

Ten such patients were from the presently reported series and 724 were collected from the literature. Three of the 10 in this series survived five years, and two ten years. From the entire group (734 patients), 126 (17.1 per cent) survived five years, and 84 (11.4 per cent) survived ten years (Table III). Women pregnant, lactating, or within one year after pregnancy are included in this, as in other series.

A superficial examination of these figures would not indicate a very bad prognosis. For example, two patients in this series (Nos. 2 and 8) can be considered cured; the first had a duct cell carcinoma of the breast without axillary nodes, removed while four and one-half months pregnant, 11 years ago; the second had an adenofibrosarcoma of the breast removed by simple mastectomy 11 years ago while three months pregnant. Both patients are now without evidence of recurrence. Seventeen of the 724 patients in the literature can be considered cured (Table IV). Insufficient information was available on the remaining 65 ten year survivors to state whether or not they were cured.

* Submitted for publication June, 1953.
As a result of this study, it seems obvious that improved results in this group of patients will follow earlier treatment. Tangible evidences of this trend are the improving ten-year survival rates in decades: none prior to 1920; 3.2 per cent 1921 to 1940; and 22.4 per cent 1941 to 1950 (Table III). Furthermore, these patients are usually seen at a more advanced stage than the non-pregnant or lactating; for example, the large number with inflammatory carcinoma, 52 of the 734 patients reported. A number of patients, including one in this series (Case 1), had incision of the inflamed area for abscess. Westburg analyzed a large series of patients from the point of view of time of reporting for treatment. He found that the pregnant or nursing woman reported a mass or other symptom of breast carcinoma two months later on the average than in a parallel series of non-pregnant women. He stated that these women often thought the mass or symptoms were part of the normal sequence of events during pregnancy or lactation. The result of this delay, in his series, was a high incidence of patients with metastases.

PREGNANCY FOLLOWING TREATMENT OF BREAST CARCINOMA

Twelve patients in the authors' series and 196 in the collected group were analyzed. Of those presently reported who survived five years, Cases 11, 12, 13, 14, 16, and 17 lived 31, 11, 9, 16, 22, and 13 years respectively without evidence of recurrence, while Cases 15 and 18 died after 16 and 17 years from distant metastases. The total cases number 208, of whom 102 (49.0 per cent) survived five years, and 55 (26.8 per cent) survived ten years (Table V). A number of cures were found in both series. The results appeared to be comparable to a series where pregnancy and nursing were not a factor.

EFFECT OF ABORTION ON THE COURSE OF CARCINOMA OF THE BREAST IN THE PREGNANT WOMAN

The statements of Adair in regard to the favorable effect of abortion on the course of carcinoma of the breast treated prior to pregnancy or discovered during pregnancy could not be confirmed in this analysis. Seven of this series and 61 in the collected series had spontaneous or induced abortions which might have some bearing on the course of disease, but, of 13 who aborted after treatment of breast carcinoma, four survived five years and one for ten years. Of 55 treated during pregnancy who aborted, eight survived five years and two for ten years. There seemed to be no definite beneficial effect determined from this event.

CASE REPORTS

Patients Treated During Pregnancy or Lactation

Case 1. Mrs. E. W. (135), Roosevelt Hospital Z24157, 28 years old, had a radical mastectomy performed November 8, 1950, for a medullary carcinoma of the breast, Grade IV, with axillary metastases. She was 7 months pregnant. One week prior to this operation an incision and drainage for abscess was performed elsewhere. Two months following mastectomy she had a normal delivery of a boy. Three months post-mastectomy she died with diffuse metastases (January 18, 1951).

Case 2. Mrs. M. K. (133), Roosevelt Hospital 13402, 33 years old, had a radical mastectomy performed by Dr. David Weeks, on February 26, 1942, for duct cell carcinoma of the breast without axillary nodes, while she was four and one-half months pregnant. This patient delivered normally, and showed no evidence of disease on February 27, 1953.

Case 3. Mrs. E. B. (135), Roosevelt Hospital B32589 and B344339, 39 years of age, noted a mass in her breast at the beginning of pregnancy. Spontaneous abortion occurred at six weeks. The mass enlarged rapidly and was radically excised three months later on October 16, 1933. At this time one-half of the breast had an orange peel appearance; there were palpable lymph nodes in the axilla, and a pathological
diagnosis of adenocarcinoma of the breast with metastases to the axilla was made. She received three courses of radiation to her chest following operation. On January 4, 1935, she had skin recurrence, metastases to both axillae and mediastinum.

Case 4. Mrs. E. W., University Hospital K36443, 31 years of age, aborted at the beginning of 1948. On March 5, 1948, she had a radical mastectomy performed at another hospital for scirrhous carcinoma of the breast without axillary metastases. Two years later she noted dizziness, headache, diplopia and tinnitus, with anisocoria, papilledema and hemorrhages of the right eye. A craniotomy was performed at the University Hospital on March 11, 1950, at which time a biopsy of the right cerebral cortex demonstrated carcinoma. The patient died in August, 1950, at home.

Case 5. Mrs. F. B., University Hospital J45864, 40 years old, had a spontaneous abortion on January 17, 1940. She had noted masses in both breasts for nearly 2 years. On September 13, 1940, because of a definite mass in the right breast, radical mastectomy was performed for carcinoma of the breast without metastases. There was no evidence of disease in August, 1947, but in April, 1948, word was received that the patient was in another hospital for custodial care, because of spread of the disease.

Case 6. Mrs. U. M., Bellevue Hospital 144334, 37 years old, had a radical mastectomy at another hospital for carcinoma of the breast, in 1936, while pregnant. She delivered her child normally, and was admitted to Bellevue Hospital on September 22, 1939, with local and remote metastases. She was transferred to a custodial hospital for terminal care on October 11, 1939.

Case 7. Mrs. H. McA., Bellevue Hospital 42889-43, 40 years old, had a right radical mastectomy on September 18, 1943, in Bellevue Hospital for carcinoma of the breast with axillary metastases. At that time she was nursing a 6-month-old child. Patient died of diffuse metastases in the summer of 1947.

Case 8. Mrs. C. K. G., Bellevue Hospital 23719-43, 22 years of age, had a grapefruit sized mass removed locally from her breast, then a simple mastectomy performed, while she was 2 and 3 months pregnant in April and May, 1942. The diagnosis was adenofibrosarcoma of the breast, originating in intracanalicular fibroadenoma (as described by Hill and Stout). She had a normal delivery of the child, as well as a second child in 1945. In 1950, another nodule was removed from the upper outer quadrant of the region where the breast had been. There was no evidence of recurrence March 13, 1953.

Case 9. Mrs. C. S., Bellevue Hospital 22334-44, 36 years old, was admitted to another hospital while 7 months pregnant. A radical mastectomy was performed August 20, 1942, for alveolar duct carcinoma with metastases to the axilla. She had a normal delivery 2 months later at the same hospital. She was admitted to the Bellevue Hospital Gynecological Service on May 16, 1944, for a therapeutic abortion of a 10 weeks' pregnancy. The operated side of the chest showed no evidence of disease, but there was a freely movable nodule in the opposite breast. Biopsy of the nodule and abortion was advised and refused. The patient was then lost.

Case 10. Mrs. R. S., Bellevue Hospital 25515-47, 28-year-old nurse, had noticed a nodule in the inner half of her left breast since she was 3 months' pregnant. At 5 months' the nodule became red and the nipple inverted. A radical mastectomy was performed on May 28, 1947, for carcinoma of the breast with axillary metastases. At the time of delivery of twins on July 16, 1947, there was a granulating area 6 x 4 cm. in size over the left chest, matting of superficial nodes extending to the posterior auricular area, stiffness of the neck, swelling of the left arm, and matted nodes in the posterior left axilla. The patient refused custodial care and died at home in August, 1948.

Case 11. Mrs. H. W., (135), Roosevelt Hospital B14753, 33 years old, operated by radical mastectomy March 4, 1922, for carcinoma of the breast without axillary nodes, had 2 babies subsequently. She was last seen, without evidence of recurrence, in January, 1953.

Case 12. Mrs. A. K. (135), Roosevelt Hospital 15920, 24 years old, had a radical mastectomy performed July 29, 1942, for carcinoma of the breast without axillary nodes, had 2 babies subsequently. She was last seen, without evidence of recurrence, in January, 1953.

Case 13. Mrs. M. H. P., (135), Roosevelt Hospital 28737, 37 years old, had a radical mastectomy for carcinoma of the breast without axillary metastases on November 9, 1944. She had a baby girl born February 16, 1946. There was no evidence of disease on February 27, 1953.

Case 14. Mrs. G. P. (135), Roosevelt Hospital B17053, 25 years old, had a radical mastectomy December 22, 1922, for carcinoma of the breast
without axillary metastases. A baby was born in March, 1926. She was last seen February 23, 1938, accompanied by a 12-year-old daughter. At this time she was free of disease.

Case 15. Mrs. B. M. (26), Roosevelt Hospital A32802, 34 years old, had a radical mastectomy May 11, 1932, for carcinoma of the breast without axillary metastases. Two years following operation she had an 8-pound boy, nursed him on the remaining breast. On November 21, 1946, right supraclavicular nodes were noticed. She later developed fluid in the right pleural cavity. She died November 2, 1948, in the Roosevelt Hospital.

Case 16. Mrs. K. P. (19), Roosevelt Hospital B30541, 38 years old, had a radical mastectomy performed November 21, 1931, for carcinoma of the breast without axillary metastases. She aborted spontaneously on April 2, 1934, at 3 months. She was without evidence of disease in January, 1953.

Case 17. Mrs. E. C. (135), Roosevelt Hospital B18588, 40 years old, had a radical mastectomy performed December 3, 1923, for carcinoma of the breast without axillary metastases. One year after operation she had a child. There was no sign of recurrence April 24, 1936.

Case 18. Mrs. M. W., University Hospital J31089, had a right radical mastectomy June 2, 1938, for adenocarcinoma of the breast with axillary metastases. The patient had a child in the early part of 1941. In July, 1943, she had nipple retraction of the opposite breast with a large, underlying mass. A radical mastectomy was performed on this breast August 3, 1943, for carcinoma with many axillary metastases. In September, 1943, her wound was still open. In October, 1943, she was bedridden, with many metastases. She died February 6, 1944.

Case 19. Mrs. N. E., Bellevue Hospital 43794, 26 years old, had a left radical mastectomy at another hospital on August 28, 1936, for inflammatory carcinoma of the breast (adenocarcinoma of the breast, no tumor in axillary nodes). A section for 5 months' pregnancy was done on July 10, 1937, because of fear that the pregnancy might accelerate the growth of this tumor. She was admitted finally to Bellevue Hospital in September, 1937, where she died on October 4, 1937.

Case 21. Mrs. R. Y., Bellevue Hospital 3927-49, 31 years of age, had a radical mastectomy on August 9, 1946, for carcinoma of the breast with secondary lymph node metastases in the axilla. She was readmitted and a therapeutic abortion done on December 23, 1946, because it was felt that pregnancy might accelerate the course of disease. In June, 1947, she had metastases to her skull, lumbar spine, and long bones visible on roentgenogram. She was sent to a custodial hospital where she died on July 15, 1949.

Case 22. Mrs. S. M. D. (41), Roosevelt Hospital J39598, 30 years old, had a radical mastectomy September 6, 1946. On January 23, 1948, a therapeutic abortion was performed because it was felt that the course of disease might be accelerated by the continuation of pregnancy. On April 8, 1948, there was evidence of local recurrence. She died on May 14, 1949, with diffuse metastases.

COMMENT

Coincidental occurrence of carcinoma of the breast and pregnancy or lactation is extremely uncommon. Only 920 patients were found after careful perusal of the world literature on this subject through 1950, and only 22 patients were found in three large hospitals in New York. A partial answer to the problem of this complication of carcinoma of the breast has been given.

Prior to this analysis, only Westburg, Adair, and Harrington have analyzed over 100 patients with this coexistence. The smallness of most series account for much of the difference of opinion. Even so, there has been general agreement that the gross five and ten year survival rates among patients who became pregnant after treatment of a carcinoma of the breast are similar to those among patients without this complication. It is possible that patients with advanced disease of the breast do not become pregnant after treatment of their carcinoma, because of the presence of metastases. Good results and relatively frequent cures may be due to this possibility.
It is probable that pregnancy is not contraindicated in patients with treated carcinoma of the breast without noticeable metastases.

The difference of opinion as to treatment and results has been greatest with regard to patients in whom carcinoma of the breast was discovered during pregnancy or lactation. The results in this group of patients are not as good as among the uncomplicated carcinoma of the breast patients. However, 84 (11.4 per cent) of the 734 collected survived ten years. Furthermore, two of ten patients presently reported could be considered 11 year "cures" and 72 of the 320 patients (22.4 per cent) reported in the decade 1941 to 1950 survived ten years or more. Seventeen of the 82 patients collected from the literature from 1921 to 1950 could be considered "cured" after periods of ten years or more, insufficient information being available in this regard on the remaining patients. On the basis of this information, it is possible that physio-
Among Patients Treated for the Breast During Pregnancy

**TABLE IV. Cures Among Patients Treated for Carcinoma of the Breast During Pregnancy and Lactation.**

<table>
<thead>
<tr>
<th>Author</th>
<th>Type Disease</th>
<th>Years Without Axillary Nodes</th>
<th>Axillary Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1924 Odermatt (88)</td>
<td>Carcinoma</td>
<td>?</td>
<td>14</td>
</tr>
<tr>
<td>1926 Chavannaz (22)</td>
<td>Carcinoma</td>
<td>?</td>
<td>25</td>
</tr>
<tr>
<td>1929 Kilgore (67, 13)</td>
<td>Medullary ca.</td>
<td>no</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Medullary ca.</td>
<td>?</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>Scirrhous ca.</td>
<td>yes</td>
<td>10</td>
</tr>
<tr>
<td>1935 Farati (38)</td>
<td>Carcinoma</td>
<td>yes</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Carcinoma</td>
<td>yes</td>
<td>16</td>
</tr>
<tr>
<td>1939 Bromeis (15)</td>
<td>Carcinoma</td>
<td>yes</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Carcinoma</td>
<td>yes</td>
<td>24</td>
</tr>
<tr>
<td>1945 Ketunnen (65, 66)</td>
<td>Carcinoma</td>
<td>yes</td>
<td>17</td>
</tr>
<tr>
<td>1949 Brooks and Proffitt (17)</td>
<td>Adenocarcinoma</td>
<td>yes</td>
<td>15½</td>
</tr>
<tr>
<td>1949 Tomlinson &amp; Eckert (126)</td>
<td>Adenocarcinoma</td>
<td>yes</td>
<td>14</td>
</tr>
<tr>
<td>1949 Santy (113)</td>
<td>A typical epithelioma</td>
<td>?</td>
<td>11</td>
</tr>
<tr>
<td>1949 Archimbaud (4)</td>
<td>A typical epithelioma</td>
<td>?</td>
<td>17</td>
</tr>
<tr>
<td>1953 White</td>
<td>Fibrosarcoma</td>
<td>?</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Duct cell carcinoma</td>
<td>yes</td>
<td>11</td>
</tr>
</tbody>
</table>

**TABLE V. Results in Women Who Became Pregnant After Treatment for Carcinoma of the Breast.**

<table>
<thead>
<tr>
<th>Years</th>
<th>Cases</th>
<th>5 yr. survivors</th>
<th>10 yr. survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>208</td>
<td>102 (49.0%)</td>
</tr>
</tbody>
</table>

Logical influences on the breast during pregnancy or lactation do accelerate the course of disease, but do not preclude cure. Delay in treatment has been an important factor in the relatively poor results to date. It is imperative that treatment be carried out even more promptly in these instances than in the non-pregnant or lactating woman. Masses and inflammations which persist short periods should be biopsied immediately. In this manner the results may be improved further.

Abortion does not show a clear effect on the course of disease in either of these groups. Abortion can not be recommended under these circumstances as effective.

**CONCLUSIONS**

1. Coincident occurrence of carcinoma of the breast and pregnancy is very uncommon.

2. The gross survival rate among patients in whom carcinoma develops during pregnancy or lactation is lower than among the nonpregnant or lactating, yet a number of these patients have been cured.

3. The poor results in patients treated for carcinoma of the breast during pregnancy or lactation may be due to delay in treatment and the advanced stage of disease when treatment is instituted.

4. The gross survival rate among patients in whom pregnancy followed treatment of a breast carcinoma is comparable to that in patients who did not become pregnant.

5. Abortion can not be shown to have a clear effect on the survival rate in either of the above series of patients.

**ACKNOWLEDGMENT**

Acknowledgment is made to Dr. John H. Mulholland, Dr. W. B. Studdiford, Dr. J. William Hinton, and Dr. J. Arthur McLean of New York University; Dr. W. C. White, Dr. Henry W. Cave, Dr. Condict Cutler, Dr. Fred W. Finn, and Dr. David Weeks, of Roosevelt Hospital, for their kind assistance and advice, as well as permission to use their private and ward cases in this report. Further acknowledgment is made to Misses McKean, Joyce, and Olson, and Mrs. Herborn, of New York University, for valuable assistance.

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THE SURGICAL TREATMENT OF CARCINOMA OF THE ESOPHAGUS AND CARDIA
AN ANALYSIS OF 457 CASES*

JOHN H. GARLOCK, M.D. AND SAMUEL H. KLEIN, M.D.

NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF THE MOUNT SINAI HOSPITAL, NEW YORK

During the past two or three years, we have noted an increasing sense of defeatism in this country concerning the efficacy of surgical therapy for cancer of the esophagus and cardiac end of the stomach. In fact, in some clinics it would appear that patients are being denied radical treatment for lesions which are frequently resectable. It is not necessary to search far for the reasons for this pessimism. A casual perusal of the literature in recent years will indicate that many authors, in reporting their cases, lump together those having obviously palliative resections and others presenting tumors which, by accepted criteria, must be considered operable and resectable for curative purposes. The resulting statistical evidence does not present a true picture of the surgical treatment of this disease insofar as it relates to the operable stage. We believe that it is important, when reporting cancer statistics of this sort, to make a sharp distinction between the grossly inoperable and the resectable groups.

Another reason is to be found in the questionable conclusions reported by one or two authors, based on an inadequate experience with the therapy of this disease. A few published reports emanate from clinics where the material is comprised mainly of patients who present themselves for treatment in the late stages of the disease. The operability rate is distressingly low and the operative mortality is correspondingly high. No valid conclusions can be drawn from reports such as these, except, possibly, that some of the figures presented may be of value in compiling data for vital statistical purposes. Upon careful examination of the details of the case reports in other publications, one is struck by the fact that the surgeon is attempting radical resection under circumstances that would indicate inoperability to the more experienced. Yet, such cases are included in the resectable and operable groups in such reports. This lack of uniformity in segregating cases into various groups based upon the local pathological setup has been a major factor in causing the confusion which has attended the general problem of appraisal of the efficacy of surgical therapy, not only of the disease under discussion, but of all surgical malignancies.

Since 1936, when an intensive study of esophageal cancer was begun in this clinic, we have followed a definite pattern of investigation, altered in minor respects as experience increased and judgment improved. Our deliberate policy of undertaking radical resections only in those instances in which a cure might be obtained was rigidly continued until five years ago. At that time, we began to do palliative resections in selected cases, not so much to accumulate material for comparative sta-

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statistical purposes as to afford some patients the chance of a return of the act of swallowing, although for an admittedly short time. This policy, we believe, has paid dividends in that we have now obtained clear-cut and incontrovertible statistical evidence of the efficacy of radical surgical excisional therapy for operable cancer of the esophagus and cardia. The effort has been rendered easier and the statistical results more valuable because the follow-up studies have been 100 per cent successful. No patient in the series reported has been lost from follow-up study.

As the study of this disease progressed, a tentative clinico-pathological classification of the various complicating factors associated with these tumors developed, and was suggested some years ago as one for general adoption by those interested in this field of surgery. Briefly, this classification embraced those tumors confined solely to the organ, those growing peripherally, requiring excision of neighboring structures, such as the right mediastinal pleura, portions of the diaphragm, parts of the pancreas, etc.; those with local lymph node spread; those with distant lymph node involvement, and those with various combinations of these complicating factors. When the surgeon was able to excise radically all gross evidence of disease, even to the extent of distant node involvement, the case was placed in the operable group. When the surgeon was unable to meet these requirements, the condition was judged inoperable and either nothing further was done or, latterly, a palliative resection was carried out. Such has been the philosophy of our approach to this complicated problem, and it is because of our rigid adherence to this general plan that we believe the facts to be presented have particular significance.

It seems superfluous to stress the fact that as one’s experience increases in the treatment of various diseases, preconceived ideas frequently fall into the discard, strong opinions undergo rapid change, and certain facts come to be accepted as almost axiomatic. In accumulating this experience, nothing can take the place of increasing numbers of cases upon whom new operative procedures may be tested and from whom our knowledge of the life history of the disease may be enlarged. We would therefore like to enumerate a number of important informative facts accumulated during 16 years of experience with the surgical therapy of this disease. We beg indulgence for re-emphasizing some that may be well-known. Others which may not be generally appreciated deserve discussion at this time.

We have noted no relationship between the duration of symptoms and operability and resectability at the time of exploration. There have been instances of a history of as short a period as three weeks associated with hopelessly inoperable tumors. On the other hand, we have seen patients with symptoms over more than a year who had easily resectable neoplasms. This emphasizes again the general problem of the biological characteristics of each individual tumor and the reaction of the patient-host to the growth.

The problem of the early symptoms of cancer of the esophagus is of great significance from the standpoint of early diagnosis. Over the years, we have tried, by careful and searching questioning, to elicit symptoms other than the cardinal one of dysphagia. While the word dysphagia has the literal meaning of disturbance of swallowing with the implication of any variety of such disturbance, it is generally considered as difficulty in swallowing food which is dependent upon the mechanical factor of a diminution in the caliber of the lumen of the esophagus. By the time this takes place, the carcinoma may be well advanced. Dysphagia, by the commonly accepted definition, is really not an early
TABLE I. 56 Patients Not Subjected to Operation.

<table>
<thead>
<tr>
<th>Reason for no operation</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper third of esophagus</td>
<td>2</td>
</tr>
<tr>
<td>Clinically inoperable</td>
<td>29</td>
</tr>
<tr>
<td>Middle third of esophagus</td>
<td>35</td>
</tr>
<tr>
<td>Bad surgical risk</td>
<td>9</td>
</tr>
<tr>
<td>Lower third of esophagus</td>
<td>9</td>
</tr>
<tr>
<td>Operation advised. Did</td>
<td>10</td>
</tr>
<tr>
<td>Cardiac carcinoma</td>
<td>18</td>
</tr>
</tbody>
</table>

Note: Inoperability decided by obvious hepatic metastases, left recurrent nerve paralysis, cervical node involvement (biopsy), tracheo-broncho-esophageal fistula, pulmonary metastases or bone metastases.

TABLE II. Cancer of the Esophagus Operability Rate.

<table>
<thead>
<tr>
<th>Operable</th>
<th>Inoperable*</th>
</tr>
</thead>
<tbody>
<tr>
<td>92</td>
<td>122</td>
</tr>
<tr>
<td>42.9</td>
<td>57.1</td>
</tr>
</tbody>
</table>

*Includes 4 palliative resections and one case with resectable tumor who went bad on the table because of a severe cirrhosis of liver. Operation not completed.

TABLE III. Cancer of the Esophagus Reasons for Inoperability.

<table>
<thead>
<tr>
<th>Reason</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local fixation</td>
<td>44</td>
</tr>
<tr>
<td>Aortic invasion</td>
<td>30</td>
</tr>
<tr>
<td>Lung root invasion</td>
<td>31</td>
</tr>
<tr>
<td>Lung root and aortic invasion</td>
<td>10</td>
</tr>
<tr>
<td>Pulmonary metastases</td>
<td>2</td>
</tr>
<tr>
<td>Pleural metastases</td>
<td>2</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>4</td>
</tr>
<tr>
<td>Distant irremovable node involvement</td>
<td>16</td>
</tr>
<tr>
<td>Local irremovable node involvement</td>
<td>18</td>
</tr>
<tr>
<td>Perforation</td>
<td>1</td>
</tr>
</tbody>
</table>

Note: There were many combinations of the above in individual cases.

TABLE IV. Cancer of Esophagus. 92 cases—Operable group—Pathological features

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor apparently confined to esophagus and no node involvement</td>
<td>34</td>
</tr>
<tr>
<td>Local node involvement</td>
<td>32</td>
</tr>
<tr>
<td>Distant node involvement</td>
<td>17</td>
</tr>
<tr>
<td>Extension of tumor beyond wall of esophagus</td>
<td>25</td>
</tr>
<tr>
<td>Right pleura excised</td>
<td>22</td>
</tr>
<tr>
<td>Adherent to bronchus</td>
<td>7</td>
</tr>
</tbody>
</table>

Note: In the lower 3 groups, various combinations of pathological extensions were, of course, encountered.

TABLE V. Carcinoma of Esophagus Operative Mortality.

<table>
<thead>
<tr>
<th>Operation</th>
<th>Number</th>
<th>Deaths</th>
<th>Mortality Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torek operation</td>
<td>16</td>
<td>10</td>
<td>60%</td>
</tr>
<tr>
<td>Infra-aortic anastomosis</td>
<td>2</td>
<td>11</td>
<td>34%</td>
</tr>
<tr>
<td>Supra-aortic anastomosis</td>
<td>3</td>
<td>14</td>
<td>32%</td>
</tr>
<tr>
<td>Combined series-total</td>
<td>1</td>
<td>35</td>
<td>38%</td>
</tr>
</tbody>
</table>

TABLE VI. Torek Operation Reasons for Mortality.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Post</th>
<th>Number</th>
<th>Mortem Examination</th>
<th>No</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulminating pneumonia</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tension pneumothorax</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mediastinitis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It is well-known that, because of anatomical confinement, tumors of the middle third may quickly become inoperable by reason of fixation to nearby structures which cannot be removed, such as the arch of the aorta, the left main bronchus or the hilus of the lung. However, the geographical location of the tumor should not deter the surgeon from exploring such a patient, unless there is obvious clinical evidence of inoperability in the form of left recurrent nerve palsy, lymph node involvement in the neck, or roentgenographic disclosure of a large peripherally growing tumor invading the adjacent lung. We are firm in
our conviction that most of these patients should be given the benefit of an exploration.

Advanced age should not, in itself, be considered a contraindication to surgery. Patients in the middle eighties have been carried successfully through the rigors of these radical procedures. Modern methods of pre- and postoperative care have done much to make this possible. Here the collaboration of a good internist will prove of inestimable value.

Patients with a history of coronary occlusion or coronary artery disease do not take kindly to this operation. The postoperative morbidity is significantly greater and operative mortality reaches prohibitive proportions. We have not, however, denied treatment because of this. An appreciable number of our postoperative deaths were attributable to this complicating factor alone.

Extensive operative experience has added considerable new information to our knowledge of the pathological history of cancer of the esophagus, especially. For instance, one encounters not infrequently a small, easily resectable tumor of the middle or lower third of the organ, and is chagrined to find extensive irremovable retroperitoneal node involvement below the diaphragm, especially along the superior border of the pancreas. This must be considered massive retrograde spread due to blockage of the lymph channels in the region of the primary tumor. Ordinarily, the direction of lymphatic flow is toward the local regional nodes in the mediastinum, as well as proximally toward the lower cervical region. Proximal microscopic spread from the site of the tumor along the submucosal lymphatic channels is a characteristic feature of squamous cell cancers of the esophagus. It is, of course, impossible to detect this in the gross at the time of operation and it therefore becomes a necessary part of the operation to transect the organ as far proximally as possible. Unless the surgeon is aware of this and accordingly makes his proximal resection as radical as circumstances will permit, he will note a high incidence of recurrence at the suture line in the follow-up period. Because of this frequently observed mode of spread, we have come to feel that practically all squamous cell tumors should have a supra-aortic anastomosis as the operation of

## TABLE VII. Infra-aortic Anastomosis Reasons for Mortality.

<table>
<thead>
<tr>
<th>Number</th>
<th>Mortem</th>
<th>Post</th>
<th>Examination</th>
<th>Mortem</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulminating pneumonia</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Right tension pneumothorax</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Leaks—fundus necrosis</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Surgical shock</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolus—14th day</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hernia of loop of bowel through diaphragm—obstruction</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary infarction</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unexplained dyspnea</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

## TABLE VIII. Supra-aortic Anastomosis Reasons for Mortality.

<table>
<thead>
<tr>
<th>Number</th>
<th>Mortem</th>
<th>Post</th>
<th>Examination</th>
<th>Mortem</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower nephron syndrome</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Fulminating pneumonia</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sudden peripheral collapse</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Right heart failure</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Vago-vagal death (?)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Bronchial obstruction</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Aortic rupture at site of ligation of esophageal vessel</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cerebral thrombosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Strangulated bowel between 2 sutures in diaphragm</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

## TABLE IX. Survivals—Torek Operation.

<table>
<thead>
<tr>
<th>Number</th>
<th>Late Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>No extension or nodes</td>
<td>3</td>
</tr>
<tr>
<td>Extension beyond wall</td>
<td>2</td>
</tr>
<tr>
<td>Extension beyond wall and local nodes</td>
<td>1</td>
</tr>
<tr>
<td>Five year and over survival—16.6%</td>
<td>1</td>
</tr>
</tbody>
</table>

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GARLOCK AND KLEIN

Annals of Surgery January, 1954
choice. A possible exception to this rule is a tumor located at the lower end of the organ just above the diaphragm. In our hands the operative mortality with supra-aortic anastomosis has been no higher than with the infra-aortic procedure.

The surgeon should think twice before attempting to separate a tumor which has invaded the outer layers of the arch or descending aorta. Experience has shown that neoplastic infiltration may be deeper than appears on the surface. Continuation of the attempt to free such a growth may result in an opening in the aorta which cannot be repaired.

During the performance of the operation of esophagectomy, the removal of the vagus nerves is most thorough. Yet, we have been impressed with the relative paucity of symptoms which might be ascribed to gastric atony, pylorospasm or disturbances of intestinal motility, frequent aftermarkets of the vagotomy operation in the treatment of duodenal ulcer. This is difficult to understand. In only three instances in this series was it necessary to pass a Levin tube to empty a dilated gastric pouch, probably on the basis of pylorospasm. The occasional patient who complains of epigastriar cramps in the early postoperative period (pylorospasms?) will usually obtain quick relief with small doses of atropine. On the basis of this experience, we do not believe it is necessary to do a pyloroplasty to overcome possible vagal effects, as recommended by one or two observers.

### Table X. Survivals—Infra-aortic Anastomosis—Lower Third Tumors.

<table>
<thead>
<tr>
<th>Number</th>
<th>Survivals</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Includes 1 case—leiomyosarcoma</td>
<td>1 alive and well 7 years</td>
</tr>
<tr>
<td>Extension beyond wall</td>
<td>1 alive and well 11 years</td>
</tr>
<tr>
<td>Local node involvement</td>
<td>5</td>
</tr>
<tr>
<td>Extension beyond wall and node involvement</td>
<td>4 Alive and well 9½ years</td>
</tr>
<tr>
<td>Distant node involvement</td>
<td>2</td>
</tr>
<tr>
<td>Local and distant nodes</td>
<td>2</td>
</tr>
</tbody>
</table>

Note: Of 12 patients operated upon before January, 1948, 5 survived more than 5 years—41.6%. 1 died after 7 years of unrelated disease. If this one is excluded, the survival figure is 33.3%.

### Table XI. Survivals—Supra-aortic Anastomosis—Middle and Upper Third Tumors.

<table>
<thead>
<tr>
<th>Number</th>
<th>Survivals</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>3—2½ years</td>
<td>2—4 years</td>
</tr>
<tr>
<td>1—6 months</td>
<td>1—2 years</td>
</tr>
<tr>
<td>1—14 months</td>
<td></td>
</tr>
<tr>
<td>Extension beyond wall</td>
<td>2 0</td>
</tr>
<tr>
<td>Extension beyond wall and local node involvement</td>
<td>2 1 2 years and 5 months</td>
</tr>
<tr>
<td>Local node involvement</td>
<td>8 4 2—26 months 1—18 months with recurrence</td>
</tr>
<tr>
<td>Distant node involvement</td>
<td>2 0</td>
</tr>
<tr>
<td>Local and distant node involvement</td>
<td>3 0</td>
</tr>
</tbody>
</table>

Note: only 4 patients were operated upon prior to January, 1948. None of these are alive after 5 years. The longest survival time was 3½ years.

Combining Tables IX, X, XI—22 squamous cell carcinomas were operated upon over 5 years ago. Six survived more than 5 years or 27.2 per cent.

In carrying out the details of the supra-aortic anastomosis, the stomach is frequently transplanted almost to the apex of the chest. As a result, there may occur an axial rotation of the second portion of the duodenum of sufficient severity to produce obstruction at this point. Four years ago, a patient developed this complication. Roentgen studies clearly indicated the site of obstruction and, at a second operation, the axial rotation of the second portion of the duodenum was found to be the cause. Section of the lateral peritoneal attachment of the duodenum resulted in prompt relief. We, therefore, recommend this step as a routine procedure in the performance of
the supra-aortic anastomosis. In passing, we would like to state that we have never seen the need of an indwelling Levin tube during the early postoperative period. Routine postoperative roentgenographic examination of the chest in our series has failed to demonstrate undue dilatation of the transplanted stomach, which would indi-

cate the need for intubation. The three cases mentioned above were the only exceptions.

The question of postoperative leak, either from the suture line or from localized necrosis of the stomach, is an important one. We believe it occurs oftener than the reports in the literature indicate. We have had 13 instances of postoperative suppuration due to leak and in six, this complication was the cause of death. The remaining seven recovered. We were concerned more about this unfortunate occurrence in preceding years than we are at present, because we believe we have learned much about the causes and how to obviate them. In the first place, clinical operative experience has shown that, in spite of the recent experimental and anatomical studies concerning the segmental blood supply of the esophagus, there are many anatomical variants in the distribution of the esophageal arteries arising from the aorta which require ligation at the time of resection. Because of this experience, we have come to feel that one should not mobilize the proximal esophageal segment too extensively after transection for fear of jeopardizing the blood supply of the cut end which is anastomosed to the stomach. More important, however, is the question of the handling of the stomach during its mobilization and the possible localized vessel thrombosis with resultant local gastric necrosis. It must be remembered that, in mobilizing the stomach for transplantation into the chest, all vessels are divided except those along the gastro-epiploic arch, which draws its sole arterial supply from the right gastro-epiploic artery. Not only must these vessels in the arch be clearly delineated, but it is most important that this part of the mobilization be carried out with the greatest care and gentleness. Accidental ligation or traumatic thrombosis of any portion of the arch will greatly increase the risk of gastric necrosis usually at the cardial end of the organ. What is not generally recognized, however, is that the same gentleness must be employed in the handling of the stomach itself during all the maneuvers necessary to effect its adequate mobilization. We are convinced that rough handling, the use of clamps, or firm finger compression are factors in the development of localized thrombosis in the gastric wall at the site of trauma which later goes on to gastric necrosis, responsible for the leaks recognized postoperatively. In our group of 13 leaks, nine were due to areas of localized gastric necrosis, three to healing disturbances at the suture line, and

| Operable......... | 89 | 45.4 |
| Inoperable*..... | 98 | 54.6 |

*Includes 15 palliative resections.

<table>
<thead>
<tr>
<th>Operative approach</th>
<th>Number</th>
<th>Deaths</th>
<th>Mortality Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left transthoracic</td>
<td>33</td>
<td>16</td>
<td>48.4%</td>
</tr>
<tr>
<td>Combined abdomino-thoracic</td>
<td>56</td>
<td>6</td>
<td>10.7%</td>
</tr>
<tr>
<td>Combined series—Total</td>
<td>89</td>
<td>22</td>
<td>24.7%</td>
</tr>
</tbody>
</table>
one to tear of the esophagus above the suture line.

In mobilizing the esophagus from the mediastinum, the surgeon's finger may inadvertently tear the longitudinal muscle fibres of the organ. If this occurs in a portion of the organ to remain, the surgeon should not fail to repair this tear with interrupted sutures of fine silk. In one patient, where this was not done, a rupture of the esophagus occurred at the exact site of a small tear, with resultant sepsis and death.

Tumors located in the lower half of the esophagus have more room for lateral growth than those situated in the close confines of the upper thoracic mediastinum. The direction of this lateral spread is often towards the right pleural sac, and fixation to the right mediastinal pleura is a frequent finding. In order to carry out a radical excision, varying sections of this reflection of the right pleura must be removed. In the early days, the subsequent bilateral pneumothorax on the operating table was considered a most serious complication. The ensuing anoxia was difficult to control and the postoperative course often became complicated, frequently to the extreme state of irreversible changes resulting in death. The anesthetist usually can tell by the pressure changes in his machine when the right pleura has been opened, but the surgeon should immediately inform him of this happening. He will then employ methods to maintain expansion of the lung and overcome the anoxic state which may develop. Temporary packing of the rent in the pleura will aid the anesthetist in accomplishing his purpose. If the opening is too large to permit suturing, the transplanted stomach can be advantageously utilized to cover the defect. At the completion of the operation, it has been our practice to remove trapped air from the right pleural cavity by needle aspiration. Rarely is it necessary to insert an intercostal tube for underwater drainage. In our series of cases, the right pleura was opened or excised 22 times. This maneuver probably contributed to the death of the patient in six instances, and these occurred in the early years of our experience.

The role of the anesthetist in the surgical care of esophageal and cardial carcinomas is an extremely important one. It is safe to say that the development of esophageal surgery in the past 15 or 16 years would not have been possible without the great advances in the field of anesthesiology. The anesthetist is an important member of the team and the wise surgeon heeds the warning signals given by the anesthetist during the course of a frequently very difficult operative procedure. Here again, increasing experience gained with larger numbers of cases fortifies the anesthetist with the assurance that is so important for a competent performance of his job.

It was not our intent to embark upon a prolonged discussion concerning the relative merits of the left-sided and the right-sided approach for esophageal cancer. We have preferred the left-sided operation from the very beginning. There is no doubt, however, that the right transthoracic approach, first suggested by Ivor Lewis, has much to commend it, especially from the standpoint of making the maneuver of

**Table XV. Transthoracic Approach—Cancer of Cardia**

<table>
<thead>
<tr>
<th>Reason for Mortality</th>
<th>Number</th>
<th>Post Mortem Examination</th>
<th>No Post Mortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary collapse-plug in bronchus</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolus—18th day</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>7</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Extensive pneumonia</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis due to perforation of esophagus above anastomosis</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cerebral hemorrhage</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Operative shock? Death 2 hours P. O.</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cause unknown</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
mobilization of the esophagus in the upper mediastinum technically easier for the surgeon. Our objection to the right approach is based on a rather simple observation. After going through all the technical details of mobilizing the stomach for transplantation through a separate abdominal approach,

### Table XVI. Abdomino-thoracic Approach—Cancer of Cardia
**Reasons for Mortality.**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Post Mortem</th>
<th>No Post Mortem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary occlusion</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Focal necrosis of stomach-sepsis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Operative shock</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

### Table XVII. Total Group—Carcinoma of Cardia—Survivals.

<table>
<thead>
<tr>
<th>Number Survivals</th>
</tr>
</thead>
<tbody>
<tr>
<td>No local extension or node involvement</td>
</tr>
<tr>
<td>11 years+</td>
</tr>
<tr>
<td>4 years</td>
</tr>
<tr>
<td>3-6 months</td>
</tr>
<tr>
<td>Extension beyond wall and local nodes</td>
</tr>
<tr>
<td>Local node involvement</td>
</tr>
<tr>
<td>1-2 years</td>
</tr>
<tr>
<td>1-4 year</td>
</tr>
</tbody>
</table>
| Note: This chart graphically demonstrates the influence of node involvement on the survival rate. Occasionally, one will encounter a long-term cure in the presence of extensive local lymph node spread.

the surgeon then explores the chest to determine operability. There is a 50 per cent chance that he will find a tumor that will not even permit of palliative removal. Under such circumstances, the abdominal part of the operation constitutes unnecessary and wasted effort. If the surgeon were to reverse the order of his steps and first explore the chest, he would then complicate matters for himself, if he were to find a resectable tumor. In spite of all that has been written about the great technical difficulties associated with the left transthoracic approach, we have really never encountered a situation which posed technical problems that could not be handled adequately. It is our impression that the proponents of the right approach are undertaking resections for tumors which we would consider inoperable and that, if the tumor is really resectable by the criteria which we have set up for ourselves, it can be removed just as easily from the left side. Certainly the operating time is cut considerably and the continuity of the operation is better maintained by the left transthoracic exposure. Of necessity, there must follow a lower morbidity and operative mortality.

We believe that one of the great technical advances in the past decade in the surgical therapy of cardial carcinomas has been the development of the abdomino-thoracic approach. As we have stressed in the past, not only are the steps of the operation made technically easier for the surgeon, but, what is more important, he is able to carry out a more radical operation under direct vision, with very much less operative trauma. In spite of the fact that the exposure is much greater than with the pure transthoracic approach, postoperative morbidity has been markedly lessened and the operative mortality has shown great improvement. We are more convinced than ever that the abdomino-thoracic incision is the one of choice for the operation of total gastrectomy when this procedure is indicated. This was first suggested by us in 1947.

The place of esophagoscopy in the diagnosis of malignancy of the esophagus and cardia deserves mention. We cannot agree with Sweet when he states that this form of examination is rarely necessary to establish the presence of a neoplasm. While our reliance on the findings of properly per-
formed roentgen examination is considerable, we have encountered instances where neither the roentgenologist nor the surgeon could be sure that he was dealing with a benign obstruction secondary to reflux esophagitis, cardiospasm or carcinoma. In fact, in three cases in our series, the roentgenologic diagnosis was unequivocally conical cardiospasm. Yet, on esophagoscopy, the biopsy specimen showed the presence of submucosal carcinoma originating in the nearby cardia. This difficulty in the interpretation of the roentgenograms is particularly noteworthy in the distal 3 or 4 cm. of the esophagus. The dangers associated with the actual performance of esophagoscopy are not very great nowadays. Our records indicate an insignificant incidence of instrumental injury of the esophagus. Certainly, the valuable information obtained by esophagoscopy examination far outweighs the small risk of instrumental injury of the organ.

The advent of the antibiotics has, of course, changed the entire complexion of the problem under discussion. In the early days, postoperative pulmonary complications, especially in the older age groups, were distressingly frequent and accounted for a considerable proportion of the operative mortality. Nowadays, it is unusual to see a serious pulmonary complication, and to have a patient die of this type of complication is indeed rare. Whether or not the antibiotics have been beneficial in other directions is somewhat doubtful. It is possible that some good derives from them in combatting infection in the mediastinal areolar tissue after inadvertent soiling. We cannot stress enough that “shot-gun” antibiotic therapy, so widely employed nowadays, can never take the place of careful surgical technic. One sees an unfortunate trend to forget or minimize the basic surgical principles of yesteryear with the thought, subconscious to be sure, that these wonder drugs will take care of any technical derelictions. In spite of the antibiotics, it is still important to carry out the steps of the operative procedures with minimal operative trauma, care in the placing of the anastomotic sutures, preservation of the blood supply of the transplanted stomach, and avoidance of gross soiling of the pleura and mediastinum.

It must be remembered, when appraising the long-term results of cancer of the esophagus and cardia, that the vast majority of these patients develop the disease in the latter years of their lives. It might be expected, therefore, that the five year survival period, almost universally accepted in surgical circles today, may coincide with the normal life expectancy of many of these patients. This has been our experience with a number of patients in our series. In the absence of an autopsy, the burden of the proof that the cancer was cured rests squarely with the surgeon. Claims that patients were cured of their cancers when death occurred under five years due to the infirmities of old age must be substantiated by postmortem studies. Otherwise, statistics will have no real significance.

The general problem of palliative surgery deserves special consideration. As mentioned earlier, we originally committed ourselves to the policy of undertaking resections only in those cases where a curative operation could be contemplated in order to obtain a real appraisal of the efficacy of radical surgical extirpation. We believe this policy has been the correct one in terms of its original purpose, but freely admit that we have denied to many patients, otherwise inoperable, the return of normal swallowing if palliative resections had been undertaken. This, essentially, is a moral problem, and rests on the conscience of the individual surgeon. In recent years, we have done palliative resections under specific circumstances. We believe that adenocarcinomas of the cardia
are in a somewhat different category. We certainly would do a resection of a removable cancer of the cardia in the presence of a few hepatic metastases. However, our experience indicates that massive hepatic involvement contraindicates any major resection of the stomach because of the associated prohibitive operative mortality. There is, also, grave doubt that resection should be undertaken in the presence of peritoneal seeding.

With inoperable squamous cell tumors there is room for considerable discussion. Not infrequently one finds a resectable tumor of the middle or lower third of the esophagus with extensive retroperitoneal node involvement below the diaphragm. If the abdominal mass does not interfere with mobilization of the stomach, a palliative resection is justified under such circumstances. Occasionally, one encounters a non-fixed neoplasm with extensively involved periaortic and mediastinal lymph nodes which cannot be removed. Here, also, a palliative resection can be done without too much increased risk. However, when the neoplasm itself is firmly fixed to neighboring important structures and cannot be removed without cutting across carcinoma, it is extremely doubtful that palliative resection should be attempted on the basis of possible restoration of the act of deglutition for a period of a very few months. There seems little doubt that this type of surgery encourages dissemination of the carcinoma. Under certain circumstances it may be possible to utilize the plastic tube recommended by Berman. We have had no experience with it and therefore can offer no opinion as to its merits. A few authors have suggested side-tracking operations as palliative procedures and it is possible that this can be done in the occasional case.

We would like to report that we have been impressed with the results of the recently developed rotation and "grid" technics of roentgen ray therapy as a palliative measure for inoperable squamous cell cancers of the esophagus. In a few instances there has been a remarkable change in the appearance of the tumor in the roentgenogram, with an accompanying improvement in the act of swallowing. We are now using this modality for mediastinal recurrences which develop after resection. Perhaps further experience will prove this form of therapy to be the method of choice for inoperable cancers of the organ. If this occurs, then many of the palliative operations carried out today will be a thing of the past.*

**ANALYSIS OF CASES**

The 457 cases reported in this paper constitute our total experience with cancer of the esophagus and cardia during the years between 1936 and December 31, 1952. Included in this total figure are 56 patients who were not subjected to surgery for varying reasons. These are indicated in Table I. It was thought wise to include this group so that we could report our complete experience. It will be noted that the majority of these patients were clinically inoperable at the time of the first examination. Others were judged inoperable from the standpoint of associated severe medical complications, and many never returned for operation, although they were considered suitable candidates. The remaining 401 cases constitute the basis for the statistical evidence to be presented because they were all subjected to operation. We will consider the squamous cell tumors and the cardial adenocarcinomas separately.

* In the past year we have been giving postoperative radiation therapy as a routine measure to all patients who have had resections for squamous cell cancers of the esophagus. Exposures have been directed to the entire mediastinal area and, in selected cases, to the upper abdomen. Radical surgical extirpation and postoperative radiation by modern methods may prove to be a most efficient combination.
CANCER OF THE ESOPHAGUS

This group comprises 214 patients. The age distribution indicates that the vast majority, 67 per cent, are in the two decades between 50 and 70. The eighth decade includes a not inconsiderable proportion of the total number. The male sex has the preponderance in the ratio of more than two to one. While 88 of the total had symptoms for a period under three months, the relatively large number over the six month period is noteworthy. Many of the operable tumors were in this group. Our attempt to define a correlation between the duration of symptoms and operability yielded little of significance, and the results of this effort are therefore not recorded.

In appraising the positive physical findings preoperatively, some interesting facts were brought to light. The weight loss varied from one pound to the extreme of 55. The average for the series was 24 pounds. In the group of 39 patients under the heading "poor general condition" are included many patients presenting the cachexia of esophageal obstruction due to extreme weight loss and water deprivation. At least in our clinic, patients of this type are rarely seen nowadays. The dissemination of the facts about the surgical treatment of this disease among the general medical profession seems to have borne results in that, during the past five or six years, we are seeing patients earlier in the course of their disease and before extreme weight loss has taken place.

Every patient in this group was esophagoscopyed, and 208 positive biopsies were obtained. It is of interest to record that four of these represented primary adenocarcinomas of the esophagus. This was confirmed at the time of exploration. There are 40 recorded instances of bronchoscopy carried out preoperatively to disclose possible involvement of the left main bronchus or trachea. In only one instance was a positive biopsy obtained.

By the criteria originally set up, our operability rate was only 42.9 per cent, a rather disappointing figure (Table II). We would like to point out that a case was not judged inoperable until every effort was exerted to bring it within the sphere of operability. Table III indicates the reasons for deciding inoperability. Liver metastases with squamous cell cancers of the esophagus were once considered a rarity. In our four examples of this direction of spread, the tumors were located in the distal esophagus.

In the group of 122 inoperable patients, there were 14 deaths, or an operative mortality of 11.7 per cent. Some of the deaths were undoubtedly due to the fact that, in the attempt to free the tumor or adherent nodes, complicating factors were engendered which caused the mortality. There is always an increased risk under such circumstances.

Table IV indicates the pathological features in the group of 92 operable tumors. The first heading of "tumors apparently confined to the esophagus" requires some clarification. It is very doubtful that all 34 patients exhibited neoplasms which had not extended, at least microscopically, beyond the outer muscular layer. We have made this classification, however, because the tumor separated in each instance with relative ease, and because there was no gross evidence of extension beyond the wall. We admit this is somewhat arbitrary, but it serves a purpose in appraising late results.

In the 91 patients in whom resection was completed, there were 35 deaths, or an overall mortality of 38 per cent. We believe it is desirable to break down these figures on the basis of the type of operation performed. The Torek operation was carried out on 16 patients, with 10 operative deaths, or 60 per cent. These were
done in the early days of our experience when we were not fully acquainted with the innumerable factors involved in the care of these patients. In 32 cases, an infra-aortic resection and anastomosis was carried out. There were 11 deaths, or an operative mortality of 34 per cent. There were 43 cases of resection and supra-aortic anastomosis, including two cervical anastomoses. The operative deaths were 14 in number, a mortality percentage of 32 per cent (Table V). Operative mortality in the excisional therapy of this disease is governed in part by factors within the control of the surgeon and in part by circumstances which, by and large, are beyond his control. The mortality in our series has varied throughout the years. Increasing operative experience, improving judgment, development of newer anaesthetic technics and the advent of the antibiotics are prominent factors in the gradual decline in the number of deaths. In the last 16 cases, the operative mortality was 13 per cent. There can be little doubt that the future holds promise for great improvement in these figures. Tables VI, VII and VIII indicate the cause of death in each instance. The high percentage of postmortem examination is noteworthy. Of the 35 deaths recorded in these tables, 12 may be classed as preventable and the remainder must be considered beyond the control of the surgeon. There were eight instances of fulminating pneumonia, three examples of coronary occlusion, three cases of right heart failure, three cases with fatal cerebral accidents, and two pulmonary embolisms. These 19 patients constitute more than 50 per cent of the mortality. The remaining four cannot be credited to an error in technic or a therapeutic oversight. It can be observed, therefore, that operative mortality looms large, not from the standpoint of avoidable technical errors, but rather because of the very nature of the disease and the advanced age groups and poor surgical risks with which the disease is associated.

FOLLOW-UP DATA

The most important part of this paper is concerned with the survival rate in the group of patients who were subjected to radical operation for curative purposes. It is upon the findings obtained by a study of this type that any logical and intelligent opinion can be formed concerning the long-term efficacy of extirpational therapy in the treatment of this disease. In addition, our analysis has disclosed certain facts, especially in the group developing recurrences, which may prove of value to the surgeon from the standpoint of employing operative maneuvers which might obviate or, at least, lessen the incidence of some of these recurrences. As stated before, we have been most fortunate in obtaining accurate follow-up data on every patient in the series reported.

Torek Operation. Six patients survived this operation. In three, there was no obvious extension beyond the esophageal wall and no nodal involvement. Two died of their disease 12 and 18 months later, one of recurrence at the upper esophagostomy stoma and also mediastinum and the other of mediastinal involvement. The third patient is alive and well 16½ years after operation. Two patients presented extension of the tumor beyond the esophagus at operation. Both died of mediastinal recurrence eight and 12 months later. One also presented recurrence at the esophagostomy stoma. The sixth patient had a tumor extending beyond the wall and also local node involvement. She died 20 months later of extensive mediastinal involvement, with perforation into the trachea and aorta. Inasmuch as these patients were operated upon prior to January, 1948, the five year survival rate can be computed at 16.6 per cent. The 40 per cent incidence of recurrence at the upper esophagostomy
stoma points the way to the need for wide ablation of the esophagus proximally to get beyond the characteristic submucosal extension of the tumor (Table IX).

Infra-aortic Anastomosis. In this group the tumors were located in the distal third of the organ. In the group of seven with no local extension, three survived more than five years. One died after seven years of cardiac disease, the other two are alive and well seven and 11 years respectively. Of the remaining four, two died of liver metastases three years and four months, and 13 months later. Two died of mediastinal recurrence two years and two and a half years postoperatively. One patient presented extension beyond the wall, requiring removal of a large segment of right mediastinal pleura. This man is alive and well 14 years after operation. There were five patients presenting local node involvement; all are dead. One died of liver metastases after seven months, and the remaining four died of local recurrence in the posterior mediastinum after two and a half years, two years, one year, and eight months respectively. Under the classification of extension beyond the wall plus local node involvement, there were four patients. One is alive and well after nine and one-half years. One died within 11 months of bone metastases, one in six months of pulmonary metastases, and one developed a suture line recurrence with later fatal spread. Two patients presenting distant node involvement died within six months. Two individuals presented local and distant node disease. One died after two years of neck and chest spread, and the other within one year of probable local disease (Table X).

Supra-aortic Anastomosis. Under this heading we include tumors located in the middle and upper thirds of the esophagus. The anastomosis, of necessity, must therefore be placed above the arch of the aorta, even as far as the cervical region. Four patients survived operation prior to January, 1948. All died of mediastinal recurrence within 11 months, seven months, three years and three and a half years respectively. Table XI indicates the survivals under each pathological classification. These patients were alive and apparently free of disease as of March 1, 1953. It is important to indicate the site of recurrence in the remaining 16 patients. Nine developed local mediastinal recurrences and succumbed to their disease. Two showed recurrence at the suture line, indicating insufficient removal of the proximal esophagus. Two died of intra-abdominal metastases, two of bone metastases and one of pulmonary spread. The longest period of survival was three and one-half years; the shortest, four months.

Adenocarcinoma of Cardia. In this group there are 187 patients who came to operation. The majority were found between the ages of 50 and 70. Thirty-four patients were in the two decades between 30 and 50. The male sex preponderated by the ratio of almost three to one. Although many neoplasms of the upper end of the stomach will give symptoms other than dysphagia at an earlier stage than is seen with tumors of the esophagus, it was noted that there were fewer cases within the one to three month period than were shown in the esophagus group. The implication of this appears obvious. Both patient and physician are still not giving heed to the early symptoms of indigestion, vague epigastric distress, unexplained anorexia and weight loss. It is when the cancer narrows the lumen of the cardia and the symptom of dysphagia becomes prominent that the patient will first seek medical advice. By that time, the tumor may be inoperable. With the modern advances in roentgenological technics as they refer to demonstrating tumors in the upper part of the stomach, the so-called silent area, there should be a very high percentage of posi-
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tive diagnosis in the early stages of this disease. The adjuvant diagnostic modalities of esophagoscopy and gastroscopy will usually confirm the findings obtained by the roentgenograms. Whenever doubt exists, we believe that exploration should be undertaken without hesitation. Under such circumstances, it is wiser to err on the side of a negative exploration than to overlook an early cancer in this region.

The weight loss varied between the extremes of five and 70 pounds. The average was 28. A rather large number, 45, were considered poor risks for various reasons.

Secondary anemia is more common with cardial cancers than with esophageal growths. We have seen a number of patients with alarming hemorrhages from tumors located near the cardia. Esophagoscopy was performed in 118 patients. The biopsy was positive in 107 and negative 11 times. As stressed before, we consider esophagoscopy of inestimable value in the diagnosis of this disease.

In this series of 187 patients with cancer of the cardia, there were 89 operable cases, an operability of 45.4 per cent. This included one case of lymphosarcoma. Among the inoperable group of 98 patients are included 15 palliative resections (Table XII). In our experience, the opportunity for carrying out a palliative resection occurs more frequently with cardial cancers than with neoplasms of the esophagus. The high incidence of metastatic liver involvement is particularly significant, almost 20 per cent.

In the group of 98 inoperable patients, there were five operative deaths, or 5 per cent. Fifteen palliative resections were performed with three deaths, an operative mortality of 20 per cent. One died of no demonstrable cause and the remaining two of suture line leaks. Table XIII denotes the pathological features in the group of 89 operable tumors. With cancers of the cardia, confinement of the neoplasm to the stomach wall is more apparent in the gross than is the case with esophageal cancers. Therefore, this classification is not so arbitrarily drawn. More than two thirds of the whole group showed local lymph node involvement and half presented extension to the lower esophagus, a growth characteristic of cardial cancers which is well-known.

In the 89 patients in whom resection was completed, there were 22 deaths, a gross operative mortality rate of 24.7 per cent. We can break this down into two classifications dependent essentially on the type of operative exposure used in each group. Thirty-three resections were carried out by the left transthoracic approach and 16 of these died, an operative mortality of 48.4 per cent. On the other hand, 56 resections were completed utilizing the combined abdomino-thoracic approach, with six deaths, or a mortality of 10.7 per cent. This marked disparity in the mortality figures between the two groups cannot be explained entirely on the basis of improving surgical and anesthetic technics or the advent of antibiotics. The type of exposure, we believe, has proved to be a major factor in simplifying the steps of the operative procedures, minimizing operative trauma and curtailing morbidity and mortality figures (Table XIV). In appraising the reasons for the operative deaths, it is interesting to note that 11 of the 22 can be attributed to acute coronary occlusions. Many of our patients have had a history of preceding coronary thrombosis and our experience leads us to believe that the risk of operation in these individuals is much greater. However, the risk must be undertaken with the realization that every preventive measure should be utilized to minimize the chance of another cardiac episode (Tables XV and XVI).

FOLLOW-UP DATA

From the pathological standpoint, cancer of the cardia presents somewhat differ-
ent problems than does the squamous cell tumor of the esophagus. In addition to spread by the lymphatic channels to regional and distant nodes and to peritoneum and pleura, a considerable percentage of patients subjected to operation shows spread by the portal system to the liver. It becomes obvious, therefore, that the rate of operability will be less and the incidence of late survivors will be proportionately decreased. Our figures substantiate these deductions. In appraising our survival data we are combining the two groups of pure transthoracic resection and operation by the combined abdomino-thoracic route. There were 67 survivors of the total group of 89 subjected to resection. Of these, 32 were operated upon prior to January, 1948. Five patients in this group are still alive and apparently free of their disease; one, thirteen years; three, eleven years; and one, seven years; a late survival incidence of 16 per cent. Among the 27 remaining patients in this particular group, one died after six years, of a coronary occlusion. The remainder died of their disease, usually with extensive intra-abdominal, pulmonary or osseous spread, after varying periods of survival ranging between the extremes of four months and five years. The average length of life after operation was 21 months. Table XVII indicates the survivals in the pathological subdivisions which have been followed in our paper. The impact of lymph node spread on the survival figures is startlingly clear in this chart. In spite of these findings, the surgeon should make every effort to do as radical an operation as is possible, because the occasional patient will live long past the usually accepted five year period.

It is not necessary to record minutely the site of recurrence in each patient who succumbed to his disease. Suffice it to say that spread was more widespread than was noted in epidermoid carcinoma and caused death in a shorter period of time.

CONCLUSIONS

1. This study has shown that there is no justification for the spirit of defeatism which has crept into the literature in the past few years and propounded by individuals who have had insufficient experience with the operative therapy of cancer of the esophagus and cardia.

2. It is important, in reporting results, to make a sharp distinction between palliative resections and those undertaken for curative purposes. The entire problem of judging long-term results in the surgical therapy of cancer has been confused in the past by the common practice of mixing both groups.

3. On the basis of an experience over more than 16 years with 457 patients with cancer of either the esophagus or cardia, many important features in the surgical management have been developed. These have been described in the body of the paper.

4. On the basis of a deliberate policy of undertaking resection in those instances in which a cure might be obtained, operability in the squamous cell tumors was 42.9 per cent and 45.4 per cent in the adenocarcinoma of the cardia group.

5. The operative mortality of the various operations employed over the period of study is presented. There is little doubt that increasing experience, better anesthetic methods and the advent of the antibiotics have been important factors in reducing these mortality figures to respectable levels. It must be remembered, however, that these operations can be of great magnitude and, because of complicating medical disabilities in older age groups, an over-all appreciable mortality must be expected.

6. A classification of the local pathological setup is suggested as an aid in tabulating survival statistics.

7. The Torek operation was carried out in the early days of this study. One, or
16.6 per cent, of the operative survivors is alive and well 16% years after operation.

8. In the group of lower third esophageal cancers (infra-aortic anastomosis) operated upon over five years ago, 41.6 per cent of the operative survivors lived more than five years. The longest survivor is 14 years postoperative.

9. In the group of middle and upper third cancers in which the supra-aortic anastomosis was employed, only four survived operation over five years ago. None are alive today.

10. The over-all five year survival rate of patients operated upon for cancer of the esophagus, excluding operative deaths, was 27.2 per cent.

11. Adenocarcinoma of the cardia presents a somewhat different pathological problem from the standpoint of routes of spread. Thirty patients were operated upon over five years ago, and 16 per cent of these are alive and apparently free of disease. The longest survivor period is 13 years.

12. This study graphically demonstrates the impact of node involvement on the survival rate. The largest number of late survivors showed no lymph node spread.

BIBLIOGRAPHY


CARCINOMA OF THE THYROID: A RE-EVALUATION*

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CARCINOMA OF THE thyroid gland continues to be the subject of much discussion and controversy. A major area of disagreement centers about the histopathologic criteria for the diagnosis of thyroid cancer; reported five-year survival rates vary from 7.8 per cent to 61 per cent. Previous experience with thyroid carcinoma at the Hospital of the University of Pennsylvania over an 11½ year period was analyzed and the results published in 1947. Since that time, impressions have been gained of an increased incidence of thyroid cancer and of changes in the relative incidence of various histopathologic types. Furthermore, the passage of years has permitted the observation of late developments in many cases.

This present study, which includes review of the data published in 1947 with continuing follow-up of those cases to date and a similar analysis of experience since that time, was undertaken primarily to test the validity of the previously reported data, especially the pathologic diagnoses, as well as to assess our more recent experience and compare it with that previously recorded.

INCIDENCE

A total of 3,856 lesions of the thyroid gland were observed in the Laboratory of Surgical Pathology of the Hospital of the University of Pennsylvania between July 1, 1933, and December 31, 1952. Whereas 2,079 thyroid lesions and 62 thyroid carcinomas were catalogued during the first 11½ years of this period, a total of 1,777 lesions and 174 carcinomas were observed in the most recent eight years. It is striking that in the earlier series, toxic diffuse goiters accounted for nearly half (44.4 per cent) of the cases, but in the later group, only 13.7 per cent, less than one-sixth. We have attributed this to increasing referral of patients with nodular goiters for surgical treatment and to the use of anti-thyroid drugs by the internist and general practitioner in the treatment of toxic patients. Table I repeats the breakdown of the 2,079 cases observed in the Laboratory prior to 1945 and compares it with the cases observed in the more recent eight-year period.

The fact that 9.8 per cent of the surgical thyroid lesions of the past eight years were carcinomas as contrasted with but 3 per cent in the earlier 11½ year period is in part explained by the great relative increase of nodular, as opposed to diffuse, goiters in the laboratory material. Table II lists the percentages of surgical thyroid lesions, exclusive of the diffuse goiters, that proved to be malignant.

The relative incidence of cancer among surgically treated nodular thyroid lesions over the past eight years (11.4 per cent) is indeed striking. It is recognized that the percentage of nodular thyroids subsequently proven to harbor malignant tumors cannot be accepted as a measure of the incidence of thyroid cancer in the pop-
ulation at large. Crile and Dempsey's have
discussed the fallacy of such reasoning. Among the cancers included in the series
under discussion, 78 were diagnosed or seriously suspected preoperatively, whereas
basis of pathologic study elsewhere, or on
clinical evidence. In addition to the 174
surgical cases in the current series, there
are 14 patients who were treated initially in
other institutions and one patient who was

<p>| TABLE I. Classification of Surgically Treated Thyroid Disease. | |
|---------------------------------------------------------------|
| Hospital of the University of Pennsylvania, 1933-1952         | |
|                                                              |
|                                                              |
|                          7/1/33 - 12/31/44 | 1/1/45 - 12/31/52 | Total               |</p>
<table>
<thead>
<tr>
<th>7/1/33 - 12/31/52</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse Toxic Goiter.... 923 (44.4)*</td>
</tr>
<tr>
<td>Diffuse Non-Toxic Goiter... 21 (1.0)</td>
</tr>
<tr>
<td>Non-Toxic Nodular Goiter... 657 (30.6)</td>
</tr>
<tr>
<td>Toxic Nodular Goiter... 279 (13.4)</td>
</tr>
<tr>
<td>Thyroiditis... 30 (1.4)</td>
</tr>
<tr>
<td>Tuberculosis... 1 (0.1)</td>
</tr>
<tr>
<td>Adenoma... 115 (5.5)</td>
</tr>
<tr>
<td>Papillary Cystadenoma... 11 (0.5)</td>
</tr>
<tr>
<td>Carcinoma... 62 (3.0)</td>
</tr>
<tr>
<td>Totals... 2079</td>
</tr>
</tbody>
</table>

*Figures in parentheses indicate percentages.

96 were first recognized only upon patho-
logic examination, an incidence of 6.6 per
cent among nodular thyroid lesions. Simi-
larly, 39 cancers not diagnosed preoper-
atively comprise 3.5 per cent of the nod-
ular lesions of the earlier series (Table
III).

It must be emphasized that many of the
cases of carcinoma here classified as un-
diagnosed preoperatively, actually came to
operation solely or largely because the
possibility of cancer was recognized, al-
though it was considered a less likely diag-
nosis than adenoma or simple nodular
goiter. Thus, the fact that a smaller propor-
tion of the tumors in the current series was
diagnosed preoperatively than in the earlier
group may well be regarded as an evidence
of a general increasing awareness of the
malignant potentialities of the nodular
goiter. Likewise, this might also account
for the increased relative incidence of can-
cer, whether diagnosed clinically or not.
Our earlier series included, in addition to
the 62 cases treated surgically, nine cases
diagnosed positively at autopsy, on the
not operated upon, but who came to post-
mortem examination. In every instance the
material of the later series has been avail-
able for histologic study.

AGE AND SEX

The age incidence of the cases of thyroid
carcinoma is presented in Table IV. This
age distribution does not differ greatly
from that previously reported by us or by
others, but it does serve to emphasize the
not infrequent occurrence of this form of
malignant disease in the youth or adoles-
cent. Most of the cancers in the younger
age group in this series have been encoun-
tered in our more recent experience. Forty-five (23.8 per cent) of the thyroid
cancers in this series occurred in males, in
contrast to a ratio of approximately 10 per
cent for surgical thyroid disease in general.
These data emphasize the important point
that, among the nodular goiters, those
occurring in young individuals and those in
males, are particularly deserving of sus-
picion of malignancy and, consequently,
of surgical attention. It was noted pre-

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CARCINOMA OF THE THYROID: A RE-EVALUATION

Previously it was noted that older patients tended to have more malignant and more advanced cancers than younger patients. In the current series in patients 60 years of age or less, about as many cancers were sufficiently advanced to permit clinical diagnosis as were diagnosed only in the laboratory. In patients over 60, however, most of the tumors were readily diagnosed clinically. As a corollary, approximately one-half of the fatalities occurred in patients found to have thyroid cancer only after the age of 50. Both points undoubtedly reflect the fact that the more malignant varieties of thyroid cancer are tumors of the older age groups.

THYROTOXICOSIS

Five patients in this series of 189 cases (2.6 per cent) presented definite evidence of thyrotoxicosis and one additional patient was equivocally hyperthyroid. This compares with a 3 per cent incidence of hyperthyroidism among the 71 cases previously reported. It is of great interest that two patients with thyroid carcinoma, who were not toxic at the time the diagnosis of carcinoma was made, gave past histories of unquestionable hyperthyroidism. One of these two patients, a 29-year-old female, had been subjected to subtotal thyroideectomy for a toxic nodular goiter in 1935 and again in 1940. In 1944, following the birth of her first child, a nodule appeared, unassociated with evidences of toxicity. This enlarged slowly, was removed in 1947 and proved to be carcinoma. The other patient was a 39-year-old female. Twenty years before noting the nodule that proved to be carcinoma, she was subjected to subtotal thyroideectomy with pre- and postoperative roentgen ray therapy at another institution for toxic goiter with exophthalmos. Unfortunately, precise data with regard to radia-

TABLE II. Relative Incidence of Nodular Goiter and Thyroid Carcinoma.

<table>
<thead>
<tr>
<th>Hospital of the University of Pennsylvania, 1933-1952</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/1/33-12/31/52</td>
<td>7/1/33-12/31/52</td>
</tr>
<tr>
<td>Nodular Thyroid Lesions</td>
<td>Nodular Thyroid Lesions</td>
</tr>
<tr>
<td>110</td>
<td>1523</td>
</tr>
<tr>
<td>Carcinoma of Thyroid 62- (5.5%)</td>
<td>174- (11.4%)</td>
</tr>
</tbody>
</table>

TABLE III. Incidence of Clinically Undiagnosed Carcinoma in Nodular Thyroid Lesions.

<table>
<thead>
<tr>
<th>Hospital of the University of Pennsylvania, 1933-1952</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/1/33-12/31/52</td>
<td>7/1/33-12/31/52</td>
</tr>
<tr>
<td>Nodular Thyroid Lesions</td>
<td>Nodular Thyroid Lesions</td>
</tr>
<tr>
<td>112</td>
<td>1445</td>
</tr>
<tr>
<td>Clinically Undiagnosed Carcinoma 39 (3.5%)</td>
<td>96 (6.6%)</td>
</tr>
<tr>
<td>Non-toxic Nodular Thyroid Lesions</td>
<td>Non-toxic Nodular Thyroid Lesions</td>
</tr>
<tr>
<td>833</td>
<td>1302</td>
</tr>
<tr>
<td>Clinically Undiagnosed Carcinoma</td>
<td>Clinically Undiagnosed Carcinoma</td>
</tr>
<tr>
<td>38 (4.6%)</td>
<td>93 (7.1%)</td>
</tr>
</tbody>
</table>

*One clinically undiagnosed carcinoma in the earlier series occurred in a toxic nodular goiter and 3 in the later series.

 Clinically Diagnosed Carcinomas have been subtracted from the total Nodular Thyroid Lesions.

TABLE IV. Age at Diagnosis.

<table>
<thead>
<tr>
<th>Hospital of the University of Pennsylvania, 1945-1952</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-20</td>
<td>14</td>
</tr>
<tr>
<td>21-30</td>
<td>27</td>
</tr>
<tr>
<td>31-40</td>
<td>31</td>
</tr>
<tr>
<td>41-50</td>
<td>44</td>
</tr>
<tr>
<td>51-60</td>
<td>33</td>
</tr>
<tr>
<td>61-70</td>
<td>25</td>
</tr>
<tr>
<td>71+</td>
<td>11</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
</tr>
</tbody>
</table>

TABLE V. Pathologic Classification of 189 Cases of Thyroid Carcinoma.

<table>
<thead>
<tr>
<th>Hospital of the University of Pennsylvania, 1945-1952</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Low degree of malignancy</td>
<td>138 (72%)</td>
</tr>
<tr>
<td>Maligant Adenoma</td>
<td>25 (13%)</td>
</tr>
<tr>
<td>Follicular</td>
<td>36 (19%)</td>
</tr>
<tr>
<td>Papillary</td>
<td>63 (33%)</td>
</tr>
<tr>
<td>Mixed (Papillary &amp; Follicular)</td>
<td>14 (7%)</td>
</tr>
<tr>
<td>II. Intermediate Degree of Malignancy</td>
<td></td>
</tr>
<tr>
<td>&quot;Adenosarcoma&quot;</td>
<td>36 (19%)</td>
</tr>
<tr>
<td>III. High degree of malignancy</td>
<td></td>
</tr>
<tr>
<td>Spindle cell</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>Round cell</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Giant cell</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>
HORN AND DULL

There is no positive evidence for relating roentgen ray radiation to the development of thyroid carcinoma 20 years later.

NODULAR GOITER

In only 48 per cent of the 174 primary cases in this series (in contrast with 74 per cent in the earlier, smaller series) was there a history of goiter of more than one year's duration. In 20 per cent of the total, the goiters had been present for five years or longer, in some for from ten to more than 30 years. This striking decrease in the proportion of thyroid cancer patients giving histories of long-standing goiters suggests a growing tendency on the part of patient, physician, or both, toward prompt attention to thyroid nodules. It also argues against the long-held dictum that most thyroid cancers arise in pre-existing adenomas, a view that more recently has been challenged.11, 12

PATHOLOGIC CLASSIFICATION

During study of this series, we were impressed by the relatively large number of invasive but exceedingly well differentiated tumors—so well differentiated that they are extremely difficult to recognize as malignant on pathologic examination. Indeed, they may escape such recognition entirely. This has led us to modify our pathologic classification, retaining under the heading of malignant adenoma only those tumors that were both well-differentiated and apparently encapsulated (Fig. 1), and classing as follicular those very well differ-
nancy is concerned, the grouping is very similar to that of the earlier series, although the proportion of tumors of low grade malignancy is somewhat higher.

Review and reclassification of the earlier cases in the light of accumulating experience do not materially change the figures. Of the 20 lesions that were classified as malignant adenomas, two are now not regarded as malignant but are replaced in the totals by two other tumors, which were originally considered equivocal and therefore excluded, but which have metastasized. Nine of the 20 have been reclassified as follicular in accordance with our present thinking.

No purely or predominantly squamous-cell tumors were observed in either of our series, although six carcinomas (three follicular, two papillary and one spindle cell) did show fairly extensive squamous metaplasia. One of the patients with a papillary carcinoma showed limited squamous metaplasia at the time of the initial incomplete removal of her tumor. She was given deep roentgen ray therapy postoperatively. Later recurrence, which proved fatal, was entirely of squamous character. Apart from this case, squamous metaplasia seemed to be incidental and did not appear to have a bearing on prognosis.

METASTASIS

Metastasis is known to have occurred in 54 of these 189 cases (29 per cent). The lymph nodes were involved in 39 cases (21 per cent); the lungs in 17 (9 per cent); the bones in 10 (5 per cent); and other sites three times (2 per cent). This is a slightly lower incidence of total metastasizing cases and of cases metastasizing to bone than in the earlier series (35 per cent and 13 per cent respectively) but the group includes many recent cases and the follow-up is much shorter than in the earlier group. However, the incidence of lymph node spread is higher in the later series (21 per cent vs 15 per cent in the earlier series), a point possibly coinciding with the greater number of papillary and follicular tumors, and the larger number of young patients in the later group.

Sixteen of the tumors that metastasized to lymph nodes were papillary, and an additional five were classified as mixed papillary and follicular. Five papillary tumors and two mixed papillary and follicular tumors metastasized to the lungs, and two predominantly papillary tumors spread to the skeletal system. On the other hand, only one “malignant adenoma” metastasized to the lymph nodes and one to the lungs, whereas three of this group spread to bones. This is entirely consistent with the generally accepted idea that papillary tumors are particularly likely to spread by way of the lymphatics, involving the regional lymph nodes first, and that the so-called “malignant adenomas” tend to invade the blood stream and produce secondary lesions in the skeleton. It is scarcely necessary to add that this “rule” is by no means without exception.

In general, the adenocarcinomas follow the pattern of metastasis of the papillary tumors—eight involving the regional lymph nodes, five the lungs, two the bones, and one the liver. The same appears to hold for the very well-differentiated follicular carcinomas, four of which metastasized to the cervical lymph nodes, and one spread to the lungs. Our earlier experience is essentially parallel to that recorded here. Six of seven “malignant adenomas” that metastasized did so to bone, and five of six metastasizing papillary tumors spread to the regional lymph nodes. One malignant adenoma involved lymph nodes. Subsequent developments in the cases of this earlier group as they were observed over the longer time period covered by the present study also follow this pattern. Four “malignant adenomas,” one follicular carcinoma and one adenocarcinoma metasta-
sized to bone. Pulmonary involvement is known to have occurred also in the case of the adenocarcinoma, as well as with two spindle celled tumors and one papillary carcinoma.

The varied tumors making up the highly malignant group appear equally capable of utilizing the blood vascular system or the lymphatic system for spread.

**Table VI. Five Year Survivals—Carcinoma of Thyroid.**

<table>
<thead>
<tr>
<th>No. Cases first seen 5 years or more ago</th>
<th>Five-year Survivals</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Diagnosed only in Laboratory</td>
<td>53</td>
</tr>
<tr>
<td>II. Diagnosed clinically</td>
<td>59</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
</tr>
</tbody>
</table>

**MULTICENTRICITY**

We have been particularly interested in the incidence of multicentric origin of thyroid cancers because of the very important therapeutic implications. Nine cases of this series are recorded as having shown obvious, apparently discontinuous, multiple nodules. Most of these were bilateral. Undoubtedly there were more, but others are not clearly recorded as such. Of these nine, four were predominantly papillary, one mixed papillary and follicular, two follicular, one an adenocarcinoma, and one of spindle cell type. Of far greater importance are six cases in which multiple foci of cancer were found only upon careful pathologic study. Some foci were so small that they could be seen only with the aid of the microscope. In two of these six cases, both lateral lobes were involved. Four of these tumors were predominantly papillary, one follicular and one mixed papillary and follicular. The percentage incidence of multicentricity is probably meaningless because of the uncertain number of tumors with obvious multiple foci, and probable additional tumors which conceivably might have begun in multicentric foci, but which are observed only after coalescence has occurred. However, the number of papillary (wholly or in part) tumors that prove to be multicentric suggests consideration of singling out this group for treatment by total thyroidectomy.

**RESULTS OF TREATMENT**

This study is not concerned primarily with evaluating methods of treatment. In general, the initial treatment has been surgical—most often lobectomy with removal of the isthmus, but occasionally subtotal or total thyroidectomy. As a rule, neck dissections have been performed only for known lymph node metastases. More recently, incomplete removal of extensive invasive tumors has been performed in selected cases when radioactive iodine therapy is contemplated or seems indicated. The general plan of treatment has usually included postoperative deep roentgen ray therapy, although it has not been routine, being withheld in the case of some well-differentiated, small, apparently localized tumors. In more recent years, I131 has been used for metastases as indicated.

Inasmuch as the current series was begun as recently as January 1, 1945, few five-year follow-ups are included. However, all of the cases in the earlier series have now been observed over a five-year period or longer. Table VI lists the five-year status of all patients first coming under our observation before December 31, 1947. The cases are separated into two groups—Group I, in which the diagnosis was made only on pathologic examination, and Group II, in which the diagnosis was made at least presumptively on clinical grounds or at operation. Of these patients, 97.4 per cent have been followed; the three cases lost to follow-up are not considered in Table VI.
These five-year results are strikingly similar to those previously reported for the smaller series—82 per cent five year survival for cases diagnosed in the laboratory, and 33 per cent for those diagnosed clinically; an overall rate of 52 per cent.

**Table VII. Five Year Survivals—Carcinoma of Thyroid (1947).**

<table>
<thead>
<tr>
<th>No. Cases</th>
<th>5-year Survivals</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Diagnosed in laboratory</td>
<td>17 14 (82%)</td>
</tr>
<tr>
<td>II. Diagnosed clinically</td>
<td>27 9 (33%)</td>
</tr>
<tr>
<td><strong>44</strong></td>
<td><strong>23 (52%)</strong></td>
</tr>
</tbody>
</table>

Five-year end results in 44 cases were presented in our earlier publication (Table VII). The further follow-up of these 44 patients is of great interest. Ten patients who survived 5 years succumbed during the next seven years. Six of these fell in Group II, the diagnosis of carcinoma having been made clinically, and four of the six are known to have died as the direct result of thyroid cancer. Four patients in Group I (diagnosis of cancer made only on pathologic examination) who survived five years, failed to survive 12, all developing metastases. Actually, as noted above, the makeup of this group has been altered slightly—two cases having been considered benign adenomas after review and replaced in the series by two cases originally considered equivocal, but in which metastases have subsequently settled the issue. One of the two added patients has died; the other is one of three patients who can be counted as 12-year survivors, but who have metastases. Table VIII presents the 12-year results in this group of 44 patients.

These figures furnish strong emphasis for the repeated observation that five-year survivals have relatively little significance with regard to thyroid carcinoma. A similar critical attitude should be maintained toward ten-year survival figures, since six patients who died within the 12-year period would have been listed as survivors in a ten-year survival table. In addition, one of the three 12 year survivors now known to have active disease showed no clinical evidence of tumor at ten years.

Of the ten patients who died in the interval between five and 12 years after operation, eight are known to have had extensive metastases of their thyroid carcinomas at the time of death. In three of these cases the tumors were "malignant adenomas"; in two, spindle cell carcinomas; and in one each, follicular, papillary and adenocarcinomas. The other two patients who survived five years, but failed to do so for 12, apparently died of unrelated causes, without evidence of active tumor, although autopsy was not performed in either case. One of these patients had a follicular carcinoma and one an adenocarcinoma. It is to be emphasized that these figures are all survival figures; three of the thirteen patients surviving 12 years are known to have active disease. It might be added that 12 patients who have been under observation less than five years are known to have active tumor, and an additional two with active disease are listed among the five year survivors in Table VI. Table IX gives the five and 12 year survivals according to pathologic classification.

Although there was no clear-cut correlation between five-year results and patho-
logic type in our earlier series, the five-year survivals in this larger group do reflect pathologic classification according to the degree of malignancy. The percentage of five-year survivals was 70 per cent for all the tumors of a low degree of malignancy, 54 per cent for the adenocarcinomas, and 21 per cent for the highly malignant tumors.

**Summary**

A series of 189 carcinomas of the thyroid encountered at the Hospital of the University of Pennsylvania between 1945 and 1952 has been reviewed and compared with an earlier series of 71 cases. The current series represents an incidence of 11.4 per cent among all nodular thyroid lesions treated surgically during an eight-year period and is compared to a 5.5 per cent incidence in the earlier eleven-and-a-half year period. Seven per cent of surgically treated non-toxic thyroid lesions considered benign preoperatively proved to be carcinoma.

A much higher proportion of non-toxic nodular goiters among the total surgically treated cases (50 per cent as compared to 30 per cent in the earlier series) suggests that more patients with nodular goiters are being referred for surgical treatment. This suggestion is strengthened by the fact that history of goiter of long standing is encountered much less frequently in the current than in the previous series. Only 48 per cent of the patients had a history of goiter of more than a year’s duration, as

**Table IX. Five and 12 Year Survivals According to Pathologic Classification.**

<table>
<thead>
<tr>
<th>Pathologic Classification</th>
<th>No. of Patients</th>
<th>No. of Patients</th>
<th>No. of Patients</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>treated more</td>
<td>treated more</td>
<td>treated more</td>
<td>treated more</td>
</tr>
<tr>
<td></td>
<td>5 yrs. ago</td>
<td>5-yr. Survivals</td>
<td>12 yrs. ago</td>
<td>12-yr. Survivals</td>
</tr>
<tr>
<td>Malignant Adenoma</td>
<td>16</td>
<td>9 (56%)</td>
<td>8</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Follicular</td>
<td>19</td>
<td>15 (79%)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Papillary</td>
<td>32</td>
<td>22 (69%)</td>
<td>11</td>
<td>6 (55%)</td>
</tr>
<tr>
<td>Mixed papillary and follicular</td>
<td>3</td>
<td>3 (100%)</td>
<td>12</td>
<td>5 (33%)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>26</td>
<td>14 (54%)</td>
<td>6</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>14</td>
<td>3 (21%)</td>
<td>6</td>
<td>1 (17%)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Tota’s</td>
<td>112</td>
<td>66 (59%)</td>
<td>44</td>
<td>13* (30%)</td>
</tr>
</tbody>
</table>

*Three patients are living with disease.
CARCINOMA OF THE THYROID: A RE-EVALUATION

Contrasted with a 74 per cent in the earlier group. In other respects, including pathologic type, incidence and site of metastasis, five year survival figures, etc., the two series are remarkably similar. Fifty-nine per cent of 112 patients first treated more than five years ago were alive at the end of the five year period. Only three patients were not followed.

The most striking finding of this study is the comparison of the five year survivals in the earlier series, with the 12 year survival figures for the same group of patients. Whereas 52 per cent of the 44 patients first treated at least five years before the 1947 report were alive five years later, only 30 per cent were alive 12 years after treatment, and of the 13 survivors, three are known to have active disease at the time of writing. Even a ten year follow-up cannot be considered adequate for thyroid carcinoma, since six patients in this series who were alive at ten years failed to survive an additional two. All but two of the patients who succumbed in the 5 to 12 year interval are known to have died with disseminated thyroid carcinoma.

In six cases, four predominantly and one partly papillary, careful pathologic study demonstrated multicentric foci, bilateral in two. Although this is a small number of cases, this finding does suggest consideration of the advisability of total thyroidectomy for papillary tumors.

This series, much larger than the earlier one, demonstrates that pathologic type has a direct bearing on prognosis, just as does the extent of disease. It appears that the tumors of a low degree of malignancy differ from the highly malignant lesions, not in being more amenable to "cure," but in running a greatly protracted course.

BIBLIOGRAPHY

AN EXTRAPLEURAL THORACOLUMBAR SURGICAL APPROACH FOR ADRENALECTOMY AND FOR RADICAL RETROPERITONEAL DISSECTION*

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FROM THE DEPARTMENT OF UROLOGY, FRANCIS DELAFIELD HOSPITAL AND THE INSTITUTE OF CANCER RESEARCH, COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS

The need for surgical incisions which provide unobstructed access to retroperitoneal structures has quite naturally been more sharply brought into focus by the increased use of extended dissections for malignant disease arising in this region. Recently, clinical trials of the value of removing essentially normal adrenal glands in patients having disseminated malignant disease, notably prostatic and mammary cancer, have prompted the development of the surgical approach described here. The operation described may well not be original. However, it has proved of value in this institution, and is reported and illustrated for the benefit of others who contemplate similar dissections.

The difficulties attending excision of normal adrenals stem mainly from the location of the glands, their fragility, and the presence of a large central vein which often is short and hard to isolate early in the course of the operation.

A surgical approach which penetrates neither the pleural nor the abdominal serous layers is desirable, particularly when bilateral adrenalectomy is performed.

TECHNIC FOR ADRENALECTOMY

Anesthesia. Inhalation anesthesia of the circle-breathing type is administered through an endotracheal tube. Inadvertent pleural injury is, under such conditions, a minor incident rather than a catastrophic event.

Positioning of Patient. The lateral recumbent position is used. The kidney rest is elevated and the operating table flexed in exactly the same fashion as if nephrectomy through a lumbar incision were contemplated.

Dissection. The incision through the skin begins at a point only 1 cm. lateral to the midline, as identified by the spinous process posteriorly. It is carried in a downward and anterior direction, beginning at the level of the upper border of the tenth rib. As the incision is brought anteriorly, it is lowered slightly until it has crossed the tenth and the tip of the 11th rib. The incision is usually above the anterior termination of the 12th rib. It is continued for a distance of about 6 cm. beyond this point, still in a slightly downward direction toward the umbilicus (Fig. 1A).

The next step in the operation is complete excision of the 12th rib. The rib is not resected, but is disarticulated from the spine and removed in toto. Removal of the 12th rib is begun by exposure of about 2 cm. of the midportion of the rib (Fig. 1B). When the blade has penetrated the peristeum on the outer surface, it is then quite easy to insinuate a grooved director between the rib and the overlying muscles and thoracolumbar ligaments. The grooved director is passed dorsally to the point at which the 12th rib articulates with the spine. The scalpel divides the muscles and ligaments at a single stroke. The muscles include the intercostal attachments and the muscular heads of the serratus posterior in-
SURGICAL APPROACH FOR ADRENALECTOMY

Fig. 1. In (A) dotted lines represent the position and direction of the skin incision. Note that the incision begins almost in the midline posteriorly and continues over the upper border of the 10th rib, past the mid-axillary line, and gradually descends over the tip of the 11th rib as it reaches the abdominal musculature. In (B) the retraction is mainly on the lower skin flap in a downward and dorsal direction, with very little retraction necessary on the upper side of the skin and muscular flap. The 12th rib which is to be excised is seen near its anterior tip. Note the small space of lumbodorsal fascia which represents the beginning point for dissection underneath the oblique and transverse abdominal muscle at a later stage. In (C) stripping of the periosteum from the body of the 12th rib is accomplished, and in (D) the entire rib is being removed following disarticulation posteriorly. The dotted line shown here does not represent the line of further dissection, which actually begins beneath the 12th rib bed in the space referred to in (B).

There are occasionally slips from the erector spinae muscles which are also divided.

When the rib has been completely stripped of periosteum throughout its entire length, it is disarticulated with the scalpel at its spinal joint (Fig. 1, C and D). The underlying nerve is dissected free from its attachments and retracted inferiorly.

Next, the pleura is bluntly teased off the superior surface of the heel of the diaphragm laterally, and allowed to move upward and medially, thereby freeing the posterior attachment of the diaphragm for safer division. Gerota’s fascia is freed from its posterior attachment to the anterior face of the lumbar muscles (Figs. 2 and 3). This is done by finger dissection and is contin-
ued upward under the dome of the dia-
phragm to a point at which it has begun to
descend medially in the region of the vena
cava. In the right-sided operation, the
outer tip and inferior surface of the liver
is exposed and followed by blunt finger
dissection to the outermost tip of the
adrenal gland. Then with the index finger,
a tunnel is made above the diaphragm in

the posterior niche created by pushing the
pleura upward and medially. This tunnel is
continued medially until almost the entire
leaf of the diaphragm has been exposed
both superiorly and inferiorly. Then with
scissors the diaphragm is divided at its
posterior attachment. It is thought to be
important to make the most posterior divi-
sion possible so that, when re-suturing is
undertaken, a wide flap of diaphragm is
free of pleura and can safely be sutured to
the posterior wall (Fig. 4). When the dia-
phragm is sectioned, along with the thora-
columbar ligaments, the thoracic cage can
be collapsed superiority and medially. This
allows the operation upon the adrenal to
continue in a direction at right angles to

the skin incision rather than underneath an
undisturbed thoracic cage. Often the
adrenal is found to lie not more than 6 cm.
beneath the skin.
On the right side it is simplest to continue the infrahepatic exposure in such a way that the upper and outer surface of the adrenal is freed by blunt dissection (Fig. 5). The remainder of the dissection for excision of the adrenal gland is based upon a knowledge of the three sources of arterial blood supply to the structure and the large central adrenal vein. Occasionally vessels of sufficient size to require ligation are encountered in the fibrous bands which run out from the liver to the adrenal. The next step in the dissection is the opening of Gerota’s fascia at a point on the medial aspect of the adrenal itself. The vena cava is exposed for a distance of about 1 cm.; the cava is followed in a cephalad direction until the large central vein is found, isolated, clamped, divided and secured with a silk ligature (Fig. 6, A and B). This step will assure proper hemostasis during the rest of the procedure. The gland is then removed by dividing the periadrenal fat between clamps from the outer and lower corner of the gland medially to the vena cava, without actually clamping or handling the adrenal tissue proper (Figs. 6C and 7). There is some danger of injury to the renal artery and vein on both the right and the left side. It must be remembered that pushing the peritoneum forward and anteriorly does not insure against injury of these vascular structures. It is helpful to palpate the renal artery at intervals during the division of the fat which contains the adrenal arterial branches which are derived from the renal artery. Although the central adrenal vein quite often empties into the renal vein on the left side, this does not materially alter the steps in the dissection. The last maneuver in excision of the adrenal consists of division of the remaining arterial branches which stem directly from the aorta, crossing the vena cava and entering the gland in multiple branches on its medial aspect. This is accomplished in much the same way as those branches from the renal artery are divided earlier in the operation.

The only technical difficulty which is commonly encountered is that of management of the central adrenal vein. The vein on the right side is ordinarily larger and shorter than the one on the left. Occasionally the adrenal gland is somewhat wrapped about the vena cava on the right side, and the adrenal vein is extremely difficult to expose. When this situation is encountered, it is perhaps best not to attempt to clamp or ligate the adrenal end of the vein, but to depend on previous control of the arterial supply before division of the central vein is undertaken. In cases of this sort, an arterial clamp of the Potts type is used and the vena cava closed beneath it with a continuous mattress suture of fine, braided arterial silk.

When the adrenal has been removed, along with a generous portion of its surrounding fat, the repair of the operative incision is begun. The diaphragm is re-es-

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**Fig. 5.** This view shows the cut diaphragm. Almost the entire right leaf is divided, not just the lateral heel of this structure. The tip of the liver is followed as a guide. The inferior surface of the liver is followed in a cephalad and medial direction, with light retraction upon Gerota’s fascial envelope, which still contains both the right kidney and the right adrenal gland.
Fig. 6. The inferior surface of the liver has been followed, and by blunt dissection a short segment of the inferior vena cava exposed. By arbitrarily exposing this segment of vena cava between the upper pole of the kidney beneath the now open fascia of Gerota and the inferior surface of the liver, the central adrenal vein must be encountered. It is shown here as a short segment joining the adrenal to the vena cava, a situation which is quite frequently found. In stripping away the fatty and areolar tissue between the vena cava and the medial border of the right adrenal, the small arterial branches directly from the aorta to the adrenal gland have been separated, ligated and divided. In (A) it is also seen that the arterial branches from the phrenic and from the renal arterial sources are still intact. The central adrenal vein is then clamped, divided and ligated. Next (B) the phrenic arterial branches to the adrenal have been divided and ligated, and in (C) the remaining arterial supply from the right renal artery is being managed. Note the close proximity of the renal vascular pedicle. It is suggested that, before the arterial branches to the adrenal from the renal artery are clamped, careful palpation of the renal artery is indicated to prevent injury to this structure.

Established in its normal position by interrupted medium silk sutures placed deeply through the posterior muscle at the point of division of the diaphragm. Care is taken not to pass the needle, on the visceral side, through the pleura (Fig. 8, A and B). When this row of sutures is completed, no further repair of the thoracic structures is required. The posterior and anterior abdominal musculature is then re-united with interrupted sutures of medium black silk. The subcutaneous and superficial fascial layers are closed with interrupted sutures of 000 plain catgut and the skin with silk. Retention sutures are employed (Fig. 9, A and B).

Even though silk is used in the depth of this incision, a single Penrose drain is left inlying to the deepest point dissected during the operation.
During the past 18 months, this surgical incision has been employed for 57 surgical operations at the Francis Delafield Hospital. Fifty-three of these were adrenalectomies, three were operations for primary renal tumor, and one for testicular cancer.

For testicular and renal tumors, it has been found feasible and convenient to continue the anterior portion of the incision in an upward direction from a point just above the tip of the 12th rib, roughly following the subcostal margin to the xiphoid process. The operation can still be kept extraperitoneal. Division of the rectus abdominis muscle on the involved side is optional.

DISCUSSION

Anterior extension of the incision to the xiphoid process permits ligation of the vascular pedicle early in the operation, a desirable feature when the primary neoplasm has arisen within the substance of the kidney. Although it is possible to visualize and even to dissect beyond the vena cava, and on the opposite side of the aorta when the right-sided approach is used, it is not suggested that this incision be employed when bilateral lymph node dissection is contemplated.

Although this incision has not been employed for retroperitoneal sarcoma and malignancies other than those arising in the adrenal, kidney and testis, it seems quite reasonable to suggest that such a surgical approach be given a clinical trial for retroperitoneal malignancy of other derivations. Since the limiting factor in dissection for retroperitoneal sarcoma is quite often the penetration of the posterior and lateral muscular structures, a fact determined in most instances rather late in the dissection, it would perhaps be of great advantage to the surgeon to determine that this sort of inoperable situation exists before the patient is subjected to a great deal of manipulation and mobilization of tissues, as well as intraperitoneal seeding of tumor. On the other hand, if a truly radical excision of adjacent muscular and fascial structures is to be undertaken in the presence of infiltrating, finger-like projections of sarcoma, the dissection can most easily be initiated from this point of view which is not ordinarily available to the surgeon who operates through an anterior abdominal wall incision.

It seems clear that, in instances in which secreting tumors of adrenal-medullary origin are suspected prior to operation, any incision which permits exposure of only one adrenal at a time is definitely contraindicated. Also, when the operation is of an exploratory nature for hyperplasia or adenoma of the adrenal cortex which may well be bilateral, this incision is not a sensible one. Tumor which has spread secondarily to the adrenal glands or to immediately adjacent structures is, however, not a contraindication to the full employment of this surgical approach. Previous flank incisions, particularly of the ordinary sort used for renal surgery, do not constitute a contra-
Fic. 8. In (A) the first silk suture has been placed to begin closure of the divided dia-
phragm. The posterior flap here is exaggerated, and with proper division it is cut flush against
the quadratus muscle. In (B) the completed line of closure of the diaphragmatic incision and
the direction in which this line runs are clearly shown. Note that at no time during the oper-
ation has it been necessary to expose the anatomical capsule of the kidney. Inspection for
pleural and peritoneal injury is done at this stage.

No originality is claimed for the technic described here. However, we have not en-
countered a description of this precise anatomical approach to the retroperitoneum.
The incision is made throughout its entire length at a much more cephalad level than
those of a similar type described elsewhere. In addition, a great deal more of the total
extent of the diaphragmatic leaf is divided. The other differences include an elective
removal of the entire 12th rib, rather than small segments of several ribs.

The postoperative complications which are peculiar to patients who have had this
kind of surgery have not been impressive. A great deal more pulmonary pathology
was expected postoperatively than has ac-
tually been encountered. A striking post-

indication; on the contrary, a secondary or
tertiary kidney operation can with facility
be performed through this route, primarily
because the incision begins and ends in tis-
sue which has previously not been mobil-
ized. In such cases there are available a
number of anatomical landmarks which
facilitate operations which otherwise
would be difficult because of scirrhous oblitera-
tion produced by previous surgery.

This incision has been employed in
adults only, but Kimbrough has found that
it is quite useful for adrenal operations and
exposure of the region in children. He
states\(^1\) that it is not necessary to divide the
diaphragm in such cases.

\(^1\) Kimbrough, J. C.: Personal communication
to the author.
operative finding is the relative absence of pain, particularly upon deep breathing. One might expect that the extensive diaphragmatic division and resuturing would predispose the patient not only to atelectatic processes in the lower lung on the affected side, but would also precipitate a considerable amount of pain upon deep inspiration. This has not been the case.

The advantages of keeping the surgical dissection extraperitoneal whenever infected or neoplastic tissue may be incised are well known. The advantages of not entering the pleura are similarly apparent. It must, however, be noted that in certain instances the pleura has been violated and re-suturing required. In all instances except one in which this accident has occurred, a tube has not been left in the chest. The procedure which has been followed includes a wider freeing-up of the pleural membrane in order to facilitate secure closure with a continuous silk suture. This re-suturing is performed with the lung expanded through forced breathing managed by the anesthesiologist through the endotracheal tube.

**SUMMARY**

1. An extrapleural and extraperitoneal thoracolumbar surgical incision for adrenalectomy and surgery of other structures in the retroperitoneum is presented.

2. Contraindications to the use of this incision, particularly for secreting tumors of the adrenal medulla and hyperplasias of the adrenal cortex, are cited.

3. Clinical experience with this incision in 57 surgical operations is briefly reviewed.

4. The low incidence of serious postoperative complications and pain due primarily to the type of surgical entry is noted.
LYSIS OF THROMBI PRODUCED BY SODIUM MORRHUATE IN THE FEMORAL VEIN OF DOGS BY HUMAN PLASMIN (FIBRINOLYSIS)*

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Thrombosis and embolism remain one of the serious complications and sources of morbidity and mortality in patients subjected to surgery, and in the many diseases of the older age groups, despite extensive studies of their mechanism of production and methods of control.

To the present time, treatment of intravascular thrombosis has consisted of methods of preventing embolism or further thrombosis by ligation of veins or by the use of chemical agents such as heparin, dicumarol, tromexan and others. No method of lysis of thrombi already formed has as yet been established, although recent studies in experimental animals with streptokinase, and in animals and patients with trypsin, have been reported.

With the preparation and partial purification of human plasminogen (Profibrinolysin) from Fraction III of human plasma, a material theoretically ideal for this purpose has been made available for investigation. We have found this material, in very low concentrations, to be actively fibrinolytic in vitro; and in vivo studies in rabbits and dogs have shown it to be relatively nontoxic and nonlethal in doses much larger than those producing marked physiological effects. Previous studies have shown conclusively that injection of this material into the general circulation will result in lysis of intravascular thrombi in the veins of the rabbit's ear. The results of our studies on the lytic effect of this material on experimentally produced thrombi in the femoral vein of dogs are reported in this paper.

In the study of intravascular lysis of thrombi in animals, one of the problems has been the establishment of an effective reproducible method of producing thrombi. In general, it may be said that in experimental animals, no satisfactory method of production of thrombi, other than by severe mechanical or chemical trauma to blood vessels, has been reported. Although Wessler recently reported production of small thrombi in isolated venous segments, these were not solid, adherent thrombi. Thrombosis has been produced in experimental animals by mechanical trauma, supplicative infection, chemical irritants, and by the injection of thromboplastic substances. Of these, sodium morrhuate has been most consistent.

In previous experiments with rabbits, we were able to produce thrombi with bovine thrombin, but this was not 100 per cent successful. Thrombosis was produced in distant organs and the thrombi were not sufficiently persistent. In dogs, we have been unable to produce intravenous clots....

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LYSIS OF THROMBI PRODUCED BY SODIUM MORRHUATE

Fig. 1. Changes in the clotting time and the spontaneous in vitro clot lysis of whole blood in normal dog No. 8, to which 80 ml. (2.8 mg./Kg.) Plasmin were given. In this, as in all subsequent graphs, the abscissa represents the time in hours, and there are three sets of ordinates: One is the amount (0 to 20 ml. inverted) of plasmin in milliliters given (each full column indicates 20 ml. of plasmin); the second is in minutes for the clotting time (Lee White method); and the third is the time in minutes in which spontaneous in vitro lysis of the blood clot appeared. In this latter (upper) graph the time is inverted, since the shorter the time of lysis, the greater the lytic activity.

Fig. 2. Changes in the clotting time and the spontaneous in vitro clot lysis observed in normal Dog No. 9, to which 160 ml. of plasmin were given. Note that the clotting time initially dropped, then as the lytic activity of the blood increased markedly, the blood became incoagulable. This occurred after one hour. The next day the clotting time and lytic activity were normal.

Fig. 3. Changes observed in Dog No. 2. Two thrombi had been formed, one in the femoral vein and one in a tributary. The abscissa and the ordinates are similar to the previous graphs. The time of lysis of the clots are indicated by the arrows marked small and large. The small thrombus lysed in 30 minutes and the large one in the common femoral vein in one hour after the appearance of an active lytic system in the blood.

Fig. 4. Changes observed in the clotting time and the in vitro spontaneous lytic activity of the blood in Dog No. 12, in which plasmin was given 24 hours after the formation of a thrombus in the femoral vein. The abscissa and ordinates are as in the previous graphs. Note that the clotting time changed very little in this animal. A total of 180 ml. of plasmin were given and the thrombus lysed in three hours. As in the previous graphs, the arrow indicates the time of clot lysis.

with thrombin with any consistency. With sodium morrhuate, however, we have produced adherent clots in 100 per cent of the rabbits" and the dogs treated as described in methods to follow.

Many studies have been made of the effect of known drugs in causing lysis of preformed clots in experimental animals. Heparin has been shown to have some thrombolytic effect in early thrombi.11, 13, 14 Tromexan, administered over a long period of time, has been found to promote recanalization of thrombi in rabbit's ear veins,18 in the femoral vein of dogs,5 and in the femoral artery of rabbits.19 Trypsin, administered over a long period of time, has been
shown to lyse thrombi in veins of rabbits and dogs. This is difficult to explain, since it is common experience that trypsin produces intravascular thrombosis. It is possible that this lytic effect of trypsin is due to its activation of plasminogen, since this is a known effect of trypsin. Streptokinase, the best known activator of human plasminogen, has also been reported to produce lysis of clots in rabbits when used in large doses over a long time interval.

**Table I. Number of Animals Used and Maximum Amount of Human Plasminogen/Kilogram of Body Weight Given Intravenously During Experiment.**

<table>
<thead>
<tr>
<th>Normal Dogs</th>
<th>Number</th>
<th>Maximum Amount Plasminogen/Kg. Body Weight</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6</td>
<td>4.9 mg./Kg.</td>
<td>0</td>
</tr>
<tr>
<td>Dogs with Thrombus</td>
<td>9</td>
<td>5.1 mg./Kg.</td>
<td>0</td>
</tr>
</tbody>
</table>

**Materials and Methods**

**Animals**

Fifteen adult mongrel dogs in good health and kept under routine laboratory conditions.

**Materials**

1. Nembutal Veterinary: 65 mg./ml.
2. Sodium Morrhuate: 5 per cent solution
3. Streptokinase (SK-SD)*: Streptokinase 100,000 units, Streptodornase 25,000, dissolved in 10 ml. of sterile saline. Two ml. of this solution were added to every 20 ml. of plasminogen used. Therefore, 20,000 units streptokinase and 5000 units streptodornase were present in each 22 ml. of plasmin solution.
4. Plasminogen: Prepared in our laboratory by a previously reported method from Fraction III of human plasma. Concentration used: 0.35 mg./ml. activated with 1 ml. SK-SD to 10 ml. plasminogen.

**Methods**

The femoral vein was exposed in the dog by a standard incision parallel to the vein.

Under direct vision, bulldog clamps were placed on the vein and its tributaries, isolating a 3 cm. segment. The blood was aspirated and 0.3 ml. of 5 per cent sodium morrhuate was then injected into the lumen. Ten minutes later the distal clamp was removed to permit filling of the vein with blood, and then reapplied. The clamps were left in place for two hours and then a partial flow of blood was permitted by releasing the distal clamp. A firm adherent thrombus, which completely occluded the vein and distended it, was formed in all animals. In eight dogs, this occurred within two to three hours, and in the other, within 24 hours. The thrombosis extended well beyond the area treated to include distal tributaries, with a total thrombus length of at least 6 cm. In several animals two thrombi were formed, a large one in the common femoral vein and a small one in a small tributary of the superficial femoral vein.

At varying times after the thrombus formation, 30 minutes in two animals, one hour in two others, and 24, 48 and 72 hours in five others, plasmin was injected into a foreleg vein. Plasmin (active fibrinolysin)
TABLE II. Dogs in Which Thrombus Was Formed in the Femoral Vein.*

<table>
<thead>
<tr>
<th>No.</th>
<th>Wt.</th>
<th>Thrombus Length</th>
<th>Time after formation thrombus</th>
<th>Duration of Plasmin Admin.</th>
<th>Lysis Thrombus Time</th>
<th>Plasmin per Kg.</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>11</td>
<td>Small 1 cm.</td>
<td>30 min.</td>
<td>2.5 hrs.</td>
<td>55 mins.</td>
<td>4.9 mg.</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>Large 2 cm.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>12</td>
<td>Large 3 cm.</td>
<td>1 hour</td>
<td>42 mg.</td>
<td>1 hr. 50 min.</td>
<td>0.7 mg.</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>11</td>
<td>Small 1 cm.</td>
<td>1 hour</td>
<td>40 mg.</td>
<td>1 hr. 15 min.</td>
<td>3.5 mg.</td>
<td>Temporary</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
<td>Large 8 cm.</td>
<td>72 hours</td>
<td>35 mg.</td>
<td>3 hrs.</td>
<td>2.8 mg.</td>
<td>None</td>
</tr>
<tr>
<td>12</td>
<td>15.4</td>
<td>Large 8 cm.</td>
<td>24 hours</td>
<td>63 mg.</td>
<td>2 hrs. 30 min.</td>
<td>4.0 mg.</td>
<td>Wound ooze temporary</td>
</tr>
<tr>
<td>13</td>
<td>6.8</td>
<td>Large 7 cm.</td>
<td>24 hours</td>
<td>35 mg.</td>
<td>2 hrs. 30 min.</td>
<td>5.1 mg.</td>
<td>Wound ooze</td>
</tr>
<tr>
<td>14</td>
<td>11.8</td>
<td>Large 6 cm.</td>
<td>24 hours</td>
<td>42 mg.</td>
<td>3 hrs.</td>
<td>3.5 mg.</td>
<td>None</td>
</tr>
<tr>
<td>15</td>
<td>11.3</td>
<td>Large 6 cm.</td>
<td>48 hours</td>
<td>49 mg.</td>
<td>4 hrs.</td>
<td>4.4 mg.</td>
<td>Wound ooze</td>
</tr>
</tbody>
</table>

*List (by number) of dogs given Human Plasmin after a thrombus had been formed in the femoral vein. The body weight in kilograms, the time and lengths of the thrombus formed in the femoral vein, the time after formation that the Plasmin was given, the amount and rate of plasmin administration, the amount in milligrams of plasmin per Kg. body weight and the time it took for thrombus lysis to occur are recorded. Side effects such as oozing from the wounds are also noted.

TABLE III. Dogs Showing Occurrence of Lysis of Thrombus.*

<table>
<thead>
<tr>
<th>Plasmin Given in mg.</th>
<th>Time Plasmin Given in Hrs.</th>
<th>Time needed for lysis</th>
<th>Plasmin per Kg. body weight</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum...............</td>
<td>63 mg.</td>
<td>4 hrs.</td>
<td>4 hrs.</td>
<td>5.1 mg.</td>
</tr>
<tr>
<td>Minimum................</td>
<td>35 mg.</td>
<td>1½ hrs.</td>
<td>55 min.</td>
<td>2.8 mg.</td>
</tr>
<tr>
<td>Average................</td>
<td>44 mg.</td>
<td>2½ hrs.</td>
<td>25½ hrs.</td>
<td>4.0 mg.</td>
</tr>
</tbody>
</table>

*List of the maximum, minimum and average amounts of plasmin in mg. given to the eight dogs where lysis of the thrombus occurred in the femoral vein. The time period of administration, the time needed for lysis and the amount of plasmin per Kg. body weight are also recorded.

was used in the concentration of 0.35 mg. per ml.

Before injection of plasmin was begun, the wound in the thigh was reopened to observe the extent and type of thrombus. In four animals, phlebography, using Urokon (20 ml.) or 35 per cent Diodrast (20 ml.), was done before and after lysis. In two other animals, sections were taken before treatment and after the lysis in the vein for histological demonstration. A tributary vein was used for the preliminary section, and the main trunk for the final section. A vein from a control animal was used for comparison.

The condition of the wounds was observed and any unusual bleeding was noted and described.

The coagulation time of the blood drawn from a distant vein was determined by the Lee-White method, and the spontaneous whole blood clot lysis time was also determined at standard intervals.

The healing of the wound in the thigh after treatment was observed daily until complete. No abnormalities of healing were noted.

RESULTS

The maximum quantity of plasmin used in this series of experiments was 5.1 mg./Kg. in the animals in whom thrombi had been produced (Table I). None of these animals showed any serious reaction other than mild to moderate oozing of blood from the fresh wounds. All animals
survived in good health until the time they were sacrificed, up to six months after treatment.

**Studies of Clotting and Lysis of Clots in Vitro.** In the group of six animals, where no sodium morrhuate was injected and no thrombus was produced, the effect of plasmin on the clotting mechanism of the blood was studied. The anesthetised animal did not show any unusual reaction or toxic effect of the plasminogen. However, in those animals where there was a fresh operative wound in the femoral area, created for the purpose of venipuncture or observation of the thrombosed vein, there was a mild to moderate oozing of blood from the raw surface when over 3 mg. of plasmin/kilogram had been administered. This ooze was temporary, ceased when the wound was sutured, and in all instances the wound healed well without hematoma formation or infection.

In most animals the clotting time lengthened soon after the administration of plasmin, and remained elevated for the duration of the experiment. In a few animals the clotting time was shortened. The *in vitro* spontaneous whole blood lysis time was used as an index of the fibrinolytic activity of the blood. Spontaneous lysis appeared within 30 minutes of the beginning of the administration of plasmin in the usual quantities, remained elevated for at least one hour after the last dose of plasmin, and returned to normal activity within two to 24 hours.

![Fig. 6](image-url)

**Fig. 6**

Fig. 6. Tributary of the femoral vein of Dog No. 10, in which a thrombus had been produced with sodium morrhuate one hour before the administration of plasmin. Biopsy of vein taken after lysis had been produced by the plasmin. Note the small fragment still attached to the intima.

**Fig. 7**

Fig. 7. Femoral vein of Dog No. 10, in which a thrombus had been produced with sodium morrhuate one hour before the administration of plasmin. Biopsy of vein taken after lysis of the thrombus.

Observations on two dogs are given in detail, as an example of the results in all animals. Dog No. 8 (control) was given 80 ml. (2.8 mg./Kg.) of plasmin. A marked drop in the clotting time from 5 minutes to 30 seconds was noted and there was a concomitant appearance of spontaneous lytic activity in the blood. This spontaneous lytic activity appeared within 15 minutes of the onset of the first injection of 20 ml. of plasmin, and persisted until about 45 minutes after the administration of plasmin was discontinued (Fig. 1). A mild ooze of blood from the femoral incision was noted, which ceased within 45 minutes, and the dog was well afterwards.

The second control animal (No. 9) was given 160 ml. (4.9 mg./Kg.) of plasmin. In this animal, the clotting time was first shortened as in dog No. 8, then with rapid injection of a larger quantity of plasmin, this trend was reversed. After 60 ml. of
plasmin had been given in 40 minutes, the clotting time rose very sharply and the blood became incoagulable and remained so for the remainder of the experiment except for one drop to a normal clotting time (Fig. 2). The spontaneous lytic activity of the blood increased very rapidly, and after one hour the lysis of the clot was immediate. This high fibrinolytic activity persisted for the remainder of the experiment, but the next day it had returned to normal, as had the clotting time. This animal also recovered in a normal fashion and appeared alert, active and normal.

These findings confirm our previously reported results of a marked increase of fibrinolytic activity of the eu-globulin fraction of the blood of dogs receiving plasmin intravenously.2

The same studies of clotting time and clot lysis time were made on several animals in which thrombi were produced by sodium morrhuate.

Figure 3 represents the changes observed in an animal (Dog. No. 2) where two thrombi had been formed in the femoral vein and a tributary. The small thrombus lysed in 30 minutes and the large one in one hour after the appearance of an active lytic system in the blood. This animal also showed a shortened clotting time, as had Dog No. 8, an increased lytic effect was observed.

The effect of plasmin in Dog No. 12, which had a 24-hour old thrombus in the femoral vein, is shown in Figure 4. The clotting time was first shortened slightly, then rose to above normal. The thrombus lysed in three hours after the animal had received 4.0 mg. plasmin/Kg. body weight. There was oozing of blood from the wound in the thigh of this animal, but this ceased spontaneously, and the next day his clotting time was normal and spontaneous lysis of the in vitro clot was absent.

Lysis of Thrombi in the Femoral Vein. In all eight dogs, where an adequate amount of plasmin was used, lysis of the thrombus in the femoral vein occurred (Table II). From this table one can see that when there were two thrombi present, one small and one large, the small one lysed first. The average amount of plasmin used was 4.5 mg. per kilogram of body weight. The minimum amount of plasmin which resulted in lysis of a clot was 2.8 mg./Kg., and the maximum needed was 5.1 mg./Kg. Lysis occurred in one to four hours, depending on the rate of injection,
and on the age and size of the thrombus. In the one animal where the thrombus did not lyse, only 0.7 mg. per kilogram of body weight was given, an amount of plasmin obviously insufficient to effect a clot lysis in vivo. Incidentally, this was one of the two short term (30 min.) thrombi in which lysis was attempted. From these few experiments, there would appear to be little difference between thrombi one hour old, and thrombi 24, 48 or 72 hours old, so far as their response to plasmin is concerned. Actually the 72 hour old clot was lysed completely, albeit only temporarily, by the smallest amount (2.8 mg./Kg.) of plasmin to produce complete lysis of a thrombus.

In Table III are given the general statistics for the eight animals in which intravascular lysis occurred. In one animal a thrombus (incidentally the oldest [72 hours]) was lysed with as little as 2.8 mg. plasmin/Kg., while the maximum amount needed for a 24-hour-old clot was 5.1 mg. plasmin/Kg. The thrombi in the small veins, 4 mm. in diameter and 1 to 2 cm. long, lysed in about one hour, while those in the common femoral vein 8 mm. diameter and 5 to 8 cm. long required 2 to 4 hours. There was no mortality from the use of the enzyme in these animals.

The patency of the femoral veins before and after lysis of the clot was determined by direct observation of blood flow through the vein in all cases. In three cases this was supported by biopsy of the vein and in four animals by phlebograms. Phlebograms were done before and after lysis of the thrombus.
and 24 hours and two weeks after lysis, in order to determine whether a thrombus had reformed.

Figure 5 is a photomicrograph of a control vein with a thrombus formed by the use of sodium morrhuate. Figure 6 is a photomicrograph of the small vein in Dog No. 10 after lysis had taken place following the use of plasmin. A photomicrograph of the common femoral vein, taken after the lysis of the thrombus in this larger vein of the same animal, is shown in Figure 7. In both these sections it can be seen that the vein has become completely patent, with a few fragments of thrombus still adherent to the intima.

The use of phlebograms gave a clear demonstration of the state of obstruction or patency of the femoral vein. Figure 8 is a phlebogram of the femoral vein of Dog No. 12, 24 hours after production of the thrombus in the left femoral vein. The complete block of flow of contrast medium through the previously obstructed area can easily be seen (Fig. 9). The wound was then sutured, and 24 hours later another phlebogram was taken, which demonstrates that the femoral vein was still patent and that the thrombus had not yet reformed, in spite of the absence of spontaneous lysis of the in vitro blood clot (Fig. 10). A fourth phlebogram in this animal two weeks later showed obstruction of the femoral vein at the site of the original thrombus formation. This dog was sacrificed, and autopsy revealed that the femoral vein lumen was patent, but compressed by dense scar tissue around it, the result of the sodium morrhuate injected.

In Dog No. 13, plasmin was given when the thrombus in the femoral vein was 24 hours old. This thrombus was 7 cm. long and extended down into the branches of the femoral vein. A phlebogram showed complete occlusion of the common femoral vein before the administration of plasmin (Fig. 11). The animal was given 5.1 mg. plasmin/Kg. body weight over a period of two hours, and at the end of this time the thrombus lysed. The only side effect was some mild oozing from the wound, but this stopped as soon as the wound was sutured, and the animal recovered in normal fashion. The phlebogram, taken after the lysis had occurred, clearly demonstrated the free flow of contrast medium through the previously obstructed femoral vein (Fig. 12).

Most of the animals were sacrificed one to three months after the experimental lysis of thrombi, and only one of these showed any evidence of old hemorrhage or any other unusual findings. In this animal (Dog No. 12) an old hematoma (4 cm. in diameter) was found in the gastric wall, along the greater curvature in the midportion of the stomach. A few focal hemorrhagic areas 3 mm. in diameter were noted in the myocardium of this same animal. This animal had been asymptomatic and clinically well. In none of the animals was there any evidence of embolic phenomena or pulmonary infarcts, either in the course of the experiments, during the survival periods of the animals, or in the complete autopsies.

_Lysis of an Arterial Thrombus._ In one animal a thrombus was formed in the femoral artery which had been cannulated for the collection of blood samples. This thrombus lysed when 3.5 mg. plasmin/Kg. body weight had been administered to the dog over a period of two hours. This is the only instance of an intra-arterial thrombus in this series. One other animal treated in another laboratory had a femo-
ral artery thrombus produced with sodium morrhuate, which lysed after the administration of plasmin.*

DISCUSSION

The results reported in this paper, lysis of thrombi up to 72 hours old within the femoral vein of the dog, in from one to doses, becomes incoagulable. However, on only one animal was there evidence at post-mortem of any significant hemorrhage, in this case, into the wall of the stomach. The fact that rather heavy wound ooze ceased immediately upon closure of the wound leads one to the probable explanation that this lack of bleeding into tissues is due to

four hours, support the previously reported results with thrombi in the marginal vein of the rabbit's ear. In addition, it has been shown that arterial thrombi react in the same way to systemic administration of activated human plasminogen (plasmin).

Complications were few and not serious. One might expect that bleeding would be a serious complication, since the blood collected lysed very rapidly and, with large

the presence of inhibitors in the tissue juices themselves.

Another serious difficulty that might be expected with rapid lysis of clots would be the freeing of emboli into the blood stream: this has been shown not to occur. If the material were injected directly into a vein distal to the clot, this could conceivably happen, but with the injection into the general blood stream, the lytic effect must act from the periphery of the clot. This is beautifully illustrated by observing the clots as lysis is taking place. First, the tip of the clot softens and begins to disappear, then the distention of the vein lessens and
the whole clot becomes softer. Oozing of blood from the needle wounds in the vein now occurs. Then in a few minutes the clot melts away completely, and a free flow of blood is observed in the vein. Even if a small segment of clot should be broken off, the marked lytic activity in the blood, probably greater than at the interface with the main clot, would make quick work of its dissolution.

The re-occlusion of the veins following the loss of the plasmin, we feel, is to be expected, because of the serious trauma to the vein, both chemical and mechanical. The surprising fact is that some stayed open for more than 24 hours, as shown by venograms. The fact that at postmortem several weeks later the lumen of some of these veins was free of clot, with the obstruction due to compression of scar from the outside, is to us even more unexpected. In practice, reformation of clots would be less likely because of the absence of severe chemical and mechanical trauma, and further protection could be furnished by the use of anticoagulants.

The fact that this material remains active in the animal organism for only a few hours at most would be an additional safety factor in possible clinical use, in case hemorrhage were a complication. Since no chemical inhibitors are known at present, this ability of the body to inactivate or inhibit the material would have to be depended upon to control its activity. In all animal species studied (dog, rabbit, cat and monkey), this control has been more than adequate.

In all animals studied to date, and in studies of local use of this material in human patients, no serious allergic or anaphylactic manifestation has been observed.

SUMMARY

Thrombi were produced in the femoral veins of nine dogs by the use of sodium morrhuate. In eight of these dogs, the thrombi were completely lysed by general systemic injection of 2.8 to 5.1 mg./Kg. of human plasmin. The one animal in which lysis did not occur received only 0.7 mg./Kg., an obviously inadequate dose. Lysis occurred in one to four hours, and the veins remained patent for at least 24 hours in some animals.

No deaths occurred in 15 dogs studied, and no serious complications occurred. A slight to moderate ooze of blood was evident in fresh wounds, but this ceased with closure of the wounds, and in only one instance was there evidence of bleeding into other tissues. No emboli were apparent.

A marked increase in spontaneous lytic activity was observed in the whole blood of all animals studied. In most animals there was a prolongation of clotting time, although some receiving the smaller amounts showed a shortening of the clotting time.

BIBLIOGRAPHY

In 1951, Moore and I described a case of pseudocyst of the pancreas successfully managed by Roux-Y cystjejunostomy and briefly reviewed the literature concerning internal drainage of pancreatic cysts. It was pointed out at that time that internal drainage was still looked upon with pessimism by certain authors, and that marsupialization was still being recommended as the preferred procedure. On the other hand, it was our feeling that internal drainage had much to commend it and that the use of a Roux-Y jejunal limb was ideal from the standpoint of ease of execution, dependency of drainage, and minimal risk of infection from regurgitation of intestinal contents into the cyst. It is the purpose of this report to describe experiences with the management of five consecutive cases by this method.

Case 1. The patient was a 31-year-old female who was involved in an automobile accident on July 23, 1950. She was said to have been unconscious for 11 days and, in addition to the head injury, she sustained multiple fractures of ribs, a fracture of the transverse process of the first thoracic vertebra, and a fracture of the right humerus, with concomitant radial nerve paralysis. Three or four weeks later she noticed an upper abdominal mass which subsequently continued to increase in size. She developed nausea, vomiting and severe abdominal pain, and was admitted to the hospital on September 15. There was a large epigastric mass and considerable abdominal tenderness. Radiologic studies showed that the stomach was displaced anteriorly and the transverse colon caudally. Serum amylase was 652.

She was operated upon on October 5. A very large pancreatic cyst was encountered. It bulged through the gastrocolic and gastrohepatic ligaments. The cyst was unilocular and contained 2,000 cc. of fluid, the amylase content of which was 1,078. An antecolic end-to-side anastomosis was made between an 18-inch long Roux-Y jejunal limb and the cyst wall. She had an uneventful convalescence and the mass was never palpable thereafter. Serum amylase was 103 on November 11, and 69 on December 5. Except for one brief episode of nausea and vomiting on November 11, she remained free of symptoms. When last seen, one year after operation, she was well and there was no evidence of recurrence of the cyst. The final diagnosis was traumatic pseudocyst of the pancreas.

Case 2. The patient was a 51-year-old white female, who was admitted to the hospital on June 30, 1951, complaining of abdominal pain. She had had epilepsy for 37 years and had had some abdominal pain off and on for 19 years, not associated with nausea or vomiting. Six weeks before admission there was an onset of rather severe upper abdominal pain, nausea and vomiting. Four weeks later the pain became so severe she was admitted to another hospital where she was told that she had cholelithiasis and that an operation would be required. She was discharged for a period of rest prior to operation.

On the day of admission she had severe pain in the epigastrium and left hypochondrium, radiating through to the back on the left side. She was rather obese and appeared to be in acute distress. There was considerable epigastric tenderness and a definite mass could be palpated in the epigastrium, extending down to the level of the umbilicus. The temperature was normal and there was no leukocytosis. The following day she was given 400 mg. of tetraethyl ammonium chloride, with transient diminution of her pain. Fasting serum amylase was 952. Values one-half, one, one and one-half, and two hours after administration of prostigmine were 832, 654, 1130, and 916. Calculae in the region of the gallbladder were visible on a plain abdominal roentgenogram. A barium enema showed displacement downward of the transverse colon by the epigastric mass, and barium swallow revealed anterior displacement of the stomach. She remained afebrile. The abdominal mass was thought to become smaller, but she continued to have abdominal pain and tenderness.
She was operated upon on July 6. There were numerous fat necroses throughout the omentum and mesentery. The gallbladder appeared diseased, with acute and chronic inflammation, and contained stones. The pancreas seemed diffusely enlarged. A cholecystectomy was performed and the common duct was explored with ease through the stump of the cystic duct. No stones were found be passed into the duodenum. Because of massive edema of the wall of the duodenum and the adjacent fat and mesentery, it was thought inadvisable to open the duodenum in order to section the sphincter of Oddi. The common duct was drained by a catheter introduced through the stump of the cystic duct. Microscopically, the excised gallbladder showed evidence of acute and chronic inflammation, and there were numerous stones within it.

She had a relatively uneventful convalescence, but continued to have pain; the mass was still palpable in the epigastrium. Bile drained well from the catheter. Serum amylase was 721 on July 7; 1,071 on July 10; 1,108 on July 12; and 1,565 on July 23. She was reoperated upon July 25. There was still present some evidence of fat necrosis. In contrast to the situation at the time of the first operation when there seemed to be only diffuse enlargement of the pancreas, there was now present a large cystic mass in the lesser peritoneal sac. The wall of this cyst was exposed through the gastrocolic ligament in its most dependent portion, and 1,000 cc. of fluid were removed from it. The end of a Roux-Y jejunal limb approximately 18 inches in length was anastomosed to the side of the unilocular cyst.

Her convalescence was uneventful. The catheter in the common duct was removed on August 2, and the patient was discharged from the hospital on August 6. At this time she was completely free of pain. Two days after operation the serum amylase was 362. On August 4 it was 233, and on August 6, it was 78. Gastro-intestinal roentgenograms made on August 2 showed no displacement of the stomach, as has been noted before operation.

The patient was readmitted to the hospital on August 18, with the story that she had had a great deal of generalized abdominal pain since her return home. The following day she had two grand mal seizures. She was severely depressed. Electroencephalographic studies were abnormal, and were interpreted as compatible with epilepsy. Physical examination was essentially normal, as were various laboratory studies, including several determinations of serum amylase. She gradually improved and was discharged on September 19 on tridione and phenobarbital medication. She was seen at fairly frequent intervals during the next 14 months and remained free of seizures and of gastro-intestinal and abdominal complaints. When last examined in September, 1953, 2½ years after operation, she said she was having occasional grand mal seizures and from time to time was depressed. She had had no gastro-intestinal symptoms and there was nothing to suggest recurrence of the cyst. The final diagnosis was post-pancreatitis pseudocyst.

Case 3. The patient was a 3-year-old white boy, who was admitted to the hospital on February 2, 1952. At the age of 2 he had had a previous admission for bilateral subdural hematomas which were treated successfully by operation. He had been admitted on a second occasion in January, 1952, because of vomiting of 3 days' duration, associated with an upper respiratory infection. At the time of his final admission the boy's foster mother stated that she had always thought his abdomen was somewhat distended, but that it had become more so on January 31, and that on this day he began to vomit everything he ate. He continued to have bowel movements. His temperature rose to 104.6° on February 1, and he became semistuporous. At the time of his admission his temperature was normal. His abdomen was distended and tympanic, except for the left hypochondrium, which was dull to percussion, though no mass was definitely outlined. The distention decreased with enemas and it was then possible to palpate a smooth, firm mass of large size occupying the epigastrium and left hypochondrium. Intravenous pyelograms revealed normal appearing kidneys. The mass in the upper abdomen was anterior to the left renal shadow. Barium studies showed the transverse colon to be displaced caudally, the stomach anteriorly. Serum amylase was 669.

Operation was carried out on February 16. A large, tense cyst was found in the lesser peritoneal sac. The cyst was unilocular and contained 800 cc. of straw-colored, cloudy fluid. The free limb of ten-inch long Roux-Y jejunal anastomosis was sutured to the side of the cyst wall through the transverse mesocolon. The patient did well and the mass was no longer palpable after operation. Serum amylase was 87 mg. on February 19. Just as he was ready for discharge, however, he developed bilateral parotid swelling, and by March 3 it was obvious that he had mumps. He was kept in the hospital until March 14, at which time he was quite well. He has been followed frequently since his discharge and has had no gastro-intestinal complaints nor has there been evidence of recurrence of the hypogastric mass. Serum amylase determinations in April and May, 1952, were normal. A gastro-intestinal barium study showed the upper...
A case has been reported of a patient who was admitted to the hospital on March 15, 1953, with the chief complaint of footdrop and numbness on the outer aspect of the right leg and dorsum of the foot of 4 weeks' duration. He was told that it was thought preoperatively that he had cholecystitis, but that at the time of operation it was evident that he had acute pancreatitis. He had an uneventful convalescence. Evidence of right peroneal paralysis developed insidiously during the third week of February.

In addition to the peroneal paralysis, physical examination at the time of admission revealed a large, round, fluctuant epigastric mass. Serum amylase was 312 mg. per cent. The glucose tolerance test was normal. Gastro-intestinal roentgenographic studies showed displacement of the stomach anteriorly, widening and downward displacement of the duodenal loop, caudal depression of the transverse colon, and posterior dislocation of the descending colon.

He was operated on March 20. A very large cystic mass was found in the lesser omental cavity. It contained approximately 2,000 cc. of brownish fluid, which subsequently was shown to have an amylase content of 3,871 mg. of reducing sugar per 10 cc. A Roux-Y anastomosis was made, the free limb being approximately 6 inches in length. A longer limb could not be constructed because the mesentery could not be divided further down due to the fact that the pancreatic cyst itself protruded between the leaves of the jejunal mesentery. An end-to-side anastomosis was created between the jejunal limb and the wall of the cyst through the transverse mesocolon. The patient had an uneventful convalescence and was discharged from the hospital on April 9. Serum amylase was 74 on April 2.

No mass has been palpable since the time of operation. At the time of operation, the gallbladder was small and no stones were palpable. When seen on April 30 and again on May 15, the patient stated that he had had some attacks of abdominal pain radiating to the back on the right side. Cholecystograms on May 8 revealed no concentration of dye in the region of the gallbladder. On May 29 he said that he had been free of all complaints for the past 3 weeks. In a letter of June 15 he stated that he continued to be free of pain. Oral cholecystograms in October revealed no visualization of the gallbladder. Genetic-intestinal studies were normal. The displacement of stomach and duodenum noticed before operation was no longer evident. The patient was free of symptoms and no abdominal mass was present. The final diagnosis was post-pancreatitis pseudocyst.

Case 5. The patient was a 52-year-old white male, who was admitted to the hospital on March 15, 1953, with the chief complaint of footdrop and numbness on the outer aspect of the right leg and dorsum of the foot of 4 weeks' duration. He had been operated upon on December 18, 1952, because of acute upper abdominal pain. He was told that it was thought preoperatively that he had cholecystitis, but that at the time of operation it was evident that he had acute pancreatitis. He had an uneventful convalescence. Evidence of right peroneal paralysis developed insidiously during the third week of February.

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HARRIS B. SHUMACKER, JR.

DISCUSSION

Sporadic reports of efforts to treat pancreatic pseudocysts by internal drainage have appeared in the literature since this principle was first advocated in 1921 by Jedlicka. He suggested anastomosis of the cyst to the stomach. Drainage of the cyst into the gallbladder was proposed by Walzel, into the duodenum by Kerschner, and into the jejunum by Hahn. Because of its anatomic location and its mobility, the jejunum is ideal for such use. The employment of the free limb of a Roux-Y jejunal anastomosis would seem the most satisfactory procedure from the standpoint of ease of performance, drainage of the most dependent portion of the cyst and freedom from threat of infection of the cyst cavity through regurgitation of intestinal contents.

In 1946 König described a case treated by this method, and in 1948 three single case reports utilizing this technic were published by Gurwitz and Hurwitz, Migiliaccio and Laurelli, and Griesmann. Just prior to the publication of the case by Moore and me, an additional case was reported by Poer and Whitaker, and in the discussion of this paper, Cole and Reynolds each added an additional successful case. During the same year Rosi presented two other cases. Subsequently single cases treated in this manner have been reported by Ryan and Murdock and Zaoussis.

Experiences which my associates and I have had with Roux-Y cyst jejunostomy in five consecutive cases indicate the validity of the impressions gained from the single case reports available in the literature and the two cases of Rosi. The procedure is technically feasible and yields excellent results. All five cases were pseudocysts, developing as the consequence of acute pancreatitis or pancreatic trauma. In one of them was there anything to suggest breakdown of the line of anastomosis nor postoperative infection of the cyst. In none has there been evidence of recurrence. There are now recorded a total of 17 experiences with this procedure. All have been successful.

When resection of pancreatic cysts does not appear to be technically a simple and safe procedure, internal drainage utilizing a Roux-Y jejunal limb would seem to be the procedure of choice.

BIBLIOGRAPHY

LEIOMYOMA AND LEIOMYOSARCOMA OF THE COLON*

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Myomatous tumors (leiomyoma and leiomyosarcoma) of the colon, exclusive of those in the rectum, are extremely rare. A search of the medical literature has revealed reports of five cases of leiomyosarcoma 17, 17, 21, 23, 24 and 19 cases of leiomyoma of the colon. 2-6, 9, 11, 12, 14, 15, 19, 22, 25 In the files of the Mayo Clinic, five cases of leiomyosarcoma and eight cases of leiomyoma of the colon have been found. We have studied thoroughly the cases reported in the literature and the complete records, including the tissue removed at operation, filed at this clinic. This combined series of 37 cases of myomatous tumors of the colon, although small, has served as a basis for construing the clinical and pathologic characteristics of this disease.

PATHOLOGIC FINDINGS

Gross Aspects. Myomatous tumors have occurred in every part of the colon (Table I), but more have occurred in the sigmoid colon than in any other portion. The preponderance in this region, however, is not great.

It was found that each tumor could be classified in one of four gross types, on the basis of the direction of its growth in regard to the lumen of the bowel as follows: (1) Intracolic type, tumors which grow into the lumen of the bowel and may be pedunculated or sessile; (2) exocolic type, tumors which grow away from the lumen of the bowel and lie in the abdominal cavity with an attachment to the wall of the bowel; (3) dumb-bell type, tumors which grow into the lumen and into the abdominal cavity away from the bowel at the same time; (4) constrictive type, tumors which encircle a variable length of bowel. The type of tumor has been determined in 26 cases (Table II); the intracolic type occurred most frequently.

The size of the tumors varied extremely. One tumor was said to be the size of a football. This tumor was malignant and nonresectable. A malignant tumor the size of a six-months-old fetus was reported to have been removed. In general, the greatest diameter of the malignant tumors varied from 5 to 8 cm. The average diameter of nonmalignant tumors was 6 to 9 cm.; however, one such tumor was 19 cm. in diameter.

The mucosa overlying the intracolic tumors showed a tendency toward ulceration in seven of eight tumors. The mucosa over the crown of the tumor was most frequently ulcerated. The tumors were coarsely lobulated and rather hard. Degeneration was noted within the substance of exocolic tumors, and in one tumor it had progressed to the extent of cavitation. The cavity was in free communication with the lumen of the colon. Less marked degeneration was noted within the substance of two intracolic tumors.

In two of the 13 cases of myomatous tumor of the colon at the clinic, free per-
foration into the abdominal cavity had occurred, and in two instances abscesses had formed around the tumor. The latter two tumors were benign, whereas the former two were malignant. It is presumed that ulceration and degeneration can progress to the point of freeing the pedicle of a tumor from the colon. One patient, who had had a leiomyosarcoma removed from the colon, gave a history of having passed a fleshy mass via the rectum three years previously. Unfortunately this mass was not available for examination.

Intussusception was commonly found in association with intracolic tumors. In seven of the 15 cases of intracolic tumor, some degree of intussusception was present, but it was not associated with any of the other types of tumors.

We do not have definite proof in any case of leiomyosarcoma of the colon that metastasis reached lymph nodes. Involvement of a lymph node was reported in the case of a patient seen in 1918; however, we were unable to find evidence of nodal involvement in the specimen. In a case reported by Scott, neoplastic nodules were found in the mesentery at operation. It is not established whether these represented metastatic neoplastic nodules in the mesentery or metastasis to lymph nodes; however, since at secondary operation hundreds of similar nodules were found in the mesentery and on the parietal peritoneum, the inference would be that these original nodules did not represent lymph nodes. In those cases in which metastasis had occurred it appeared to involve the peritoneum only, and it was not noted within the substance of other viscera.

Microscopic Aspects. Sections from all specimens were stained with phosphotungstic acid hematoxylin in order to demonstrate the myoglia. Mallory\(^\text{16}\) pointed out that tissue must be perfectly fresh in order to demonstrate the myoglia, because postmortem changes take place rapidly. In general, this was found to be true, as in most cases the fibrils in the cytoplasm were not demonstrable.

Histologically the myomatous tumors varied from those that contained almost normal smooth muscle cells to those that contained an immature type of cell and numerous cells containing mitotic figures. Little stroma was present in the tumors and in general it was rather low in vascularity. Degeneration and hemorrhage within the substance of the tumor were occasionally seen.

Whorling of the cells was a common characteristic. The cells were spindle in type, but as the degree of differentiation decreased, the cells became shorter and broader, with more rounded ends. The amount of cytoplasm varied considerably in relation to the size of the nucleus. In general, as the size of nucleus increased, the amount of cytoplasm decreased, and the presence of a large nucleus and scant cytoplasm was considered a sign of lack of differentiation. Irregularity of shape of

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<th>Table I. Location of 35 Myomatous Tumors of the Colon.</th>
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<td>Benign</td>
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<td>Cecum</td>
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<th>Table II. Classification of 26 Tumors According to Gross Type.</th>
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<td>Type</td>
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nuclei was characteristic as cells became less differentiated. In many tumors having undifferentiated cells, the nuclei were hyperchromatic; however, the only criterion by which a tumor was classified as malignant was the presence of mitotic figures in the nuclei. The tumors were graded on a basis of 1 to 4, depending on the number of mitotic figures seen in each high-power field. The presence of malignancy was based on the criteria of Evans. Giant cells were not seen in any of the specimens studied. In all tumors in which mitotic figures were seen, other signs of lack of differentiation in the individual cell were noted. In some cases it was impossible to determine the muscle layer from which the tumor originated.

CLINICAL FINDINGS

History. In our series of 37 cases of myomatous tumors of the colon, 22 of the patients were females and 13 were males. The sex of two patients was not stated. Six of the females and four of the males had malignant tumors. The ages of the patients ranged from five to 79 years.

Benign tumors were seen with about equal frequency among patients in each of the age groups from the third through the sixth decades, whereas the peak incidence at which malignant myomas were found was in the sixth decade. The incidence of myomatous tumors gradually increased among patients whose ages ranged from the first through the sixth decade, after which it gradually decreased. Of the tumors seen among patients in the sixth decade of life, four were malignant and five were benign.

The presenting symptoms were frequently difficult to ascertain from the reports of cases. In 26 cases, however, the presenting symptoms were known. In 15, pain was one of the main factors. In two cases it was due to perforation at the site of the tumor resulting in an acute abdomin
ated with intussusception. Only one patient had intussusception who did not have a history of having passed blood in the stool. Blood, however, was frequently noted in the stool in the absence of intussusception.

Eleven patients complained of constipation. Frequently constipation was unrelenting and the patient required enemas for relief. In at least two instances, alternating constipation and diarrhea were noted. The constipation tended to occur rather suddenly in a patient who previously had had normal bowel habits. Five patients complained of diarrhea; two had intermittent attacks, two had diarrhea continuously, and one patient had diarrhea at the onset of acute perforation. Mucus was usually present in the loose stools, and blood was also frequently present. The presence or absence of blood was mentioned in 22 cases, and in 12 the patients gave histories of blood in the stool. The amount of blood lost was extremely variable; some patients had gross hemorrhages, others had streaks of blood in the stool, tarry stools, or benzidine-positive stools. Occult blood was noted in only two cases.

Various degrees of obstruction were caused by these myomatous tumors. Even in the cases of intussusception, however, complete obstruction of the colon had not occurred. The only case in which obstruction was considered to be complete was the case of Heurtaux, in which the tumor had sloughed free from the hepatic flexure of the colon and had become impacted at the anal outlet.

Loss of weight was noted by seven of the 37 patients, and ten patients denied any loss in weight. This factor was indeterminate in the remaining cases. The amount of weight lost varied from 35 pounds (15.9 Kg.) in ten months to five pounds (2.3 Kg.) in two weeks. Loss of weight was mentioned by three patients having malignant tumors and by four patients having benign tumors. The exact amount of weight lost was not always definitely mentioned, although whether the tumors were benign or malignant did not make any demonstrable difference.

The duration of symptoms was variable and, in general, this factor was measured in months. Two of the ten patients with leiomyosarcomas had symptoms for three years, one had vague symptoms for ten years and acute symptoms for ten days, three had symptoms for approximately one month, and one had symptoms for one year. One patient had not had any symptoms prior to intestinal perforation. Of those patients who had leiomyomas, two had symptoms for four years, two for two years, and one for 12 years. Twelve other patients with leiomyomas, in whom the duration of symptoms was known, had had symptoms for an average of six months. It can then be stated that in cases of leiomyoma or leiomyosarcoma of the colon, most patients will have symptoms for a few months only before consulting a physician.

In a review of the symptoms of leiomyoma and leiomyosarcoma of the colon found in a series of cases from the Mayo Clinic and the literature, differentiative features between benign and malignant tumors have not been found.

Physical Findings. In general, physical examination of the patients revealed them to be normally developed individuals. Abdominal masses were found frequently. Such masses could be palpated in 18 patients; in two patients, perforation of the colon had occurred and adequate examination for a mass could not be carried out. In eight patients a mass could not be palpated, and in nine cases the presence or absence of an abdominal mass was not mentioned. Frequently the patients in whom a mass was not felt had considerable pain and tenderness, which possibly obscured the presence of a mass. The mass itself, when palpated, was frequently tender. This fact was mentioned in six cases;
in four of these the tumors were malignant. In the two cases in which perforation had occurred the masses were found to be 8 cm. and 6.5 cm. in diameter, respectively. In another case the mass was described as the size of a tennis ball. In each of five cases the mass was less than 4 cm. in its greatest diameter.

Digital examination of the rectum revealed abnormal physical findings in only one case, that of Heurtaux, in which the tumor was impacted at the anal outlet. Proctoscopic examination was of value in only one instance. In that case an extra-rectal mass was noted, which proved to be a tumor adherent to the bladder.

In general, the blood was relatively normal as reflected by the values for hemoglobin in the cases in which it was known. The concentration of hemoglobin was known for six patients with malignant tumors and ten with benign tumors. In one instance the value was 7.5 Gm. per 100 cc. of blood; this was the only case in which the hemoglobin was lower than 10.5 Gm. per 100 cc. This patient gave a history of occult blood in the stool. The tumor was malignant. All other patients with malignant tumors had values for hemoglobin of more than 11 Gm. per 100 cc. and the average, excluding the afore-mentioned case, was 11.7 Gm. In the ten cases of benign leiomyoma of the colon in which the value for hemoglobin was known, the average value was 12.4 Gm. per 100 cc. of blood.

The sedimentation rate of erythrocytes was known in four instances of malignant tumor. The values were 18, 118, 27 and 62 mm. in one hour (Westergren). In the two instances of benign tumors in which the erythrocyte sedimentation rate was known, the values were 12 and 55 mm. in one hour. It is seen that a variable amount of elevation of the sedimentation rate has occurred in those patients with leiomyosarcoma of the colon. The instance of the higher value in the presence of a benign tumor was possibly due to concomitant abscess formation.

Radiologic Findings. Good reported the roentgenologic findings of intramucosal tumors arising in the small intestine as follows: "(1) Preservation of the mucosal relief pattern; (2) production of a rounded deformity of the barium filled intestinal lumen by a mass which is firmly attached to the bowel." He stated that "submucosal and intramural tumors of the colon produce the same roentgenologic features as their counterparts in the small intestine." He further stated that "the distinction from carcinoma can be made."

It is obvious that the roentgenographic findings differ in each of the four types of myomatous tumors in the colon. There were nine cases of intracolic tumor in the collective series in which roentgenologic findings were known. A filling defect indicative of a polypoid lesion was reported in six cases. In three of these cases some degree of intussusception was present at operation, but was not noted in the roentgenograms. In two patients, the retrograde flow of barium was completely obstructed, and intussusception was present in one of these patients. In the other case the first roentgenographic examination did not show evidence of obstruction; such evidence was reported on re-examination only. The tumor was in the sigmoid. In another instance in which the tumor was found in the cecum the roentgenologic examination did not show evidence of its presence. In one instance in which a leiomyoma was found in the sigmoid colon the roentgenologist suggested that this might be a lipoma.

Results of roentgenologic study were known in four cases of exocolic type of growth. In one instance evidence was noted of a deep cavity which communicated with the bowel. This represented the cavitation formed by the degeneration within the central area of a malignant neoplasm. Also in
In one instance, a filling defect was reported in the cecum. In another instance it was noted that the stomach was pushed to the left and that the ascending colon and hepatic flexure were pushed to the left and downward. Roentgenologic examination of the colon was not carried out in this case. In one case from the literature, roentgenologic examination of the colon was interpreted to show the presence of an extra loop of bowel.

In three cases of circumferential type of growth in which roentgenographic findings were known, narrowing of the lumen of the bowel for a distance of 8 cm. was noted in one. This anomaly had the appearance of an external pressure defect except that it was nondistensible. In a second case, evidence was reported of a tumefactive lesion in the transverse colon which appeared as a semicircular deformity of the bowel. The mucosal pattern was preserved, and the findings suggested an intramural extraluminal tumor. In a third case evidence seemed to indicate partial obstruction with spasm of the sigmoid colon, which was suggestive of diverticulitis. In the former instance the growth was malignant and in the latter two the growths were benign.

In one instance of a dumb-bell type of growth, roentgenologic findings were reported. Evidence of a polypoid tumor was noted in the bowel when barium was given by enema. A dense region outside the lumen of the bowel appeared to be continuous with the polypoid growth and to cause a pressure defect on the wall of the bowel. The flow of barium was not obstructed.

TREATMENT AND PROGNOSIS

The treatment available for myomatous tumor in the colon is either surgical or roentgenologic, or a combination of the two. According to Golden and Stout in their review of smooth muscle tumors of the gastro-intestinal tract, "in general it may be stated that proper surgical treatment of the benign smooth muscle tumor will result in a cure unless the lesion is rectal or extraperitoneal." They further stated that "the malignant leiomyoma is usually of low grade malignancy and if adequately treated, even in the presence of metastases, the patient may enjoy years of uneventful health. In those poorly differentiated with many mitoses and bizarre forms, the duration of life, even with radical removal, appears to be little more than a year or two following the onset of symptoms. Fortunately these are uncommon."

Resection was carried out in nine of ten cases of leiomyosarcoma. In two cases, metastasis was present at the time of operation: one patient, who had neoplastic nodules in the mesentery, died about a year after operation of recurrence of tumor; the other patient, in whom involvement of a mesenteric node was reported, died a year and a half later of influenza. Necropsy was not performed in the latter instance. Three patients in the Mayo Clinic group were alive and well without evidence of recurrence of tumor 21 months, four and a half years and nine years, respectively, after operation. The first and second patients were each considered to have leiomyosarcoma, grade 2, and the third patient was considered to have leiomyosarcoma, grade 3. In the cases reported by Golden and Stout and by Neugebauer, each patient was alive and well at the end of one year. One patient died of recurrence of tumor two years and three months after surgical removal of the primary tumor.

In one instance a palliative procedure was done for a tumor that was judged inoperable. One patient who had advanced intraperitoneal spread of a tumor considered to be a leiomyosarcoma, grade 4, underwent transverse colostomy. This patient died six months after operation of hemorrhage from the colostomy.
LEIOMYOMA AND LEIOMYOSARCOMA OF THE COLON

Eleven patients who had leiomyomas of the colon underwent resection of the colon and seven patients underwent local removal of the polyps by enterotomy. The pedicle of the polyp was ligated in two instances and the method of removal was unknown in seven instances. In one case in which resection was carried out, the patient died postoperatively of an overwhelming peritonitis. In another instance in which a transverse colostomy had been performed at the clinic for a lesion with formation of abscess in the pelvis, secondary resection was carried out elsewhere a year and a half later, and the patient died postoperatively.

Recurrence of a tumor has not been reported in any case in which a diagnosis of leiomyoma of the colon was made. Follow-up studies in five cases were for periods of one year and three, ten, 13 and 14 years. Golden and Stout reported a follow-up study of their case of four years' duration; the tumor had not recurred.

Among the postoperative complications in the group having malignant tumors were jaundice in one case and wound dehiscence in one. In most instances the postoperative course was uneventful.

Roentgen therapy has not been used sufficiently in this series of cases of leiomyosarcoma of the colon to warrant any conclusions regarding its effect on growth of the tumor.

COMMENT

Leiomyosarcoma of the uterus has always been considered to be an extremely malignant condition. Evans found that of 13 patients in whom the tumors showed from 2,200 to 12,000 mitotic figures per cubic millimeter of tissue, 11 had recurrence of tumor within one to 18 months. The condition of the other two patients was followed only seven and four months, respectively, after operation. In the remainder of his 72 cases of actively growing myomatous tumors in the uterus, mitotic figures were absent or fewer than 800 per cubic millimeter. In none of the cases in which follow-up studies were made did death result from recurrence. Proper and Simpson found that if mitotic figures were present in uterine myomas to any extent the prognosis was almost hopeless. The result of the present study of a limited number of cases would suggest that the outlook for patients having malignant myomatous tumors of the colon removed before obvious extension has occurred, is much better than it is when similar tumors occur in the uterus.

In order to compare the frequency of occurrence of myomatous tumors in the colon with those in various other parts of the gastro-intestinal tract, we would like to mention that ten cases of leiomyosarcoma and ten cases of leiomyoma of the rectum have been reported at the Mayo Clinic. Also 40 cases of leiomyosarcoma of the stomach and five cases of leiomyosarcoma of the esophagus have been reported.

As noted in the microscopic study, all gradations of cellularity and activity from cells of normal smooth muscle type to large actively growing cells with many mitotic figures have been seen in the various tumors. This might be construed as evidence that benign leiomyomas do become malignant. It is to be noted that Neuman has followed the transition of a leiomyoma of the rectum, by succeeding microscopic studies during seven years, into a malignant leiomyosarcoma with many mitotic figures.

Clinically, the patients complained of moderate to severe abdominal pain, accompanied by constipation or diarrhea and with blood and mucus in the stools. Frequently, a large palpable mass was present. The patients did not tend to appear cachectic in the presence of the foregoing signs and symptoms as would be expected if carcinoma were present with a mass of...
corresponding size. Roentgenologic examination frequently will not help differentiate these tumors from other intra-abdominal growths. The evidence, however, of a cavity leading away from the bowel seen on use of a barium enema is suggestive of an exocolic myomatous tumor. It is to be noted that roentgenologic examination may not show any positive evidence in the presence of an exocolic tumor. The roentgenologic findings in a dumb-bell or hour-glass type of tumor have been described. In most cases, myomatous tumors do not present sufficiently characteristic symptoms to be recognized clinically.

Leiomyosarcoma does not tend to spread by the lymphatic route, and distant viscera have not been found to be involved. Hence, if peritoneal implantation is not evident, a reasonable chance of cure by removal of the tumor itself might be expected. Removal of surrounding tissue need not be nearly as extensive as in the case of carcinoma. In the nine cases of leiomyosarcoma in which information regarding survival was available and in which surgical removal of the lesion was performed, three patients are known to have died from their disease. Two of these patients had extension beyond the primary growth at the time of operation. Five patients were alive without evidence of recurrence at the time their case was reported. The periods of survival in these cases as reported were nine years, four and a half years, 21 months, 12 months and 12 months. One patient died of influenza a year and a half after operation but evidence of recurrence was not present. The duration of survival in four cases is too short to permit any conclusions; however, the survival periods of nine and four and a half years are significant.

SUMMARY AND CONCLUSIONS

Smooth muscle tumors of the colon are extremely rare. Only five cases of leiomyosarcoma of the colon have been encountered at the Mayo Clinic since its inception and five other cases have been reported in the literature. During the same period, eight patients having benign leiomyomas of the colon have been seen at the clinic and 19 cases of such tumors have been reported in the literature. The tumors in our series of cases were classed as malignant only when mitotic figures were present.

Smooth muscle tumors of the colon were found among patients of all ages, with a gradual increase in each decade up to the sixth, and then with a sharp decline in incidence in succeeding decades. The highest incidence of malignant tumors is seen in the sixth decade, whereas benign tumors were found with approximately equal frequency in each of the decades from the third through the seventh.

The following classification of myomatous tumors of the colon according to gross characteristics has been suggested: intracolic tumors; exocolic tumors; circumferential or "stenosing" tumors, and dumbbell tumors.

It is suggested that surgical removal of the tumor is the treatment of choice. Roentgen therapy has not been used in a sufficient number of cases to determine its efficacy. It is important that the tumor be considered operable in so far as size and degree of fixation are concerned, as many of these tumors are large and more are benign than are malignant. Furthermore, the benign tumors may be fixed to surrounding tissues owing to inflammation and formation of abscesses. It is suggested that the prognosis for patients having leiomyosarcoma of the colon, treated by surgical means, is much better than the prognosis for patients having leiomyosarcoma of the uterus.

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PULMONARY CYSTIC CHANGES IN XANTHOMATOSIS*

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The lung of the newborn is not a mere miniature of the adult, as growth of new lung units and further development of existing ones continues until puberty. Metabolic, glandular and connective tissue changes occurring during this period influence the development of the lung. The disorder xanthomatosis is, we believe, occasionally associated with pulmonary cystic changes in the lung which are not well understood. Thannhauser and Magendanz's classification of primary essential xanthomatosis as either hypercholesteremic or normocholesteremic permits of considerable accuracy in predicting the clinical features likely to be observed. This presentation is concerned with the normocholesteremic type and emphasizes the pulmonary cystic changes which have been observed in four patients at Fitzsimons Army Hospital (Table I).

Widespread tissue involvement characterizes xanthomatosis. The skin, dura, orbit, pituitary gland, brain, liver, spleen, lymphatics, bone, tracheobronchial tree, lung and pleura have been reported involved. Several clinical entities such as Letterer-Siwe disease, Hand-Schuller-Christian disease, lipid granulomatosis and eosinophilic granuloma of bone or lung may be facets of primary essential normocholesteremic xanthomatosis.*-9, 11, 21, 23, 30

CASE REPORTS

Case 1. A fascinating case problem was presented in a 24-year-old soldier admitted to another hospital December 4, 1950, and transferred to Fitzsimons Army Hospital May 1, 1951, with the symptom of expectorating a slight amount of bloody sputum almost daily for the past 5 years. A slightly painful mass in the left axilla was present which had been slowly enlarging for one year and was now 5 x 3 cm. in size. Six years earlier he had had a small "blood blister" surgically excised from the left shoulder which had been observed for one and one-half years, and at the time of removal was elevated 1 cm. above the surrounding skin. Histopathologic study of this tissue was not made. In 1949, four years after its removal, the lesion recurred and was again excised. The roentgenogram of the chest revealed most interesting findings. Throughout both lung fields there were areas of round densities which often varied in appearance during the intervals between examination. These were interpreted as fluid containing areas which would empty and refill, producing minimal symptoms (Figs. 1 and 2). The mass in the axilla was widely excised and the histopathologic interpretation was a metastatic tumor, probably vascular in origin. Bronchoscopy revealed a tumor mass on the posterior wall of the left lower lobe bronchus. An excisional biopsy of the mass was accomplished and the histopathologic examination was indicative of a metastatic tumor, type undetermined (Fig. 3).

A right exploratory thoracotomy performed May 17, 1951, was revealing. Only a few fine adhesions between the pleural surfaces were encountered and the mediastinum was normal. Innumerable cyst-like lesions, measuring 0.5 cm. to 3.0 cm., were present throughout the lung, especially subpleurally. Small yellowish flecks could be visualized through the thin overlying pleura. On palpation, the masses felt soft and were easily compressible, their contents could be partially emptied and the cysts would refill with air as the anes-
PULMONARY CYSTIC CHANGES IN XANTHOMATOSIS

The patient applied positive pressure. The pleural surface overlying a cyst, 4 cm. in diameter, was of a confluent orange-yellow appearance. Several cysts were removed for further study. The contents of the cysts appeared as a serous bloody fluid.

On cross section the cyst wall was thin. Microscopically, the wall was made up of columnar epithelium, shading into cuboidal, with large areas of squamous metaplasia (Fig. 4). There were areas showing foam cells surrounding spaces interpreted as cholesterol clefs. In other areas small irregular and spindle shaped cells with hyperchromatic nuclei were observed. Mitotic figures were rare. A few days after operation he coughed up a 0.7 cm. fragment of pulmonary tissue which microscopically was the same as that noted in the excised cysts. About 6 months later a 1.5 cm. mass was observed in the right upper arm. Upon exploration, the mass was found to be a part of the deltoid muscle, and the microscopic findings on this tissue were again characterized by the presence of foamy phagocytes, foreign body giant cells and cholesterol clefs (Fig. 5). On reviewing the histopathologic picture of the lesion from the right axilla, bronchus, lung and left shoulder, similar characteristics prevail in each. The patient has remained well, carried on his full military duties for one and one-half years until discharged, and two years after being first seen he has no complaint except the expectoration of a slight amount of bloody sputum each morning. Roentgenograms of the chest reveal an increase in the extent of cystic lesions. The blood cholesterol levels were repeatedly within normal limits, bone marrow studies were normal, long bone survey was negative except for a cystic lesion seen in the left radius (Fig. 6).

That definite pulmonary changes should occur in association with xanthomatosis seems logical. Rowland indicated such changes in 1928, and others have described this interesting phenomenon27 (Table II). The alterations in the lung seen in xanthomatosis are considered as being due to two factors: first, a granulomatous process involving the pulmonary interstitial tissues; second, bronchiolar obstruction. Rowland described the papillary outgrowths into the lumina of the bronchioles, suggesting that partial bronchiolar obstruction was significant in producing the cysts.27 In the above patient there was noticeable squamous metaplasia with piling up of bronchial epithelium. There was a xanthomatous tumefaction partially obstructing the left lower lobe bronchus (Fig. 7).

**Table I. Xanthomatosis Showing Pulmonary Cystic Changes.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical and Laboratory Findings</th>
<th>Pulmonary Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>M</td>
<td>Blood-streaked sputum 7 years. Sputum loaded with foamy histiocytes. Cholesterol normal. Excisional biopsy of lung, peripheral lymph nodes, bronchial epithelium, skin, and muscle have shown xanthomatous lesions.</td>
<td>Chest roentgenogram showed innumerable bilateral air and fluid-filled cysts measuring 2 to 3.0 cm. in diameter. Tumor of L. L. L. bronchus.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>M</td>
<td>Cough, sputum, fatigability, chest pain, 32-pound weight loss and afternoon temperature elevation. Attempts to incriminate tubercle bacilli, fungi, parasites or an allergic process were unsuccessful.</td>
<td>Roentgenogram showed bilateral nodular infiltrations throughout both lung fields. Excisional biopsy of lung was performed. One of the removed nodules contained a cystic lesion 1 cm. in size and histopathological examination revealed changes considered due to xanthomatosis.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>19</td>
<td>M</td>
<td>Looseness of teeth, sore gums, fatigability, cough, chest pain, 20-pound weight loss, afternoon temperature elevation. Bone survey showed destructive lesions of the left mandible, both humeri, left scapula and left first rib. Excisional biopsy of gum histologically reported eosinophilic granuloma.</td>
<td>Extensive soft-appearing infiltration throughout both lung fields with several areas of lucency which were thought to represent small areas of cavitation. Exised lung tissue reveals changes considered due to xanthomatosis.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>24</td>
<td>M</td>
<td>Slight cough, 5-pound weight loss, daily afternoon temperature elevation. 10% peripheral eosinophilia. Cholesterol normal. Attempts to incriminate tuberculosis bacilli, fungi, parasites or an allergic process unsuccessful.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FORSEE AND BLAKE

ner, Davidson and White report similar findings with extensive xanthomatous changes present throughout the larynx, trachea and smaller bronchi. Others have reported similar observations concerning transitions between them, may be seen in this case problem. The proliferative phase is seen in the periphery of the tissue removed from the left axilla where areas of histocytic proliferation with the local involvement of the upper respiratory tract (Table III).

Holm and his co-workers have described four histological phases encountered during the course of generalized xanthomatosis. First, there is histocytic proliferation and local accumulation of eosinophils. Foam cells are not seen in this phase. Second, a granulomatous reaction characterized by the appearance of young blood vessels, reticular cells, histocytes, eosinophils, giant (Touton) cells and beginning lipoid phagocytosis. The third is the xanthomatous phase characterized by the appearance of isolated or groups of foam cells. The fourth phase is that of fibrosis and healing. These histological features overlap considerably just as the clinical characteristics merge. Each of these phases, and accumulation of eosinophils are present. Approaching the more mature center of this lesion the granulomatous phase becomes quite evident, and young blood vessels characteristic of this phase were so striking as to suggest the diagnosis of malignant tumor, probably vascular in origin. Large numbers of foam cells seen characteristically in the xanthomatous phase are seen best in the lesion removed from the deltoid muscle. The fibrous or healing stage is represented by the lesion removed from the skin of the left shoulder and was first thought to represent a sclerosing heman-giofibroma. It is believed that the pulmonary cystic changes herein described are the most severe yet reported in primary normocholesteremic xanthomatosis.
Case 2. A 32-year-old white male was admitted to Fitzsimons Army Hospital April 4, 1949, complaining of a chronic cough productive of 85 cc. of sputum daily, bilateral chest pain of moderate severity, easy fatigue, night sweats, and a 32 pound weight loss during the preceding 12 months. Frequent afternoon temperature elevations were noted during hospitalization. Past medical history revealed a 5-month period of exposure to considerable dust while employed in a cement factory a year prior to onset of present complaints. Physical examination revealed a few moist rales bilaterally. Eosinophils were absent in the peripheral blood. Skin tests were positive for tuberculosis and histoplasmosis and negative for coccidiodomycosis. Sputum studies were repeatedly negative for tubercle bacilli and fungi. Bronchoscopy was negative. Chest roentgenograms revealed extensive bilateral parenchymal nodular infiltrations. There were no enlarged peripheral lymph nodes. A left thoracostomy revealed marked 0.5 to 2 cm. nodules throughout both lobes. These nodules were hard and irregular to palpation, becoming confluent at the hilus. The involved apex of the lower lobe was removed as a biopsy specimen. One of the nodules in this removed portion of lung tissue contained a cystic lesion 1 cm. in diameter. Histopathologic examination revealed many histiocytes, eosinophils and xanthomatous macrophages. A few lymphocytes and foreign body giant cells were scattered in the fibrous trabeculae. Special stains for parasites, fungi and tubercle bacilli were not helpful. This case and case 4 have been previously considered as an eosino-

![Fig. 3](image1)

**Fig. 3** (Case 1) Photomicrograph of lesion removed from left lower lobe bronchus. Note large histocytes, eosinophils and cholesterol clefts.

**Fig. 4** (Case 1) Photomicrograph of lesion removed from right lung. Note the extensive squamous metaplasia of the epithelium with narrowing of the bronchial lumen. Observe as well the numerous cholesterol clefts.

philic granuloma of the lung. The granulomatous phase of xanthomatosis is considered to be represented by the pulmonary changes in these two patients.

Case 3. A 19-year-old white male soldier was admitted to Fitzsimons Army Hospital March 16, 1950. His symptoms were soreness of the gums, moderate cough productive of about 30 cc. of sputum daily, bilateral chest pain and a 20 pound
TABLE II. Collected Case Reports of Generalized Xanthomatosis Associated With Pulmonary Cystic Changes.

<table>
<thead>
<tr>
<th>No.</th>
<th>Year</th>
<th>Reported By</th>
<th>Age</th>
<th>Sex</th>
<th>Clinical and Necropsy Findings of Systemic Xanthomatosis</th>
<th>Specific Pulmonary Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1928</td>
<td>Rowland?</td>
<td>5</td>
<td>M</td>
<td>Exophthalmos, cystic lesions of skull. Blood cholesterol not done.</td>
<td>Describes pulmonary reticulation with definite cystic changes. There were papillary outgrowths into the bronchial lumina with partial obstruction. Large numbers of interstitial lipid cells with interstitial fibrosis.</td>
</tr>
<tr>
<td>2</td>
<td>1942</td>
<td>Farber, Hampton and Mueller?</td>
<td>1½</td>
<td>F</td>
<td>Liver, kidney, lymph nodes, uterus and tongue involved.</td>
<td>Describes pulmonary reticulation, blebs and cystic changes. There were large numbers of interstitial lipid cells and interstitial fibrosis.</td>
</tr>
<tr>
<td>3</td>
<td>1943</td>
<td>Currens and Popp?</td>
<td>29</td>
<td>F</td>
<td>Cystic lesions of skull. Excisional biopsy histologically confirmed xanthomatosis.</td>
<td>Roentgenographic examination showed pulmonary reticulation and cystic changes suggestive of honeycomb lung. No microscopic study made of pulmonary tissue.</td>
</tr>
<tr>
<td>4</td>
<td>1949</td>
<td>Oswald?</td>
<td>9</td>
<td>F</td>
<td>Liver and lymph nodes involved. Roentgenograms showed lesions of skull and spine. Necropsy showed xanthomatous foci in skull, basi-sphenoid, pituitary fossa, body of 9th thoracic vertebra, and 9th left rib.</td>
<td>Roentgenographic examination showed scattered opacities in both lungs, giving a trabeculated appearance. Necropsy showed diffuse honeycombing of lung. Cysts 0.9 cm. in size. Microscopically there was a granulomatous infiltration of lungs with giant cells of Touton type, many containing lipid.</td>
</tr>
<tr>
<td>5</td>
<td>1949</td>
<td>Parkinson?</td>
<td>56</td>
<td>M</td>
<td>Diabetes insipidus, cystic lesion, right femur. Biopsy typical of eosinophilic granuloma.</td>
<td>Generalized reticulation with miliary mottling of both lung fields. The reticulation formed small shadings 0.5 cm. in diameter. Tomogram by confirmed presence of cysts.</td>
</tr>
<tr>
<td>7</td>
<td>1951</td>
<td>Lewis?</td>
<td>21</td>
<td>M</td>
<td>Diabetes insipidus. Normal cholesterol.</td>
<td>Chest roentgenogram and tomograms showed multiple small cysts, both lungs, which did not fill at bronchography.</td>
</tr>
</tbody>
</table>

Weight loss during the past 4 months. Roentgenograms of the right mandible showed a destructive lesion of the right alveolar ridge. Temperature averaged 99 to 100°F. Roentgenograms of the chest indicated extensive bilateral, irregular stringy densities with numerous cystic-like areas. Additional cystic bony involvement noted on roentgenograms included areas in the mandible, right, first rib, left, both humeri, and the left scapula (Fig. 8). Repeated excisional biopsies of the left lower gingiva showed on histopathologic examination collections of large swollen foam cells, numerous young blood vessels, and infiltration of plasma cells, lymphocytes and many eosinophils interpreted as an eosinophilic granuloma of the gums. Although no biopsy of the lung was obtained, the authors feel justified in regarding the lung lesions as being part of the generalized xanthomatous disease process. This seems rational in view of typical cystic bone lesions in the ribs, humerus, scapula and the microscopic picture of eosinophilic granuloma upon gingival biopsy.

**Case 4.** A 24-year-old soldier was hospitalized October 21, 1950, following abnormal findings noted on a routine re-enlistment chest roentgenogram. The patient had had a mild chronic productive cough for 3 years. There was a 5-pound weight loss during the preceding 8 months. After hospitalization, the patient was observed to have a daily low grade afternoon fever. He denied chills, fever, malaise, hemoptysis, or other symptoms. Past history was not helpful. Physical examination was not remarkable. Skin tests for tuberculosis, histoplasmosis and blastomycosis were positive, that for coccidioidomycosis negative. Peripheral blood smear showed a 10 per cent eosinophilia. Examination of the sputum was...
repeatedly negative for tubercle bacilli and fungi. The roentgenograms of long bones, hands and feet were negative. The chest roentgenograms showed an extensive soft appearing infiltration throughout both lung fields, with several scattered areas of lucency, probably representing small areas of cavitation. Cholesterol and cholesterol esters were normal. In the inability positively to establish a diagnosis, a left thoracotomy was performed. The lung was found to contain innumerable small, pea-sized nodules throughout all lobes. Several excisional biopsies of lung tissue containing these nodules were studied microscopically and are considered to represent the granulomatous phase of xanthomatosis. During a 2-year follow-up period he has worked regularly and has attended school. He is asymptomatic.

CONCLUSION

The diagnosis of many intrathoracic lesions requires surgical exploration and histopathologic examination of the excised tissue, but even then some may be equivocal. Differentiation of the proliferative and granulomatous phases of xanthomatosis from neoplasm may be difficult, as the characteristic xanthoma cells are seen only in the more mature lesions. Widespread tissue involvement, undifferentiated microscopic findings, and little deterioration of health suggest xanthomatosis. The cystic changes depicted in the patients described are thought to be due to pulmonary interstitial involvement and bronchiolar obstruc-
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FORSEE AND BLAKE

FIG. 8. (Case 3) Roentgenogram of chest showing extensive cystic areas throughout lung. In addition, cystic lesions are seen in end of first rib, scapula and the humerus.

<table>
<thead>
<tr>
<th>Year</th>
<th>Reported By</th>
<th>Respiratory System Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1873</td>
<td>Fagge®</td>
<td>Xanthomatous changes in trachea.</td>
</tr>
<tr>
<td>1908</td>
<td>Pusey®®®®®</td>
<td>Pulmonary changes present.</td>
</tr>
<tr>
<td>1925</td>
<td>Thompson16</td>
<td>Xanthomatosis with interstitial lipid histiocytosis and pulmonary fibrosis.</td>
</tr>
<tr>
<td>1925</td>
<td>Turner12</td>
<td>Extensive xanthomatous involvement of trachea and bronchi.</td>
</tr>
<tr>
<td>1926</td>
<td>Kyrklund13</td>
<td>Xanthomatosis with interstitial lipid histiocytosis and pulmonary fibrosis.</td>
</tr>
<tr>
<td>1928</td>
<td>Urbach®®</td>
<td>Severe laryngeal involvement.</td>
</tr>
<tr>
<td>1930</td>
<td>Chester®</td>
<td>Pulmonary fibrosis.</td>
</tr>
<tr>
<td>1931</td>
<td>Finney®®®</td>
<td>Laryngeal xanthomatosis.</td>
</tr>
<tr>
<td>1935</td>
<td>Horsfall®®®®®</td>
<td>Pulmonary changes present at autopsy.</td>
</tr>
<tr>
<td>1937</td>
<td>Thannhauser®®</td>
<td>Xanthomatous nodules of larynx and trachea.</td>
</tr>
<tr>
<td>1941</td>
<td>Freund12</td>
<td>Granulomatous infiltration of lungs with enormous deposits of cholesterol within lipophages.</td>
</tr>
<tr>
<td>1942</td>
<td>Gross®®®®®®®®</td>
<td>Diffuse mottling, both lung fields.</td>
</tr>
<tr>
<td>1944</td>
<td>Jaffe17</td>
<td>Pulmonary fibrosis.</td>
</tr>
<tr>
<td>1947</td>
<td>Weinstein®®®®®®®®</td>
<td>Granulomatous nodular infiltration, both lungs.</td>
</tr>
<tr>
<td>1948</td>
<td>Schuknecht®®®®®®®®®</td>
<td>Granuloma of lungs.</td>
</tr>
<tr>
<td>1948</td>
<td>Ponset®®®®®®®®®®®®®</td>
<td>Infiltrative lesions throughout both lungs.</td>
</tr>
<tr>
<td>1949</td>
<td>Schaefer®®®®®®®®®®®®®</td>
<td>Pulmonary fibrosis.</td>
</tr>
<tr>
<td>1949</td>
<td>Kruger®®®®®®®®®®®®®</td>
<td>Extensive linear infiltration, both lungs.</td>
</tr>
<tr>
<td>1951</td>
<td>Farinacci®®®®®®®®®®®®®®®®®®®</td>
<td>Extensive eosinophilic granulomatous processes, both lungs, on two patients.</td>
</tr>
</tbody>
</table>

Observations in these patients suggest that Hand-Schuller-Christian disease, Letterer-Siwe disease, lipoid granulomatosis and eosinophilic granuloma of bone and lung may be mere facets in primary normocholesteremic xanthomatosis.

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PULMONARY CYSTIC CHANGES IN XANTHOMATOSIS


MYCOTIC ANEURYSMS*

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Mycotic is the descriptive term applied to those aneurysms which arise due to inflammatory destruction of the arterial wall in association with embolization. They are so named because of their relation to bacterial endocarditis, called "mycotic" by Osler.

PATHOLOGY

Mycotic aneurysms have no characteristic shape; they are often associated with gross hemorrhage, and occasionally an embolus may be identified grossly. The actual aneurysm is often found in relatively small arterial branches. Microscopic examination reveals an acute or chronic inflammatory reaction involving and disrupting the vessel wall. Fragments of the emboli may be recognized in the peripheral portions of the diseased vessel wall, presumably in the vasa vasorum.

PATHOGENESIS

The role of the gross embolus may be of importance, but cannot be of primary significance because of the infrequency with which sterile emboli cause aneurysms. In order for mycotic aneurysms to occur, two factors are necessary. First of these is mural damage, which may be on the basis of embolism, obstruction of the vasa vasorum, atherosclerosis, congenital defects or external trauma. Second is sepsis, which may come from infected emboli or a bacteremia, or may be due to a contiguous infection.

Once an aneurysm has developed, the common course is rapid and progressive dilatation and rupture, but spontaneous thrombosis and cure may follow instead.

CLINICAL FEATURES

Some form of sepsis is essential, and in 90 per cent of cases this sepsis is bacterial endocarditis. The history of rheumatic fever is therefore of value in making a diagnosis of mycotic aneurysm.

The local findings may be described in four stages. The first stage is embolism, which has no features differing from any other kind of embolism. The second stage is the formation of the aneurysm. Local pain and a pulsating mass may then be demonstrated. A systolic bruit is often audible over the mass. During this stage arteriography may be useful in establishing the diagnosis and in elucidating the exact anatomical relationships. The third stage is that of rupture. Rupture does not always occur, however, and the fourth stage of thrombosis and spontaneous healing may follow. It is probable that many small aneurysms undergo spontaneous thrombosis and resolution.

TREATMENT

In those cases in which the anatomic relationships allow possible surgical care, direct attack should be made on the aneurysm if the patient can be brought into appropriate condition by general supportive measures, with special attention to the

* Submitted for publication May, 1953.
diseased heart. Excision of the involved segment of vessel is indicated in most instances. If repair is necessary, end to end anastomosis or the use of an autologous vein graft is recommended. Regional sympathectomy is of dubious value in acute occlusions, and should be utilized only if there is objective evidence that the procedure will enhance the chance of the extremity for survival.

Prognosis is poor partly because of the gravity of the basic disease, and partly because of the inaccessibility of 80 per cent of the aneurysms. Appropriate antibiotic therapy has improved the outlook for bacterial endocarditis in recent years, and more opportunities for surgical intervention and cure of the aneurysms should be expected. Very few cases of cured mycotic aneurysms have been reported, and most of these have occurred since the era of chemotherapy and antibiosis began (Table I).

### CASE REPORTS

The following five cases have been seen at Wadsworth General Hospital since January, 1947. Several other cases were rejected because of inadequacy of information.

#### TABLE I. Summary of Successfully Treated Cases of Mycotic Aneurysm.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Site</th>
<th>Size</th>
<th>Etiology</th>
<th>Treatment</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clutton &amp; Dudgeon</td>
<td>78</td>
<td>M</td>
<td>femoral</td>
<td>—</td>
<td>pneumonia</td>
<td>ligation, drainage</td>
<td>cure, after suppuration</td>
</tr>
<tr>
<td>Gage</td>
<td>18</td>
<td>F</td>
<td>iliac</td>
<td>—</td>
<td>SBE</td>
<td>ligation</td>
<td>thrombosis and cure</td>
</tr>
<tr>
<td>Nicolson</td>
<td>12</td>
<td>F</td>
<td>aortic</td>
<td>—</td>
<td>SBE</td>
<td>none</td>
<td>thrombosis and cure</td>
</tr>
<tr>
<td>Klein &amp; Crowell</td>
<td>22</td>
<td>M</td>
<td>ulnar</td>
<td>2.9X2 cm</td>
<td>SBE</td>
<td>excision</td>
<td>cure</td>
</tr>
<tr>
<td>Hurwitz &amp; Arst</td>
<td>20</td>
<td>M</td>
<td>brachial</td>
<td>4.0 cm</td>
<td>SBE</td>
<td>excision</td>
<td>cure</td>
</tr>
<tr>
<td>Goadby et al</td>
<td>35</td>
<td>M</td>
<td>femoral</td>
<td>“orange sized”</td>
<td>SBE</td>
<td>ligation, excision</td>
<td>good, but died of SBE</td>
</tr>
<tr>
<td>Goadby et al</td>
<td>46</td>
<td>M</td>
<td>radial</td>
<td>“cherry sized”</td>
<td>SBE</td>
<td>penicillin</td>
<td>thrombosis and cure</td>
</tr>
<tr>
<td>Martorell &amp; Serra</td>
<td>32</td>
<td>M</td>
<td>common</td>
<td>“orange sized”</td>
<td>SBE</td>
<td>ligation; ligation &amp; excision</td>
<td>good, but died in 3 months of SBE</td>
</tr>
<tr>
<td>Martorell &amp; Serra</td>
<td>40</td>
<td>M</td>
<td>deep</td>
<td>3.0 cm</td>
<td>SBE</td>
<td>ligation</td>
<td>good at 3 months</td>
</tr>
<tr>
<td>Fernbach et al</td>
<td>10</td>
<td>F</td>
<td>common</td>
<td>5.0 cm</td>
<td>SBE</td>
<td>ligation</td>
<td>good</td>
</tr>
<tr>
<td>Barker</td>
<td>24</td>
<td>M</td>
<td>deep</td>
<td>5.0 cm &amp; femoral (bilateral)</td>
<td>SBE</td>
<td>excision</td>
<td>good at 3 months</td>
</tr>
</tbody>
</table>

*Probably mycotic, but not absolutely identified as such.

Case 1. (McC.) This 32-year-old white man was admitted in a stuporous condition after complaints of headache for nine days. Examination of the heart and lungs was normal. A diagnosis of meningitis and acute cavernous sinusitis was made. The patient deteriorated and died two days after admission.

Autopsy revealed that the primary disease had been an acute sphenoidal sinusitis. There were mycotic aneurysms in both carotid arteries. On the right the aneurysm had ruptured into the middle and posterior fossa, and there was thrombosis of the right cavernous sinus. On the left side the aneurysm was partially thrombosed.

Case 2. (W. L. A.) This 64-year-old white man was admitted in shock with a ten-day history of pain in the chest and dyspnea. Physical examination revealed an enlarged heart, a precordial friction rub, and an otherwise undescrbed "mitral" murmur. He died shortly after admission.

Autopsy revealed an acute ulceration of the mitral valve consistent with acute bacterial endocarditis. There was an unruptured mycotic aneurysm of the anterior cerebral artery (Figs. 1 and 2) and a focal embolic glomerulonephritis. Other emboli were present in the brain and spleen. The terminal episode was believed to have been cardiac decompensation.

Case 3. (R. W. H.) This 25-year-old white man was admitted four hours after the onset of pain in the right leg, a convulsion and unconsciousness. For two days the patient had complained of drowsiness and pain in the right hand. There had been a 50-pound weight loss and a change in personality in the past six months. No
history of rheumatic fever or other cardiac symptomatology was obtained.

Temperature was 40°C; pulse rate, 84; respiratory rate, 36. The patient was unconscious. There was diffuse muscular spasticity and Cheyne-Stokes respiration. The left pupil was dilated and did not react to light. There were bilaterally positive Babinski toe signs. The heart and lungs were reported as normal.

Shortly after admission, burr holes were made under local anesthesia and extensive hemorrhage found deep in the left cerebral hemisphere. Subtemporal decompression was performed. Shortly after termination of the operation, respiratory failure occurred.

Autopsy revealed a bacterial endocarditis on a bicuspid aortic valve. A nodule, 0.8 cm. in diameter, was present in the wall of the gallbladder. This was identified microscopically as a mycotic aneurysm (Fig. 3). The spleen was enlarged and contained an area of infarction and a microscopic mycotic aneurysm. There was a focal embolic glomerulonephritis, and occasional small renal arteries showed typical mycotic inflammation and necrosis (Fig. 4). Extensive intracerebral hemorrhage was present, but no source of bleeding was identified.

Case 4. (C. T.) This 52-year-old Italian male was admitted in a coma. For the last two months he had been seriously ill, complaining of pain in the left groin, jaundice, melena, epistaxis and hematuria. There was a recent weight loss of at least 30 pounds. For two weeks he had been persistently febrile. Increasing mental confusion caused his admission. No history of rheumatic fever or of other specific cardiac disability could be elicited.

Physical Examination. The temperature was 36.5°C, pulse rate 120, respiratory rate 26. The patient was semicomatose. The heart was not enlarged and the rhythm was normal. There was a harsh, high-pitched, systolic murmur, best heard at the apex and transmitted over the entire precordium. The lungs were clear. Both the liver and spleen were enlarged and tender. There was clubbing of the fingers, but no petechiae or splinter hemorrhages. A non-hemolytic streptococcus fecalis was obtained on blood culture.

The patient was started on large doses of penicillin and showed some improvement for a time, but on the sixteenth hospital day he suddenly became comatose, developed a right hemiplegia, and died in spite of heroic supportive measures.

Autopsy revealed a bacterial endocarditis of the mitral valve and evidence of old rheumatic heart disease. The spleen weighed 1220 Gm., and contained one infarction and one abscess. The kidneys were enlarged and showed many small infarcts. There was gross blood over the surface of the left cerebral hemisphere. Fresh hemorrhages appeared in the pons and midbrain. There was extensive encephalomalacia on the left. Dissection
of the left middle cerebral artery revealed a ruptured mycotic aneurysm.

Sections through the aneurysm of the cerebral artery showed the vessel involved in an acute inflammatory and destructive process, and the architecture was barely recognizable by the shape and the presence of a few elastic fibers. The wall of the artery was formed on one side by an outpocketing of purulent exudative material containing areas of focal calcification.

Case 5. (R. L. R.) This 24-year-old white male was admitted on August 29, 1951, complaining of pain in the legs, malaise, weakness, chills and fever. Past history revealed episodes of rheumatic fever as a child, and again five months before admission. System review was unremarkable except for frequent respiratory infections.

Physical Examination. The patient was well developed and well nourished, pale, and in acute distress. His temperature was 38.6°C, respiration rate 28, pulse 120, and blood pressure 132/45. The lungs were clear. The heart was of normal size and showed a normal rhythm. A systolic thrill was present over the fourth left intercostal space just off the sternum, and a systolic murmur was present over the entire precordium, most marked and harsh at the apex. There was a soft, blowing, systolic murmur at the aortic area that was best heard in the third left intercostal space.

Laboratory data. Urinalysis revealed a specific gravity of 1.020, albumin of 3 plus, and negative sugar. Microscopic examination of the urine showed occasional red blood cells, several coarsely granular and white cell casts, and many white cells. Sedimentation rate was 43 mm./hr. (Wintrobe's method) corrected for hematocrit. The white blood cell count was 6600, with 75 per cent polymorphonuclear leukocytes, 18 per cent lymphocytes, and 7 per cent monocytes. The red blood cell count was 3.1 million, with 9.9 Gm. per cent hemoglobin. Serologic test for syphilis was negative. Blood urea nitrogen was 37 mg. per cent. Roentgenograms of the chest were unremarkable.

The patient was admitted with the diagnosis of subacute bacterial endocarditis and a mycotic abscess of the left femoral triangle. Massive penicillin therapy was begun. Three weeks after admission the patient's condition began to deteriorate. The leg became extremely painful and tender. Signs of cardiac failure were noted, and the
patient was given digitalis. The mass in the femoral triangle enlarged rapidly, and filled the entire medial surface of the thigh. Surgical intervention was advised and streptomycin therapy was added to the penicillin.

On the twenty-fourth hospital day, exploration of the thigh was undertaken. The preoperative diagnosis was a mycotic aneurysm of the deep femoral artery. This anatomic localization was based on the general position of the mass and the presence of a persistently bounding popliteal pulsation distal to the mass. Under continuous spinal anesthesia, a long incision was made over the course of the femoral artery, and the common femoral artery was identified and temporarily controlled with tapes. The superficial femoral artery was found to contain a large embolus lodged 2 cm. distal to the bifurcation of the common femoral artery. The deep femoral artery led directly into the previously described mass, which was found to consist of about 500 cc. of old clotted blood, lying anterior to the adductor magnus and under the edge of the vastus medialis at the level of the first perforating artery. With this clot was found a sac-like membrane, also filled with lamellated clot. A small, grey, granular piece of material believed to have been a platelet embolus was found near the site of a thrombosed artery, which measured about 2 mm. in diameter. The embolus was then removed from the superficial femoral artery. The two emboli were identical in appearance. The common femoral vein was divided and ligated because of its proximity to the inflammatory mass. The wound was closed with a rubber tissue drain in the cavity of the hematoma.

A continuous paravertebral block was maintained for 48 hours after operation, using a polyethylene catheter placed in the paravertebral space to administer a mixture of procaine, penicillin and hyaluronidase.

The patient improved rapidly. His temperature returned to normal in four days; his appetite improved, and his cough and hemoptysis diminished. Some edema of the left leg remained, but the pain and tenderness rapidly disappeared. His cardiac treatment was continued with rest, penicillin, streptomycin and digitalis. He had no further complaints of pain in the left leg, but did have several episodes of pain in the right femoral triangle. Examination of this area was non-contributory.

On the forty-eighth hospital day, the patient complained of severe pain in the right thigh, and a mass 5 x 9 cm. was felt in the right femoral triangle. The superficial femoral artery could be felt stretched over the surface of the mass itself, and the mass did not appear to pulsate. A diagnosis of mycotic aneurysm of the right deep femoral artery was made, and on October 14, the right femoral triangle was explored under spinal anesthesia. A hematoma was found in a location almost identical with the contralateral aneurysm, lying anterior to the adductor magnus and under the edge of the vastus medialis at the level of the first perforating artery. The aneurysm here had also ruptured, but the hematoma was not so large. A platelet embolus, similar to the first two emboli, was found and removed with the clot and aneurysmal sac. A biopsy of the muscle and lymph node was performed and the wound closed with drainage of the hematoma cavity.

The skeletal muscle was normal and the lymph node revealed only a nonspecific lymphadenitis. The patient made a prompt recovery. The mitral and aortic murmurs persisted. There was no evidence of arterial impairment in the legs. He was discharged on the seventy-second hospital day.

No positive blood cultures were ever obtained. Subungual "splitter" hemorrhages and conjunctival petechiae which occurred during the patient's hospitalization substantiated the presumed diagnosis of subacute bacterial endocarditis.

**SUMMARY**

Five cases of mycotic aneurysm are presented. One of these is remarkable because of the occurrence of multiple major emboli and the development of surgically tractable aneurysms in symmetrical areas in each deep femoral artery. Certain features of the diagnostic and therapeutic problems of mycotic aneurysms are reviewed. Increasingly successful antibiotic therapy should make more of these aneurysms amenable to surgical therapy, but a large number of patients will succumb before the appropriate operation can be performed. Prompt surgical intervention is indicated as soon after the diagnosis as the condition of the patient warrants.

**BIBLIOGRAPHY**

**MYCOTIC ANEURYSMS**


**SIXTH INTERNATIONAL CANCER CONGRESS**

Physicians and scientists are invited to present papers at the VIth International Cancer Congress to be held in Sao Paulo, Brazil, on July 23 to 29, 1954, under the sponsorship of the International Union Against Cancer. The program will include sections on fundamental cancer research, on clinical studies on cancer and on cancer control. Registration blanks are available from the Chairman, National Committee on the International Union Against Cancer, National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D. C.

It is expected that round trip transportation by air from Miami to Sao Paulo will be available for about $480. Detailed information regarding travel arrangements and hotel reservations may be obtained from Dr. Brewster S. Miller, American Cancer Society, Inc., 47 Beaver Street, New York 4, New York.

In accordance with similar arrangements being made in other countries to coordinate participation in the Congress, residents of the United States who desire to present papers must send five copies of an abstract of each paper proposed for presentation to the Chairman, National Committee on the International Union Against Cancer, at the above address by January 15, 1954. Abstracts are not to exceed 250 words and must be accompanied by a title and the name, address, academic or professional title, and institutional affiliation of the investigator or physician. These requirements do not apply to people who have been invited to participate by the President of the Congress unless application is made for travel allotments as described below.

Travel allotments of approximately $600 each will be available to a limited number of individuals requiring such assistance. Applications for travel allotments must be submitted in quintuplet to the Chairman, National Committee on the International Union Against Cancer, at the above address by January 15, 1954. They should be in letter form, giving information concerning age, training, publications in cancer or related fields, and academic or professional status. Applicants not planning to present papers should include five copies of abstracts, as described above, of major current investigative work. A letter from the laboratory director, or appropriate administrative officer, approving the application, is also necessary.
RUPTURE OF THE INFERIOR EPIGASTRIC VESSELS*
S. DOUGLAS MURRAY, M.D. AND RAY E. BURGER, M.D.
WELCH, WEST VIRGINIA

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RUPTURE OF THE inferior epigastric vessels is not considered a very common lesion. Many of the standard texts on surgery entirely omit a description of this clinical entity, which is important chiefly because of the abdominal lesions with which it may be confused. It is the purpose of this communication to state some of the diagnostic pitfalls and to outline several of the clinical clues which aid earlier diagnosis. Early diagnosis results in early treatment, and this will obviate many of the time and effort consuming laboratory procedures commonly undertaken when the patient presents himself to the surgeon. Therapy is relatively easy and so far as the literature attests, cure is permanent.

BACKGROUND

The first case of rupture of the inferior epigastric artery was reported in this country by Richardson in 1857. Payne was able to collect 165 cases in the literature up to 1938. Since that time Herman, Bowles, Lord, Bassett, and Johnson have added their cases. In the foreign literature, Hughes, Dwyer, Kotzareff, and Blond have written rather extensively of the syndrome.

ANATOMY

In general, the rectus abdominis and the muscles of the cheek are the only groups in the body that do not lie on some form of skeletal support. This doubtless makes them prone to injury under the stimulus of sudden strains, as in the case of the recti with coughing or assuming the upright position.

Max Brödel described the long, narrow belly of the rectus muscle as made up in reality of separate muscles that act as one because of the tendinous bands that run transversely. It can expand and contract as much as nine finger-breadths. Terrific pressure is thus exerted as in the act of defecation, straightening up or violent coughing spasms. Running beneath this muscle in loose areolar tissue is a long anastomosis between the femoral vessels below and the internal mammary above. Lying beneath the vessels is the posterior rectus sheath as far as the semilunar line of Douglas, and below that, transversalis fascia and peritoneum. The inferior epigastric vessels send many branches to the muscles, especially at the tendinous inscriptions. The proximity to the peritoneum, especially below the umbilicus, probably causes the signs of peritoneal irritation so often observed when the vessels bleed. It can be seen, too, from this, that in the exceptional case, bleeding may extend as far as the thoracic cage superiorly, and to the perivesicle space inferiorly. Indeed, Kotzareff reports a case where the hemorrhagic mass could be palpated per vagina.

PATHOLOGY

The rupture of the epigastric vessels occurs most usually below the fold of

* Submitted for publication April, 1953.
RUPTURE OF THE INFERIOR EPIGASTRIC VESSELS

Douglas. Conceivably either the artery or the vein, or both, may be involved, but such a distinction is often impossible to make at operation. Most observers feel that the last situation is the one obtaining in the majority of cases.

The lesion has been classified as traumatic as in puncture wounds of the abdominal wall, as in one of our cases, and spontaneous, as reported by Epstein and others. The last category is probably very rare, as careful inquiry most often will elicit a history of sudden strain, as in coughing or twisting.

Just what causes these vessels to bleed aside from their anatomical situation? Infectious processes such as tuberculosis, typhoid, tetanus, typhus, influenza and low states of muscular inanition seen in the wasting diseases have been indicted. In the blood vessel itself hypertension, arteriosclerosis, lues and medial degeneration have been mentioned. Hughes reports a case occurring during pregnancy. Others feel that pregnancy may be of predisposing importance in the disease in later years. This factor was ruled out in all of our cases. Aneurism, localized to the site of the lesion, has been advanced as a possible cause of rupture, but this has never been substantiated.

Another etiological agent may well be the anticoagulants so much in use today for thrombo-embolic disease. This appears to have been the major offender in one of our patients.

Untreated or unrecognized cases may result in abscess formation, as occurs in hematomata elsewhere.

SIGNS AND SYMPTOMS

The average patient presents himself with the complaints of pain in either the right or left lower abdominal quadrant. Nausea and vomiting, anorexia and constipation may be present. The onset may be sudden or gradual, depending upon the amount of bleeding.

Pertinent signs are confined to the abdomen. A tense, tender mass is most generally palpable either to the right or left of the midline in the lower abdomen. The mass is fixed, and there may be an associated spasm and rigidity of the muscles. Slight to moderate intestinal distention is not unusual. Peristaltic sounds may be hypo-active or not affected. Ecchymosis of the abdominal wall has been described, but was not observed in our cases.

If a mass is palpable and remains so when the patient sits up, and cannot be moved from side to side, the diagnosis becomes more certain. This sign was first described by Fothergill.

Prostration and shock may be present, but are rare. Slight elevation in the temperature, pulse and white blood count is the rule.

The lesion is said to afflict primarily the middle-aged patient. Signs of arterial and venous disease elsewhere are often found. Laboratory and radiological examinations are not contributory, save in a negative way, to rule out other conditions. As intimated previously, such tests are time and energy consuming when the diagnosis can and should be made without them in the majority of cases.

DIFFERENTIAL DIAGNOSIS

Among the myriad intra-abdominal conditions confused with rupture of the inferior epigastric vessels are carcinoma of the colon with perforation, pelvic inflammatory disease, chronic appendicitis, cyst of the ovary, tumors of the abdominal muscles, mesenteric thrombosis, volvulus, intussusception, gallbladder disease, tubal pregnancy, degenerating fibroids of the uterus, abscess of the abdominal wall, muscle rupture, and in one of our cases, incarcerated hernia. Bassett reports a case associated with intercurrent appendicitis.
TREATMENT

Conservative treatment, consisting primarily of pressure with a tight abdominal binder, has been advocated by some, including Lichtenstein. The majority opinion, however, holds that direct surgical attack upon the bleeding point is the safest and surest therapy. To leave a blood clot in the tissues is to invite chronic pain, abscess formation and calcification. Operative interference, also, clearly obviates the occasional case of mistaken diagnosis, which in certain instances may be catastrophic.

CASE REPORTS

Case 1. Mrs. R. M., Hospital No. A-2576, 40-year-old white, married female, Gravida O, was admitted to Grace Hospital on February 2, 1953. She stated she had had the “flu” for the past week, and after a paroxysm of coughing two days prior to admission, had developed a painful mass in the lower right abdomen at the site of a right rectus incision made nine years previously for appendicitis. She had vomited intermittently ever since. Bowels had moved the day before. She had passed neither stool or flatus on the day of admission.

Physical examination revealed a well developed woman in considerable physical distress. Blood Pressure was 134/78, pulse 92, temperature 99°. Abdomen was moderately distended. There was a fixed, tense, exquisitely tender mass in the right lower abdominal quadrant at the inferior angle of the previous laparotomy scar. Peristalsis were hypo-active. Rectal and vaginal examination were negative. Preoperative diagnosis was “incarcerated incisional hernia.”

Under spinal pontocaine anesthesia on the day of admission, an incision was made over the mass. The fascia was found to be intact. The right rectus muscle was torn and shredded. A large hematoma was found under the muscle. This was evacuated, and the inferior epigastric artery was seen to bleed actively after the clot was removed. The vessels were doubly ligated. Wound closed without drainage. The postoperative course was uncomplicated, and the patient was discharged asymptomatic on February 11, 1953.

Comment. The history of “flu” and violent coughing, plus the fixed tender mass, were the chief clues in the diagnosis in this case. The vomiting and obstipation were clearly on an irritative basis. Absence of obstructive sounds should have made the preoperative diagnosis somewhat untenable, save were it a case of a hernia of the Richter type. Decoulx, Driessens and Demarey in 1939 reported a case in which rupture of the epigastric vessels followed an attack of bronchitis in a patient who had had four previous laparotomies, the last one eight years previously. The authors believed that the multiple irritative actions of the repeated operations were the etiological factor in the case. Our case is somewhat similar, but it is difficult for us to believe that the previous surgery contributed to the accident.

Case 2. Mrs. A. H., Hospital No. A-4975, a white, married, Gravida O, 68-year-old female, was admitted to Grace Hospital on March 10, 1953. This patient had been treated both as an in- and as an out-patient for many years for arteriosclerotic cardiovascular disease, and for hypertrophic arthritis of the spine.

On the present admission, she was complaining of pain and swelling of the left leg for the past two days.

Examination showed an elderly woman in no distress. Weight, 160 pounds; blood pressure, 195/100; pulse, 112; temperature, 99°. Heart was clinically enlarged. There was an occasional extra-systole. There were no murmurs. Lungs were clear, abdomen was virginal, slightly distended, otherwise negative. Left lower leg was slightly swollen and red. There was tenderness over the calf muscles and Homan’s sign was positive. Pelvic and rectal examinations were negative. Diagnosis of thrombo-phlebitis of the left leg was made.

Patient was placed on bed rest, elevation and warm packs to the left leg. Three hundred mg. of Dicoumarol were given on the day of admission, and 200 mg. each day for the next two days. Cardio therapy was also administered.

Process in the leg had clinically subsided in 5 days. Patient began to complain of arthritic pain in the knees and back, and on March 16, 1953, was placed on 25 mg. of Cortone every six hours. The following day the patient complained of constipation. There was some distention and slight tenderness of the right lower quadrant. No masses were palpable. Ampulla of the rectum was some distention.
RUPTURE OF THE INFERIOR EPIGASTRIC VESSELS

Physical examination showed a small, thin, negro female in no distress. Blood Pressure was 114/70; pulse, 80; temperature, 99.6°. There was moderate left costo-vertebral angle tenderness. The abdomen was scaphoid. There were no masses or tenderness. The right lower rectus incision was well healed. Pelvic examination revealed the cervix to be firm and closed. There was a large, firm, fixed mass in the right fornix; the left fornix was very tender. Diagnosis of pyelitis, left, and possible ectopic tubal pregnancy was made.

Cystoscopy on February 21, 1953, was negative, as were retrograde pyelograms, save for many white blood cells in the urine specimens from both sides. Friedman test for pregnancy was negative on February 23, 1953.

The abdomen was explored on February 25, 1953, under spinal anesthesia through a lower mid-line incision. No active bleeding was encountered from the epigastric vessels. Both adnexal areas were masses of adhesions with the tubal and ovarian architecture completely destroyed. Bilateral salpingo-oophorectomy was performed. Abdomen closed in layers using silk on the fascia and skin.

Pathological Report. Sclerotic and cystic ovaries; chronic inflammatory oviducts.

Postoperative course was uncomplicated, and the patient was discharged on March 3, 1953, asymptomatic. The patient was checked in the out-patient clinic one week later and was doing well.

Patient returned to the hospital on April 14, 1953, complaining of a painful tender swelling of the left side of the abdomen for the past two weeks. Physical examination was negative except for the presence of a tense, tender, non-mobile mass to the left of the surgical incision. Pelvic examination revealed no masses.

Diagnosis of hemorrhage from the left inferior epigastric artery was made and patient was re-admitted to the hospital. On April 15, 1953, under Sodium Suritol anesthesia, a small incision was made over the mass, and deep to the substance of the left rectus muscle about 40 cc. of sanguino-purulent material was evacuated. The incision was closed around a small rubber tissue drain. Postoperative course was uncomplicated. The patient was discharged on April 19, 1953. Pathological report was Staphylococcus Aureus.

Comment. Johnson reported a case of postoperative hemorrhage from the deep epigastric vessels in 1943. His case occurred about two weeks following laparotomy through a right para median inci-
sion for pelvic pathology. Our case occurred about one month following operation. Operative trauma undoubtedly contributed to the lesion, possibly from self-retaining abdominal retractors. Why the clots became infected is conjectural. Blond’s case also underwent purulent transformation.

CONCLUSIONS
1. The surgical entity of rupture of the inferior epigastric blood vessels has been reviewed from a historical, pathological, anatomical, diagnostic and therapeutic viewpoint.
2. Although the disease is said to be rare, the three cases herein reported occurred within a space of three months.
3. Its importance is chiefly in differentiating it from more serious intra-abdominal conditions.
4. Surgical attack on the bleeding point is relatively simple and no case of recurrence has been reported.
5. The possible etiological role of the anticoagulants has been stated, and a report of one of our cases in which one of these agents had been used, is the first, so far as we know, to be recorded.
6. Pregnancy, at least in our cases, either proximately or remotely, was not a factor in this lesion.

BIBLIOGRAPHY
CONGENITAL INTRINSIC OBSTRUCTION OF THE DUODENUM
WITH REPORT OF THREE CASES*

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INTRODUCTION
Duodenal atresia and stenosis are relatively rare conditions, but in the past few years an increasing number of cases have been reported. In the past 27 months, one infant with atresia and two with stenosis have come under our care and have been operated upon successfully. This paper briefly summarizes the important aspects of these congenital deformities and reviews our three cases.

INCIDENCE
The exact incidence of congenital intrinsic duodenal obstruction has not been determined; however, Webb and Wangensteen in 1931 estimated atresia or stenosis of some part of the intestinal tract occurred about once in every 20,000 live births. Davis and Poynter in 1922 estimated duodenal atresia to occur in about 58,500 live births. Ladd and Gross in 1941 recorded five treated cases of duodenal atresia and 11 cases of duodenal stenosis. The malformation is probably more prevalent than previously supposed, and its detection requires only alertness on the part of the first examining physician. A majority of these babies can be cured if diagnosed promptly.

SYMPTOMS AND SIGNS
These, in early cases, include persistent vomiting of bile (usually the atresia or stenosis is distal to the ampulla of Vater) with distention of the upper abdomen on the first day or two of life. Visible peristalsis is a valuable sign and almost surely means duodenal obstruction because hypertrophic pyloric stenosis occurs so rarely at this age. The vomitus may contain meconium. There are either no stools at all (in atresia) or scanty ones containing meconium or milk curds (in stenosis). While these are all clues to the diagnosis, they serve only to arouse suspicion, and indicate necessity for an abdominal roentgenogram.* In atresias, the stomach and proximal duodenum will be gas-filled, with no gas in the remaining intestinal tract. In a duodenal stenosis, some gas will appear distally, as the obstruction is incomplete. If still in doubt, air or a thin mixture of barium may be instilled into the stomach through a catheter. The barium, in our experience, does no harm, and may be withdrawn through the catheter after completing the studies. A high index of suspicion and observation on the part of the first examining physician, followed by simple roentgenographic studies, should leave few cases undiagnosed.

TREATMENT
The greatest advances have been made in treatment. Of the 16 cases of Ladd and Gross up to 1941, eight were successfully treated. Glover and Barry in 1949 reported eight operative cases with three survivals. Individual reports seem to indicate a greater number of survivals than formerly, probably because of more accu-

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rate and rapid diagnosis and because of better preoperative preparation and postoperative care. Routine use of blood, parenteral fluids, and antibiotics to prepare these infants for surgery has been the deciding

![Fig. 1 (Case 1). Roentgenogram of abdomen without use of barium, showing gas-filled stomach and duodenum and absence of gas in remainder of intestinal tract, consistent with a duodenal atresia.](image1)

factor. The surgical technic has changed little with the years. Enough fluid to restore balance should be given, but overhydration should be avoided. Elaborate blood chemistry studies give little aid to the physician, but much discomfort to an already dangerously ill infant.

Preoperative preparation should take a minimum of time. Following this, the infant, with a catheter in the stomach, is taken to the surgical theater, a cannula is inserted in an ankle or other suitable vein, a source of heat is placed near the baby, and the anesthetic given. An incision of the surgeon's choice is made. The stomach and duodenum are examined, with mobilization of the duodenum. This latter step may be difficult, but will be aided by elevation of the right and transverse portions of the colon. The distended duodenum will narrow at one point and distal to this the jejunum will be completely collapsed (in atresia) or partially collapsed, and of definitely smaller than normal caliber (in stenosis). Care must be taken to avoid trauma to the bowel wall and to delicate omental and mesenteric vessels. When the

![Fig. 2 (Case 1). At two years of age.](image2)
site of the pathologic portion is accurately determined, a duodenojejunostomy or gastrojejunostomy is made, by-passing the point of obstruction. We feel the former to be preferable, but believe a poor risk infant to be better off with a more cursory exam-

Case Reports

Case 1. A 4-day-old female was admitted December 11, 1950. The birth weight had been 6 pounds 8 ounces; present weight was 4 pounds 12 ounces. The infant had vomited bile periodically since birth and had retained no feedings. There had been no bowel movements.

She was severely dehydrated, with a barely perceptible heart beat and irregular respirations. There was moderate distention of the upper abdomen. No other congenital defects could be found. The red blood cell count on admission was 7,240,000, with 21.7 Gm. of hemoglobin.

Fluids and penicillin were given, and after 36 hours, the red blood cell count was 4,100,000 and the hemoglobin 15.2 Gm. A roentgenogram of the abdomen (Fig. 1) confirmed the diagnosis of congenital duodenal atresia.

Following insertion of a cannula into an ankle vein and a catheter into the stomach, a vinethene-ether anesthetic was administered and a transverse incision was made above the umbilicus, with section of a portion of both rectus muscles. The stomach and first and second portions of the duodenum were distended. The jejunum was col-

Fig. 3

Fig. 3 (Case 2). Roentgenogram of abdomen using thin barium showing distended stomach and duodenum with the point of obstruction. Gas is present in lower intestinal tract, showing the obstruction to be a stenosis rather than an atresia.

Fig. 4

Fig. 4. Roentgenogram of abdomen using thin barium. The point of duodenal obstruction is evident. Gas in lower intestinal tract shows this to be a duodenal stenosis.
lapsed, as was the remainder of the small and large bowel. No gas could be manipulated into the jejunum, so a complete atresia was presumed to be present. The duodenum was not completely mobilized because of the infant’s poor condition, but it was sufficiently examined to confirm the diagnosis. A brief examination of the remaining bowel showed no obvious obstruction. It was thought that the quickest procedure would be an anterior gastrojejunostomy rather than a duodenojejunostomy, so this was done, using a two layer anastomosis, continuous 4- chromic to the mucosa and muscularis and interrupted 4-0 silk to the serosa. The abdomen was closed in layers with interrupted 3-0 silk, and 4-0 chromic subcuticular suture was used in the skin. During the operation, blood and fluids were given through the cannula.

Postoperatively the baby regurgitated some early feedings, but began to have curds in the stool on the fourth postoperative day, and by the eighth day the weight was 5 pounds, 14 ounces. The baby made uneventful progress and was discharged on the eighteenth postoperative day weighing 6 pounds 15 ounces. She is entirely normal at the present time (Fig. 2).

Case 2. An 18-day-old female was admitted August 8, 1952, weighing 5 pounds 13 ounces (birth weight 7 pounds). She had started, on the third day after birth, to vomit bile 1 to 3 hours after eating. There were scanty bowel movements. The red blood cell count was 5,420,000; the hemoglobin, 15.8 Gm. There was some upper abdominal distention. A roentgenogram of the abdomen (Fig. 3) was diagnostic of congenital duodenal stenosis.

The infant received preoperative fluids and, after the usual cannula and gastric tube were placed, was operated upon through a transverse upper abdominal incision. The stomach and first, second, and third portions of the duodenum were distended; the remainder of the small bowel was collapsed, but a small amount of gas could be manipulated into the jejunum from the duodenum. The duodenum was mobilized laterally and dissection carried to the point of marked narrowing in the third portion. The jejunum was anastomosed to the dilated duodenum using the two layer technique as described in the first case report.

There was some regurgitation for 3 days postoperatively. Following this, well formed stools appeared and the vomiting stopped. The infant was discharged on the seventeenth postoperative day, and at that time was showing normal weight gain. The baby was seen 2 months after operation and was normal.

SUMMARY AND CONCLUSIONS

Three successfully treated cases of congenital intrinsic duodenal obstruction have been presented. We suggest that duodenal atresia and stenosis are more common than supposed and that the first examining physician can make the diagnosis by being aware of the triad of persistent vomiting soon after birth, upper abdominal distention, and a characteristic roentgenogram. Early diagnosis followed by proper surgery should give a high percentage of cures.

BIBLIOGRAPHY

PERFORATED PEPTIC ULCER IN THE NEWBORN:
REPORT OF A CASE WITH MASSIVE BLEEDING*

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"IT IS SIGNIFICANT that only two cases of massive bleeding from peptic ulcer in children under one year of age followed by recovery have been reported." This statement recently published prompted the reporting of the following case.

CASE REPORT

Infant female was born on the Obstetrical Service, Fitzsimons Army Hospital, at 7:00 P.M., January 18, 1953; the first living child of a 19-year-old gravida II para 0 Negro female whose prenatal course had not been remarkable. Labor was difficult because of the fact that the cervix effaced slowly and delivery was accomplished by manual rotation with a low forceps extraction. Birth weight was 5 pounds, 10 ounces. The positive findings on physical examination at birth were those of a weak cry, poor Moro reflex and the usual amount of molding of the head.

The child was placed on routine neonatal care and the first suggestion of any difficulty was at 8:00 p.m. on January 20, 1953, when the child was approximately 48 hours old. The pediatrician was asked to see the baby because she had vomited some "coffee ground" material after nursing poorly. To examination, the infant was active, lightly jaundiced, and the abdomen was moderately distended. There were active bowel sounds present and rectal examination was negative. A gavage tube was passed into the stomach without any resistance, and at this time the child had an emesis of brown stained material.

C CBC was within normal limits. A plain roentgenogram of the abdomen revealed a moderate amount of gas in the stomach, and the left side of the abdomen showed one or more loops of dilated bowel. From this film it was not possible to determine whether this was small or large bowel. There was no gas noted in the region of the sigmoid or rectum; it was felt by the radiologists that these findings were consistent with the diagnosis of mechanical obstruction.

One-half hour later the infant vomited 65 cc. of bright red blood with clots and had very suddenly gone into profound shock. The abdomen became more distended and no bowel sounds could be heard. She immediately received 75 cc. of whole blood by syringe, with definite clinical improvement, good peripheral pulse, and the decision was made to explore the abdomen.

At 3:35 A.M. on January 21, 1953, when the child was 56 hours and 35 minutes old, the abdomen was entered through a right paraumbilical incision. When the peritoneum was opened, a considerable quantity of clotted and bright red blood presented. It was estimated that approximately 135 cc. of blood were removed from the peritoneal cavity. There was moderate distention of the small bowel and through the thin bowel wall could be seen intraluminal blood. Exploration of the abdomen was negative until the right upper quadrant was reached. Over the dome of the right lobe of the liver there was considerable clotted blood, and initial impression was that there had been a traumatic laceration of the liver. However, with the clotted blood removed, the dome of the right lobe of the liver was found to be intact, and was retracted for examination of the stomach and duodenum. Exposure revealed a 7 mm. perforation of the anterior aspect of the first part of the duodenum approximately 5 mm. distal to the pylorus, from which clear bile extruded. The perforation was repaired with interrupted vertical mattress sutures of No. 80 cotton, securing a tag of omentum over the perforation. With the perforation closed, two small Penrose drains were brought out through a stab wound in the right subcostal region from the right infra-hepatic space. The abdomen was closed and the patient was returned to the ward in fair condition. The child re-

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William H. Moncrief, Jr.

Received 140 cc. of blood during the procedure and immediately postoperatively.

Postoperatively the infant was maintained on IV fluids and in addition was given penicillin, streptomycin, vitamin C and vitamin K daily. The evening of January 22, 1953, the child was started very cautiously on very small amounts of electrolyte and glucose solutions by mouth. She continued to do fairly well on this regimen, with the amount of fluid intake being increased rather slowly; however, at 11:00 P.M., January 22, 1953, the infant vomited some bile stained material that was not bloody. The rest of the general physical examination was negative except for the distention of the abdomen, but at the same time there was noted active peristalsis. The oral feedings were discontinued and the child was continued on parenteral fluids. By January 23, 1953, good bowel sounds again were heard, the child was active and the abdomen was less distended than it had been. She was restarted on oral feedings at 5:00 P.M., January 24, 1953, being offered small amounts of electrolyte solution by mouth. A dilute "Alacta" formula was started on January 25, 1953, which she tolerated very well. This was increased slowly, both in strength and amount, and the rest of the child's hospital stay was uncomplicated. She was discharged February 26, 1953, in good general condition. Her weight was 5 pounds 14% ounces.

Fig. 1. (A and B) Note pneumoperitoneum under right leaf of the diaphragm and over dome of liver missed at initial reading. Lipiodol fills the colon, demonstrating small bowel distention.

Discussion

The problem of peptic ulceration in newborn and infants has been the subject of occasional review since Holt published his series in 1913. Bird, Limper and Mayer, Guthrie, Hollander and Stark, and Mcaleese and Steber have reported peptic ulcers in newborn, infants and children in excellent summaries. From these it can be seen that peptic ulcer in the early age group is a relatively rare condition, but is...
being recognized with increasing frequency. While approximately 375 cases have been reported in the literature, there are undoubtedly many others which have not been reported. The general incidence of duodenal ulcer in the newborn can be appreciated by the report of Bonnaire, Durante and Ecalle, who showed in 4000 autopsies of newborns only two cases of duodenal ulceration. The disease in newborn and infants appears equally distributed between the sexes and has been reported in every age group. Lee and Wells report a perforation in utero, and numerous authors report ulceration in the first few days of life. The case of Bird, et al, at 34½ hours of age, appears to be the earliest treated surgically with recovery.

The etiology of peptic ulceration in newborn and infants is unknown, but undoubtedly many of the adult factors pertain to the very young. The condition has been attributed by different authors to various causes, and more than likely is due to a combination of factors. External trauma, vascular, bacterial, chemical and neurogenic theories have been invoked to explain the etiology. It is of interest to note the more than casual relationship between difficult labor with intra-cranial damage, and intracranial new growths in the newborn, and peptic ulceration. Vonderahe reviewed 51 cases of gastroduodenal ulceration and noted well marked, localized, pathologic alterations of the brain or its membranes in 21.6 per cent of them.

Cushing wrote that trauma or new growths may produce a functional release of the vagus from paralysis of the antagonistic sympathetic fibers leading to hypersecretion, hyperchlorhydria, hypermotility and hypertonicity, especially marked in the pyloric segment. Localized mucosal ulceration, questionably associated with the asphyxia of difficult labor, and the relative hyperacidity in the first few days of life as reported by Miller, may have a significant role in the etiology.

Ulcers varying in size from a few millimeters to 1.5 cm. have been reported, and multiple ulcerations may occur. As many as five separate and distinct ulcers have been found in the same infant. In the newborn, ulcers are of the acute type. They occur so rapidly that there is usually no evidence of acute inflammatory reaction adjacent to the ulcer, and may be associated with necrosis and hemorrhage, including surrounding tissues, rather than with inflammation.

The condition is practically never diagnosed or suspected until hemorrhage or perforation occurs, because peptic ulcer symptoms in newborn and infants are atypical. Perforation is commonly accompanied or preceded by clinically detectable bleeding. Protocols commonly report sudden profuse hematemesis and death within a few hours, occasionally preceded by a day or two of black stools. There may be vomiting, loose stools and dehydration, to be followed suddenly without warning by bloody vomitus or melena. A previously scaphoid abdomen may become distended due to perforation of the ulcer. Early diagnosis is important in the treatment inasmuch as hemorrhage is usually, and perforation always, a surgical problem. Transfusion should be resorted to early, and must be given in adequate amounts to sustain the infant until an operation can be performed.

SUMMARY

As far as can be determined, the third case of bleeding peptic ulcer with perforation in a newborn with recovery is reported. Only one younger case, with recovery, that of Bird, et al, can be found. The importance of early diagnosis, supportive therapy and good nursing care is emphasized.
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ANNOUNCEMENT

On February 18, 1954, the Buffalo Surgical Society will sponsor the Roswell Park Lecture, this year to be given by Dr. Isador S. Ravdin, John Rhea Barton Professor of Surgery, University of Pennsylvania Medical School, and Surgeon in Chief at the Hospital of the University of Pennsylvania.

Dr. Ravdin at that time will be awarded the Society’s Gold Medal, being given for the seventh time, in honor of Dr. Roswell Park, Professor of Surgery, University of Buffalo, 1883–1914. Previous lecturer and recipients of the Medal are as follows: Dr. Allen C. Whipple (1948), Dr. Evarts A. Graham (1949), Dr. Dallas B. Phemister (1950), Dr. Frederick A. Coller (1951), Dr. Edward D. Churchill (1952), and Dr. Warren H. Cole (1953).
PANCREATODUODENECTOMY FOR LEIOMYOSARCOMA OF THE DUODENUM*

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Radical pancreateoduodenectomy, as originally reported by Whipple and his associates in 1935, was first performed in two stages for carcinoma of the ampulla of Vater. It was later applied to carcinoma of the head of the pancreas, duodenum, and distal portion of the common bile duct. The operation is now performed in one stage by most surgeons. Cattell feels, however, that in occasional poor risk patients, the operation is done more satisfactorily in two stages. He recommends a first-stage cholecysto-jejunostomy, followed by the second stage in two to three weeks, which time enables the patient's condition to improve. He believes that this technic extends the operation to a certain number of patients with long-standing jaundice and hepatomegaly who could not withstand such radical surgery otherwise, and he feels that a lower over-all mortality is attained.

Trimble, in 1941, advocated a technic wherein there was no attempt made to anastomose the remaining portion of the pancreas to the jejunum. Brunschwig also adheres to this technic. Occasionally, however, persistent pancreatic fistulae or intra-abdominal abscesses have developed when this technic was used.

Restoration of the continuity of the gastro-intestinal tract usually is accomplished most satisfactorily by doing a gastrojejunostomy distal to the site of the implantation of the common duct or the gallbladder into the jejunum, to avoid ascending cholangitis.

At the time of operation, the diagnosis of a lesion is sometimes still in question, confusion existing regarding common duct stone, chronic pancreatitis, and carcinoma of the ampullary region. Resectability may be determined occasionally after mobilization of the duodenum and head of the pancreas. If necessary, a palliative procedure only may be done.

The results of pancreateoduodenectomy in treatment for carcinoma of the pancreas are discouraging. Roughly, only one-third of the lesions for which laparotomy is done are amenable to the radical operation, most cases being too far advanced. Local invasion or metastases to lymph nodes are usually contraindications to resection. In Cattell’s series of 30 operative cases, the operative mortality was 16.7 per cent, and there were no cures or five-year survivals reported. Brunschwig has recently described a seven-year survival, and Miller and Clagett a five-year survival, however. Cattell suggests total pancreatectomy as a further radical measure to prevent recurrence, and to obviate the danger of the spread of cancer cells where the involved pancreas and its ducts are transected.

Results in the treatment of carcinoma of the ampulla of Vater are more encouraging. Cattell having three cases surviving more than five years, and six cases surviving more than three years, in a series of 12 operative cases.

Familiarity with and improvements in the technic of pancreateoduodenectomy have facilitated the performance of the operation more frequently. In addition, the increasing advancements in the surgeon’s
armamentarium of anesthesia, blood transfusions and antibiotics, have enabled surgeons to increase the applicability of the operation, as in the following case.

**CASE REPORT**

A 31-year-old Filipino man was admitted to Queen’s Hospital, Honolulu, on May 5, 1952, with the complaint of vomiting of bloody material and the passage of black stools. He had had similar symptoms 5 months previously, but there was no history of abdominal pain, indigestion, excessive alcoholic beverage ingestion, or weight loss. Examination revealed pallor, a normal temperature, a pulse of 120, and a blood pressure of 90/70. The abdomen was soft and non-tender. Rectal examination produced reddish-brown stool on the examiner’s gloved finger. The remainder of the physical examination was negative. The red blood cell count was 3,820,000, and the hemoglobin 9.8 Gm. A urinalysis was non-contributory. The patient was admitted to the medical service. A surgeon was called immediately in consultation, and the patient followed jointly thereafter by both services.

The patient was sedated, and a transfusion of low-titer “O” blood was started. He was cross-matched for two more pints of blood. A Foley catheter was inserted into the bladder, and measurement of the hourly urinary output was commenced. The vital signs were recorded at frequent regular intervals, and the patient was re-evaluated every one to two hours. He improved after the initial transfusion, but 12 hours later, after the administration of 1000 cc. of blood, he vomited black material, and passed a large amount of tarry stool. The urinary output was less than 15 cc. per hour. The blood pressure had dropped to 66/24. The patient was perspiring, pale and lethargic.

It was felt that the hemorrhage was continuous and severe, despite an initial response to the first transfusion. Laparotomy was performed despite the lack of a definitive diagnosis. An extensive gastrotomy was unrevealing. Further exploration revealed a large, soft tumor in the region of the head of the pancreas, which had eroded the posterior wall mucosa of the second portion of the duodenum to cause the bleeding. A biopsy was taken, but definitive surgery was felt to be contraindicated because of the patient’s poor condition. The abdomen was closed. Further transfusions were given in order to restore the patient’s blood volume. The pathological report on the biopsy was neurofibroma.

Four days later, he had recurrent passage of large amounts of tarry stools, along with tachycardia and lowered blood pressure. Another laparotomy was done, and through a duodenotomy opening, the bleeding point in the duodenal wall was ligated. The stomach was transected, and the distal segment closed. A gastrojejunostomy was done as a preliminary to later radical surgery, and to divert the flow of gastric contents away from the duodenum. Following this, the patient’s hemorrhage ceased.

Three weeks later, a radical pancreatoduodenectomy was done. The lesion appeared to be a smooth muscle tumor, 6 or 7 cm. in diameter, which had arisen from the wall of the second portion of the duodenum, and which had extended into the head of the pancreas. There was no evidence of metastasis. It was felt that local excision was impossible, due to involvement of the head of the pancreas and proximity of the tumor to the common bile duct. Approximately two-thirds of the stomach, the entire duodenum, the distal portion of the common bile duct, and the head and part of the body of the pancreas were removed. The jejunum was transected near the ligament of Treitz, and its proximal segment re-
moved with the specimen. The distal cut end was brought up through the transverse mesocolon for purposes of anastomosis. The duct of Wirsung, in the stump of the remaining tail of the pancreas, was catheterized with a small segment of \#18 polyethylene tubing. A pancreaticojejunostomy was done, capping the open end of the jejunum over the tubing and end of the pancreas. Two layers of interrupted inverting 5-0 silk sutures were used. A T-tube was placed in the common duct, and an end-to-side choledochojejunostomy was performed distal to the pancreaticojejunostomy, using the T-tube as a splint. An end-to-side cholecystojejunostomy was also performed, distal to the choledochojejunostomy. The above three anastomoses were performed retrocolic. A distal loop of jejunum was then brought anterior to the transverse colon, and a gastrojejunostomy was performed. Interrupted silk suture technic was used throughout.

The patient withstood the procedure well, and the convalescence was uneventful. Within 6 months, he had gained 15 pounds and resumed his job as a carpenter. A follow-up 11 months postoperative revealed continued improvement and no evidence of recurrence or metastasis.

Histological study of the tumor revealed spindle cells with oval blunt-ended nuclei (Fig. 1). The cytoplasm of these cells contained intracellular fibrils (on special stains), and the nuclear chromatin was cross-hatched. The cells were collected into bundles and whorls. Degenerative changes were present, and occasional mitotic figures were seen. No capsule was present microscopically, and the lesion faded imperceptibly into adjacent structures. Special stains, including Masson and van Gieson, indicated that the lesion was of a myomatous nature. It was felt to be a grade I leiomyosarcoma.

The above tumor represents a typical myomatous tumor of the "outer" or subserosal type, which is frequently a source of massive exsanguinating gastro-intestinal hemorrhage, due to necrosis and erosion of the mucosa. The lesion was regarded as of very low malignancy. Smith states that metastasis is the only positive proof of malignancy in these lesions. A local excision was impossible because of the size of the tumor, its extension into the pancreas, and its proximity to the common bile duct. A pancreateoduodenectomy was performed after two preliminary laparotomies. The postoperative result to date has been satisfactory. It is felt that the radical operation, pancreateoduodenectomy, is occasionally applicable to lesions such as this.

**BIBLIOGRAPHY**

A review of the medical literature from 1940 to the present yields only two documented reports of accidental division of the femoral artery during surgery for varicose veins. The purpose of the following case report is twofold: first, to re-emphasize this hazard of surgery for varicose veins; and secondly, to present a review and critique of the plan of management of a major arterial injury of the lower extremity, in the light of recent knowledge.

CASE REPORT

V. W., 32-year-old wife of an Air Force sergeant, was admitted to the USAF Hospital, Ellington Air Force Base, Texas, on June 28, 1952, as a transfer from a small, local civilian hospital, 3 days following an operation for varicose veins of the left lower extremity.

She had had no significant illnesses previously, except for mild bilateral greater saphenous varicosities of about 10 years’ duration, more marked on the left. Operative treatment had been advised and, on the morning of June 25, 1952, the patient had reportedly undergone high ligation of the left greater saphenous vein, together with interruption of several small varicosities on the lateral aspect of the thigh, and the retrograde injection of sclerosing solution into the distal trunk of the saphenous vein.

On recovery from anesthesia, the patient experienced excruciating pain throughout the entire left leg and slight numbness of the foot. During the ensuing 72 hours, mottled areas of grey-brown discoloration developed over the course of the greater saphenous vein, along the medial thigh and lower leg, and over the entire great toe. The pain increased progressively; it could not be controlled by opiates, and the entire extremity, particularly the lower leg and foot, became noticeably swollen.

On June 28, 1952, her husband arranged for her transfer to the USAF Hospital, Ellington Air Force Base.

On examination at the time of admission, the patient’s general appearance was that of a well-developed and well-nourished young white female. She was pale, perspiring generally, and was in severe discomfort from pain throughout the left lower extremity. Temperature was 100 degrees F; pulse, 90/minute; blood pressure, 130/60.

Remarkable physical findings were limited to the left lower extremity, which was diffusely swollen. There was a recently-made, 5 cm. transverse incision, a finger’s breadth below the groin crease, and a 2 cm. vertical incision on the lateral thigh, 10 cm. above the patella. The areas of discoloration (Figs. 1 and 2) over the medial aspects of the lower thigh, leg and foot, including the entire great toe, the medial surface of the second toe, and a large portion of the ball of the foot, were anesthetic to pin prick, and were cooler than the surrounding skin, which, in turn, was cooler than corresponding skin surfaces on the right side. There was a moderate degree of muscle tenderness in both the calf and thigh regions. Normal pulses were palpable throughout the right lower extremity, but none were detectable on the left below the external iliac artery, which was easily felt above the inguinal ligament.

Laboratory studies revealed the following: RBC 4.2 million/cubic millimeter; hemoglobin, 14.0 Gm./100 cubic centimeters; WBC 8,100/cubic millimeter, with normal differential count; urinalysis within normal limits, and chest plate negative.

One hour after admission, 2 per cent procaine lumbar sympathetic blocks were performed at L1 and L3 on the left. A prompt hyperemic response resulted, with increase in skin temperature and decrease in pain, which gave way to a tingling sensation. A noticeable blanching of the areas of mottled discoloration occurred, and the extremity became dry, but the pulses remained impalpable.

It was then elected to explore the left groin incision under local anesthesia. The partially-studies

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healed incision was reopened bluntly down to Scarpa’s triangle, where the femoral vein and nerve were found to be intact. The saphenous vein could not be readily identified, and was presumed to have been ligated and divided. The femoral artery was noted to have been divided proximal to the profunda branch, about 3 cm. below the inguinal ligament, and both ends had been ligated with heavy catgut suture material. The distal end was palpably thrombosed and was separated from the proximal stump by approximately 3 cm., probably due to retraction. The catgut ligature previously placed about the pulsating proximal stump was reinforced with two 000 silk ligatures, and the

end of the second week, the swelling had nearly disappeared.

Although no pulses reappeared, it was clear by the third week after admission that the blood supply would sustain the extremity. All the gangrenous areas remained dry and were permitted to separate spontaneously to avoid the trauma of surgical debridement. Spontaneous sloughing of the gangrenous areas began at 5 weeks. The patient’s general condition was excellent, and she became completely pain-free, so that crutch walking could be initiated at 6 weeks. She was discharged to her home at this time, and was instructed in the scrupulous care of the local areas, including the daily application of aqueous zephiran.

Progress was satisfactory at home for the first week, when pain, redness and swelling about the base of the blackened and shrivelled great toe was noted. She became febrile, and was readmitted for a period of 15 days, during which time the mild infection subsided uneventfully with the aid of antibiotics and bed rest. Surprisingly, 7 weeks after onset (August 21, 1952), all the
bones in the foot, including the great toe, continued to appear viable by roentgenographic examination.

No further episodes of spreading cellulitis developed, but a persistent red flair about each of the separating eschars, indicating a low-grade inflammatory response, prompted elective debridement of all necrotic tissue, including disarticulation of the great toe at the metatarsophalangeal joint. This was done on October 10, 1952, under intravenous thiopental sodium anesthesia, sodium anesthesia, the necrotic tissue was debrided and the distal two-thirds of the first metatarsal bone was removed with an osteotome. Again, only minimal bleeding was encountered. Histologic examination of the specimen failed to reveal any evidence of osteomyelitis. The patient remained in good condition following surgery, continuing moist dressings at home, and she was able to ambulate well with crutches.

All the areas of ulceration along the lower medial thigh and the lower leg were completely epithelialized by early January, 1953 (5½ months after onset), but a 3 cm., indolent, encrusted ulceration overlying the remaining third of the first metatarsal bone persisted, without any diminution in size. Accordingly, the patient was readmitted for removal of the remaining segment of the first metatarsal. This was accomplished under intravenous thiopental sodium anesthesia on January 21, 1953.

The patient was again followed in the outpatient clinic, continuing saline dressings at home, until March 12, 1953, when she was admitted for the sixth time, for more vigorous therapy of the chronic ulceration, which now measured 1.0 cm. in diameter, at the site of removal of the metatarsal bone. At this time, all other areas were soundly healed, and the depressed scars had softened and filled in to a considerable extent (Fig. 5). In particular, the skin covering the ball of the foot had improved remarkably, having become soft and pliable. Treatment consisted of strict bed rest, with elevation of the left lower extremity; antibiotics parenterally; and enzymatic debridement of the shaggy, undermined, avascular ulceration with streptokinase-streptodornase solution following 2 days of intensive preparation, consisting of frequent saline dressings, antibiotic therapy, and 500 cu. cm. of whole blood. Only a small amount of bleeding was encountered under each of the eschars, and this was controlled by pressure alone, except about the ball of the foot, where 2 small bleeders were ligated. The head of the first metatarsal was left in situ, although its exposed portion appeared blackened.

Following surgery, a general supportive regime, plus antibiotics parenterally and neomycin ointment locally, was rewarded with only sparse granulations, which precluded any attempts at skin grafting. After a month of hospitalization, the patient was again discharged to her home, where she continued applying frequent tepid, sterile saline dressings.

On November 19, 1952, the patient was readmitted for further debridement. The previously-debrided areas had not completely epithelialized, and there was an indolent area of ulceration on the ball of the foot. The distal two-thirds of the first metatarsal bone projected from this ulcerated area, and was surrounded by necrotic tissue (Figs. 3 and 4). Under intravenous thiopental
(Varidase). At the end of 6 days of treatment, the ulcerated area had filled in nicely with clean, friable granulations. Saline soaks and radiant heat were then substituted for the enzymatic debridement and, at the time of discharge on March 28, 1953, the ulcer measured only 0.25 cm. in diameter and was healing rapidly. Re-examination of the pulses at this time continued to reveal absence of arterial pulsations below the external iliac on the left.

Complete healing was secured by the first week of April, 1953, and the patient was advised a suitably designed shoe in order to commence weight bearing. At this time, her ankle motion and the motions of the third, fourth and fifth toes were essentially normal. She had been carrying out active movements faithfully and, whenever she had been on bed rest, her left ankle was supported at 90 degrees, so that there was no heel cord shortening. However, the skin on the medial border of the second toe had been involved in the original gangrenous process, so that after separation of the eschars, the toe was held in about 45 degrees of fixed flexion at the metatarsophalangeal and interphalangeal joints. This flexion deformity persisted unchanged despite intensive physiotherapy, and prevented her from putting her foot into a shoe.

Accordingly, she was hospitalized for the seventh time on April 9, 1953, for excision of the proximal bony phalanx, left second toe, to overcome the flexion deformity. This procedure was accomplished on the following morning under thiopental anesthesia. The proximal bony phalanx was removed subperiosteally without the necessity of ligating a single bleeder. With the aid of strict bed rest and prophylactic antibiotic therapy, the incision healed per primam, and the patient was discharged on April 18, 1953.

On the following week, she was fitted satisfactorily with a shoe and commenced weight bearing with crutches. Progressive ambulation has been instituted and, to the present, there has been no suggestion of intermittent claudication.

**DISCUSSION**

Luke and Miller, reviewing surgical complications following the ligation of varicose veins and retrograde injection of sclerosing solution in a series of 756 operations, reported two instances of accidental ligation and injection of the femoral artery, which subsequently came to mid-thigh amputation. They also reported the occurrence of five cases of transient but severe arteriospasm of the femoral tree, manifested by unusually severe extremity pain of a burning nature, together with objective findings of pallor and absent pulses. The arteriospasm resolved spontaneously in about 30 minutes in each of these cases, but the authors suggested that arterial thrombosis might well have supervened.

The operation of vein ligation with retrograde injection of sclerosing solution has been abandoned by many surgeons in favor of vein stripping procedures, partly because of the all-too-frequent systemic reactions to the sclerosing solutions and the complications or arteriospasm or deep vein thrombosis with or without embolization; and partly, of course, because the latter procedures have been shown to effect a more satisfactory permanent result.

In the case presented, it was not possible to ascertain whether the retrograde injection of sclerosing solution had been accomplished through the distal segment of the femoral artery or through the saphenous vein; but it was deemed more likely that the vein had been sclerosed, since the pattern of gangrenous areas followed the course of the vein so closely. It is well recognized that the arterial pulse may be obliterated by arteriospasm, but there is little excuse for confounding the anatomical landmarks of Scarpa's triangle to such a degree as to mistake the femoral artery for a venous channel.

In contrast to upper extremity arterial injury, which is often associated with little or no loss of function, injuries of the femoral artery usually result in extensive loss of both tissue and function. In a series of five cases of war wounds of the common femoral artery, Rose, Hess and Welch reported that all developed gangrene, with a line of demarcation at or above the ankle. Illustrating the importance of the profund branch, the same authors reported that eight of 21 cases of wounds of the
superficial femoral artery failed to develop any areas of gangrene. DeBakey and Simeone, summarizing experiences with battle wounds of the peripheral arteries during World War II, found that of 517 cases of femoral artery injury, 275, or 53.2 per cent, sustained loss of the limb. When the injury involved the common femoral artery, there was an 81.1 per cent incidence of limb loss, whereas injuries of the superficial femoral artery were associated with a 54.8 per cent incidence of limb loss.

These statistics, however, were derived from battle injuries, where the arterial injuries were often associated with extensive soft tissue damage, resulting in impairment of collateral circulation, and where there was an average time lag of about 15 hours prior to treatment.

The ideal treatment of a vascular injury is the re-establishment of normal circulation. Accordingly, wound exploration is indicated in every case. In the case presented, re-establishment of arterial continuity by anastomosis or vein graft was impossible due to thrombosis of the distal arterial segment. DeBakey and Simeone state that thrombosis of the distal tree often occurs within six to eight hours after arterial injury. Certainly after 72 hours there is little point in attempting primary arteriorrhaphy. Effort was, accordingly, devoted to improving collateral circulation.

As pointed out by Leriche and Werquin, in-continuity ligature of an artery leads to reflex vasoconstriction of the distal arterial tree, interfering with the establishment of an adequate collateral circulation. By resecting an arterial segment between ligatures, thereby accomplishing a periarterial sympathectomy, much of this reflex vasospasm can be relieved. In our case, the artery had already been divided between ligatures, yet there was a decided circulatory response to lumbar paravertebral blocks and to subsequent lumbar sympathectomy. This corresponds with the experience of Crutcher, who observed considerable improvement in circulation following both delayed (three cases) and immediate (one case) lumbar sympathectomy in cases of superficial femoral artery ligation.

The question of whether circulation is improved or impaired by ligation of the concomitant vein is still the subject of debate. Some recent reports favor conservation of the vein. Because the femoral vein was left intact, we thought it expedient, once the danger of bleeding had
passed, to employ anticoagulant therapy to avert the hazards of thromboembolic phenomena, to which a patient confined to bed with circulatory impairment is particularly vulnerable. Anticoagulants may be employed early, in the absence of extensive soft tissue damage, to prevent occlusion of collateral pathways by retrograde thrombosis.

The affected extremity, whether exposed to the air on sterile sheets or maintained in a supportive swathe, should be kept at heart level and at room temperature. Gentle applications of a 1:1000 solution of aqueous zephiran are helpful in reducing the skin bacterial count. If the gangrenous areas are dry and uninfected, more tissue can be conserved by letting these areas separate spontaneously than by performing early surgical debridement. If infection burrows under the eschars, then surgical debridement must be performed without delay.

General supportive measures should include the repletion of blood volume and administration of oxygen to provide maximum sustenance of tissues which may be critically deprived. Tetanus toxoid or antitoxin, as indicated, and broad spectrum antibiotic therapy are administered to minimize the dangers of clostridial infection and cellulitis. There is evidence to indicate that vasodilator drugs are ineffec-tual and may be detrimental, but intravenous 5 per cent ethyl alcohol serves to allay much anxiety and discomfort, thereby reducing the need for narcotics.

SUMMARY

1. A case report illustrating the results of inadvertent ligation of the femoral artery during surgery for varicose veins has been presented for the twofold purpose of re-emphasizing this hazard of vein surgery and of reviewing newer concepts of the management of major arterial injury.

2. A program for the management of a major arterial injury of the lower extremity is outlined; initiated by exploration of the wound with restoration of arterial continuity, if feasible. Failing this, various methods of improving collateral circulation are evaluated. Ligation of the concomitant vein and the employment of anticoagulants are discussed, and the importance of antibiotic therapy and scrupulous conservative local care are stressed.

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COMPLETE RUPTURE OF THE LEFT LOBE OF THE LIVER AND SPLEEN WITH RECOVERY

A CASE REPORT*

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The reported mortality rate from massive rupture of the liver is high. Wright lists the mortality rate, as reported by various authors, at 30 to 60 per cent. According to Pilcher, liver injury mortality is reported to be 60 per cent. Because there have been few published reports of complete rupture of the left lobe of the liver with recovery, this case report is submitted.

CASE REPORT

J. B., a 17-year-old white male, was admitted to the Atascadero Hospital, Atascadero, California, on May 10, 1952, with a history of driving a "hot rod" which overturned and pinned the lower portion of his chest and upper portion of his abdomen beneath the upper portion of the windshield. About an hour elapsed from the time of injury until he was brought into the hospital. On admission the patient complained of pain in his chest and was coughing up small amounts of bright red blood.

Examination at the time of admission revealed his lips to be slightly pale, his blood pressure, 100/60; pulse, 88; respiration, 20; temperature, 98.4°. There were numerous abrasions over the chest wall, respiratory sounds were clear and normal, and the heart sounded normal. The abdomen was extremely tender, particularly in the left upper quadrant, and there was moderate rigidity in this area. Peristaltic sounds were present, but subdued. The patient was given 1000 cc. of 5 per cent dextrose in water on admission and 50 mg. of demerol for pain. Following this, his pressure rose to 110/70.

Roentgenograms of his chest showed considerable clouding in the right upper lung field. Roentgenograms of the abdomen in the lateral recumbent position revealed no evidence of free air and no other definite intra-abdominal pathology.

About 3 hours after admission to the hospital, the patient, in addition to complaining of chest pain, complained of upper abdominal pain and pain in both shoulders. At this time there was diminished resonance and fainter breath sounds in the right side of the chest. There was moderate rigidity and tenderness throughout the abdomen, but this was particularly marked in the left upper quadrant. At times the lower portion of the abdomen was soft. Rectal examination and urinalysis were negative.

A diagnosis was made at that time of contusions of the right lung with the possibility of a ruptured spleen, and it was decided that if the abdominal signs became more pronounced, an abdominal operation would be indicated. Two hours later there was progression of the abdominal signs, with no marked change in the pulse or blood pressure; and at this time, approximately 6 hours after injury, an abdominal exploration was performed. Endotracheal anesthesia with Pentothal D-Tubocurarine was used. This was supplemented with nitrous oxide. At this time the blood pressure was 110/50, the pulse between 72 and 100. Because it was believed that we were dealing with a ruptured spleen, a left subcostal incision was made.

On opening the abdominal cavity, several hundred cubic centimeters of blood were found in the abdominal cavity; and the spleen, which had a laceration in it, was removed by individual ligation of its blood vessels. However, on removing the spleen, a large quantity of fresh blood continued to be noted in the abdominal cavity. Because of this, the left costal incision was extended across the midline of the abdomen over to the right costal margin and extended vertically upward in the mid-portion (Fig. 1a). On doing this we were very much surprised to note a vertical laceration of the liver just to the left of the falciform ligament. This laceration extended through
COMPLETE RUPTURE OF LEFT LOBE OF LIVER AND SPLEEN

Fig. 1 (a). Abdominal incision and appearance of laceration through entire thickness of left lobe of liver. (b). Liver remaining after removal of most of the left lobe. The vessels already have been isolated and ligated individually and are plainly visible. Through-and-through sutures are being taken through the entire thickness of the liver. Note how they overlap. Some sutures are purposely left long.

the entire thickness of the liver in such a manner that the left lobe of the liver was torn completely free of the right portion and was suspended in the abdominal cavity by only the left triangular ligament (Fig. 1a).

At this point, some 50 minutes after operation had begun, the blood pressure and pulse disappeared. The left lobe of the liver was immediately removed from the abdomen by cutting through the triangular ligament. Hot, moist packs were placed against the raw surfaces of the remaining liver while blood was forced into both the right and left arms at the same time under positive pressure. Nitrous oxide was stopped and oxygen under positive pressure was given. Also, 1500 cc. of blood were given in the next 50 minutes. The carotid pulse during this period was barely perceptible, and the pulse was between 140 and 165 for the next hour. The pupils remained contracted and the patient remained warm and dry.
After 50 minutes, the blood pressure returned, the pulse improved, and active surgery was resumed. No anesthetic agent of any kind was given for the next hour, the patient being carried on oxygen under positive pressure. The pulse stayed at about 120 and the blood pressure at an average of 140/50 for the duration of the operation. The packs were kept against the liver approximately 45 minutes, at which time the anesthesiologist advised us that the peripheral circulation had improved sufficiently to permit us to proceed with the operation. On removing the hot, moist packs from the raw surfaces of the liver, blood spurted freely from numerous cut blood vessels in the liver. These were separately caught with hemostats and individually ligated (Fig. 1 B). Next, through-and-through stitches were taken through the entire thickness of the liver, as shown in Figure 1 B, and the ends of these sutures were left long. Then Gelfoam was placed over the entire raw edge of the liver and the sutures that were left long were tied over the Gelfoam to hold it in place (Fig. 2). (After the free blood was removed from the abdomen there appeared to be no further bleeding.)

Further examination revealed several areas of subserosal hemorrhage in the wall of the large bowel, but no additional injuries were noted. A Penrose drain was placed in the region of the raw edge of the liver and another Penrose drain in the left gutter. The latter was brought out through a separate stab wound in the left flank and the former through the superior portion of the vertical incision. The wound was closed in layers. Cotton was used on the splenic vessels, No. 1 chromic on the liver blood vessels, and No. 2 chromic for the mattress sutures in the liver.

During the operation we used 2500 cc. of blood, 1000 cc. of saline, and 500 cc. of 5 per cent dextrose. The operative procedure took three hours 25 minutes, of which 45 minutes was spent waiting for the blood pressure to return to an acceptable level while the hot, wet packs were kept against the raw liver margin. The patient left the operating room fully reacted, with a blood pressure of 140/50 and a pulse of 120.

Following surgery, a Levine tube was inserted and continuous Wangensteen suction started. Penicillin and streptomycin were given, along with sufficient intravenous fluids to maintain proper water balance as determined by charting his fluid intake and output.

For the first four days following operation, his temperature ranged between 102°F. and 104°F., rectally, and his pulse between 110 and 136. For 48 hours his abdomen became quite distended and there was complete absence of bowel sounds. About 72 hours after surgery his bowel sounds were readily heard, gas passed per rectum, and his abdomen became soft. On changing the dressings, only a small amount of bile drainage was noted and the wound appeared clean. On the sixth postoperative day the drains were pulled out about one inch and this procedure was continued daily until the drains were completely removed. The patient ran a low grade fever until the thirteenth postoperative day, and for a similar length of time he complained of some abdominal distress. Both drains were removed on May 25, 1952, and a slight amount of bile drainage was present, which subsided a few days thereafter.

The patient was discharged from the hospital on May 28, 1952, 18 days after admission. At this time the wound was well healed other than at the site of the drains. These areas healed within 2 weeks after discharge from the hospital. He has been seen many times in the past year since this accident. The boy is now attending school and shows no ill effects of the injury he sustained.

**COMMENT**

It is believed that this case is worth reporting in order to stress the fact that with ample blood, hemostatic agents such as Gelfoam, proper anesthesia, and antibiotics, massive tears of the liver, instead of being considered hopeless cases, can now be attacked vigorously with a reasonable hope of success. To emphasize this point, we wish to state that this procedure was done in a 20-bed, rural hospital, without the many niceties one would have in a large hospital. If such a procedure can be done in such a place, it can be more readily done in larger institutions.

The patient was operated upon approximately six hours after his accident. Mad-ding, in a comprehensive report on war wounds of the liver, stated that the average time elapsing between time of injury of the liver and time of operation was 11.3 hours. Wright wrote that symptoms of intra-abdominal injury were not recognized for six or more hours after rupture of the liver develops. This will emphasize the fact that there may be temporary spontaneous coagulation of a bleeding liver, as
a result of which many hours may elapse before a definite diagnosis can be made. This permits enough time for the operating room to be prepared and ample blood to be made available. Blood, of course, is most important. The facilities of a county blood bank were available at this particular hospital, otherwise this procedure could not have had a successful outcome.

We wish to stress the point that when the anesthesiologist reported the absence of the peripheral circulation during the operation, all manipulation was stopped. Firm pressure was applied to the liver and kept there while the anesthesiologist forced blood into veins in both arms under positive pressure. Cooperation between the anesthesiologist and the surgeon is necessary for the successful outcome of such cases.

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There is now a trend away from placing packs against the raw bleeding liver edge. The packs do not drain, but rather act as tampons, causing pocketing of bile and exudate and formation of abscesses. On removal of a pack several days later, secondary hemorrhage may follow. The bile leakage and the damage done by necrotic liver tissue left behind may be of greater importance in the cause of death following liver injuries than loss of blood from hemorrhage. For this reason it is felt that removal of all devitalized tissue is essential, as is adequate external drainage such as can be obtained by Penrose drains. Bleeding should be stopped permanently by individual tying of bleeding vessels plus placing Gelfoam against the raw surfaces. It is important to mention that removal of the Penrose drain should not be started until the fifth day, at which time a fistulous tract will form about the drain so that any bile present will continue to drain. This drain should be removed rather slowly, at the rate of an inch or so a day, so that no abscess cavities or collections of bile will be left behind. It is best to defer complete removal of the drain until all drainage has ceased.

**SUMMARY**

1. A case report of complete laceration and removal of the left lobe of the liver and spleen, with recovery, is recorded.

2. The successful outcome of this case depended upon:
   a. Ample blood.
   b. Cooperation of the anesthesiologist.
   c. Hemostatic agents, such as Gelfoam.
   d. Drainage by means of Penrose tubes rather than gauze packs.

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PNEUMOPERITONEUM therapy, although of relatively recent origin, is well established as an effective form of collapse therapy in the treatment of pulmonary tuberculosis. That it is not entirely without hazard has been pointed out by Rack and Clement and others, who list among the complications occurring with it, ascites, aggravation of certain types of herniae, intra-abdominal adhesions, omental torsion, and many others. Of more importance to the clinician is the altered symptomatology in some of the relatively common types of abdominal pathology.

Foremost among these is acute appendicitis, and already scattered reports of the pitfalls encountered in its recognition and management in the presence of pneumoperitoneum are appearing in the literature. The authors have had the opportunity of reviewing 31 cases of this condition during the past five years and offer these as a basis for comparative evaluation of its management. Ten of these were operated on at the Western North Carolina Sanitarium, 20 at the Veterans Administration Hospital at Oteen, and one in private practice.

INCIDENCE

Rilance and Warring have computed the incidence of acute appendicitis in patients receiving pneumoperitoneum and in those receiving other forms of therapy in a ratio of 11:1. Schaff and Bornstein found a similar ratio of 5:1 Knoepp reports a ratio of 7:1, but adds the important observation that the incidence in the presence of pneumoperitoneum is roughly the same as in a general hospital population, while among tuberculous patients receiving other forms of therapy including rest, the incidence is distinctly but unexplainably lower. We feel that too many variables enter in to permit an accurate determination of the incidence factor. However our figures of approximately 3:1 confirm the impression that pneumoperitoneum is complicated by acute appendicitis more often than one would expect, a fact which we are unable to explain. This is all the more puzzling since the five-year period during which these cases were observed occurred after the advent of streptomycin, and the majority of these patients were receiving streptomycin-PAS therapy. An explanation may be found in the fact that whereas the natural intra-abdominal defenses are able to forestall many cases of incipient appendiceal infection, pneumoperitoneum hampers the defense mechanism sufficiently to allow the condition to fulminate into a dangerous disease. This will receive more consideration in a later section.

PHYSIOLOGIC CONSIDERATIONS

The injection of air into the peritoneal cavity creates an altered physiological
RAIFORD AND THOMPSON

state which, we feel, has a definite bearing on the intra-peritoneal response to inflammatory disease. First, there is an increase in intra-abdominal pressure varying from 5 to 10 cm. of water. Anderson and Winn have estimated that 4 per cent of patients receiving pneumoperitoneum complain of pain sufficient to require sedation, either at the initial injection or a subsequent refill. Our impression is that the incidence is considerably higher, particularly following the first few injections of air, and especially if the injection is excessive. While the pain is ordinarily of minor degree and disappears within two or three days as the patient becomes adjusted to the change, it can and does produce a symptom complex almost indistinguishable from the early manifestations of intra-abdominal pathology. Peritoneal effusion, usually asymptomatic but sometimes in sufficient quantity to necessitate aspiration, is not an infrequent occurrence. The peritoneum and serosal surfaces in the majority of cases show some degree of inflammatory change varying from a mild hyperemia with thickening to patches of whitish exudate. We are unable to state the type and degree of histopathology represented, but believe it to be a non-specific inflammatory reaction. Routine peritoneal biopsy is now performed in an attempt to determine this factor. The creation of an air space in the peritoneal cavity prevents the continuous close approximation of organs, parietal peritoneum, and especially the omentum. The ability of these structures, especially the latter, to wall off or localize infection is thereby materially diminished. Finally the presence of an artificial cushion of air prevents accurate palpation of the abdominal viscera, masking and altering the established signs of abdominal pathology.

CLINICAL FACTORS

Sex and racial incidences are of little significance in this series of cases, since in one institution the majority of patients are male of both white and colored races (Oteen Veterans Administration Hospital), while in the other, all patients are white of both sexes (W. N. C. Sanitarium). The average age was 28 years, which corresponds roughly to the average age of the sanitarium populations.

The average duration of pulmonary tuberculosis in our group of patients was 32 months prior to the development of the appendicitis. This, we feel, is of less significance than the duration of the pneumoperitoneum. In this analysis it is found that the patients developed appendicitis on an average of 11 months after institution of therapy. When these statistics are examined more closely, it is seen that 23 of the 31 cases appeared within 12 months, and of these, 12 appeared within six months. Furthermore, in five of the six month group tuberculous infection was associated with the pyogenic infection. Two of the 11 cases developing between six and 12 months showed similar pathology while no tuberculous infection was found in the remaining cases which had received pneumoperitoneum more than 12 months.

The time elapsing between the previous pneumoperitoneum refill and the onset of symptoms appears to be of some significance. The majority of these patients were receiving weekly refills of air. The onset of appendicitis in ten occurred within 24 hours of the most recent injection of air, while the remaining 21 were scattered throughout the week, with an average of four days after refill. At least three patients attributed the onset of pain directly to the air injection. It should be recalled, however, that physiological pain following the institution of air is not an uncommon occurrence.

SYMPTOMS

The average duration of symptoms before operation was 37 hours. Excluding
four of the earlier cases with durations of five, seven, eight, and nine days respectively, the average duration was 18 hours, with a maximum of 48 and a minimum of four hours, figures which are not particularly flattering to the diagnostic acumen of the attending physicians, since these patients were hospitalized and under constant medical surveillance, but which again emphasize the difficulties of diagnosis encountered during our early experience with pneumoperitoneum.

Pain was by far the most characteristic and consistent premonitory symptom, occurring in all 31 cases. In ten, the pain started and remained in the right lower quadrant. In 15 it started elsewhere, usually in the peri-umbilical region, and shifted after a few hours to the right lower quadrant. In the six cases pain started as above, but remained generalized and never localized at a particular point. Pain was preceded by nausea in 17 cases, vomiting in 14, and diarrhea in seven.

PHYSICAL SIGNS

Tenderness to direct pressure was the most consistent finding on physical examination and was located in the right lower quadrant in 30 cases despite the fact that subjectively, the pain was felt elsewhere in six. In the remaining case, tenderness to pressure was elicited in the lower mid-abdomen (operation revealed the acutely inflamed appendix lying over the brim of the pelvis). Rebound tenderness was present in varying degree in 20 cases. Rigidity, spasticity, and muscle guarding were conspicuously absent, being noted in four cases only. Rectal tenderness was noted in only three cases. This examination, however, was either omitted or not mentioned in the majority of instances.

Temperature was, as expected, elevated above the patient's established normal, an average of 1.6° F. Similarly the pulse rate was elevated above the established normal on an average of 13 beats per minute. The leukocyte count was uniformly elevated, averaging 15,900 W.B.C., with an average neutrophile of 80 per cent.

OPERATIVE FINDINGS

The most consistent operative finding (84 per cent) was the presence of free fluid in the peritoneal cavity regardless of the degree of appendiceal inflammation. As pointed out previously, this can be caused by air alone, but unquestionably the inflammatory disease was largely responsible. The fluid varied widely in amount and in character, from clear amber to frankly purulent in cases of rupture.

Plastic exudate on the surface of the appendix and adjacent viscera was present in 17 (77 per cent) of the 22 cases in which its presence or absence was noted. Perforation had occurred in none of the 19 cases recognized and operated on within 18 hours after onset of symptoms. Of the 12 coming to operation 18 or more hours after onset, perforation had occurred in seven (57 per cent) with varying degrees of peritonitis of a particularly malignant and fulminant nature. In only two of the seven was there any evidence of walling off with abscess formation.

PATHOLOGY

The appendix appeared grossly inflamed in all but two cases of this series, and acute infection was confirmed by microscopy in all but one. In this case a tuberculoma was found occluding the lumen and producing distal distension. That it was not acutely inflamed, we feel, was due to the fact that it was recognized clinically and removed within a few hours after the initial symptoms. This was the one case in which the temperature and leukocyte count were normal.

In addition to the pyogenic infection, tuberculous disease of the appendix was
found in seven cases. It would be interesting to know if this represented a part of a generalized tuberculous enteritis or peritonitis, but unfortunately biopsies were not made nor observations recorded in more than a few instances. It is of possible significance that all seven cases of appendiceal tuberculosis occurred in individuals receiving pneumoperitoneum less than 12 months. It is possible that this can be explained by the fact that these patients were in an earlier and theoretically more active stage of the disease.

RESULTS

All but one patient recovered from the effects of the appendiceal disease. This individual, one of the earliest in our series, was not operated on until nine days after the onset of symptoms due to the confusion in the clinical evaluation of the disease at that time. Although the patient survived the operation death intervened several days later, ostensibly due to effects of the generalized peritonitis.

DISCUSSION

The signs and symptoms of acute appendicitis in the presence of pneumoperitoneum, although altered somewhat by the presence of intraperitoneal air, are fairly typical. Pain, either starting or localizing in the right lower quadrant, is the most constant symptoms, although localization is less consistent. It should again be emphasized that this pain can be aped by the presence of air pressure alone, but again localization is inconstant. Nausea, vomiting and diarrhea occur with variable frequency, and cannot be relied on as pathognomonic findings. Tenderness is the most constant physical sign, is located over the diseased organ, and is direct rather than rebound on character. Due to the cushion of air, rigidity and muscle spasm are conspicuously absent. We have found that palpation of the abdomen in the upright or prone position is a valuable adjunct to physical examination. By this maneuver the intraperitoneal air is allowed to rise, leaving the viscera in closer proximity to the abdominal wall. It is obvious that evaluation of the temperature, leukocyte count and urinalysis should be routine procedures in establishing the diagnosis.

For obvious reasons we feel that aspiration of the air in any suspected case of appendicitis is advisable. First, if the pain of which the patient complains is due to air pressure, it will immediately be relieved. Second, removal of the protective cushion will permit far more accurate palpation of the abdominal viscera. A possible third reason concerns itself with readjustment of pulmonary function before the added insult of anesthesia and surgery. In one of our cases, a 23-year-old girl with minimal pulmonary disease, the sudden release of air at operation combined with transient hypotension coincident to spinal anesthesia was followed six hours later by massive pulmonary edema. Only the prompt institution of drastic combative measures avoided a probable fatality.

Lack of peritoneal and omental response to inflammatory disease constituted the most common operative finding. This bears out the opinions voiced by other authors as well as the expected behaviour of these structures in view of the altered physiology. It is immediately evident that in such a situation the appendiceal infection can develop into a rapidly spreading, malignant type of peritonitis, rather than being limited to a small area or an abscess in which surgical therapy can be converted into an elective procedure. It is, therefore, in our opinion, of utmost importance to operate upon individuals in this category unless appendicitis can be positively ruled out. The risk of spreading infection is far too great to permit an attitude of watchful
waiting in spite of the protective action of the antibiotics. To re-emphasize, whenever the diagnosis of appendicitis is equivocal, it is imperative to operate.

It is obvious that in following these principles the incidence of normal appendices removed will be higher than that found in the average general hospital. The percentage of correct diagnoses in this series was, for instance, only 70 per cent. However, this should be completely excusable in view of the dire results of conservatism.

Although it has not been encountered in our series, Rilance and Warring have pointed out the influence of pneumoperitoneum in bringing about disappearance of intra-abdominal adhesions. In view of this, it is interesting to conjecture what influence artificial pneumoperitoneum would exert in cases of chronic recurring obstruction due to adhesion formation in patients with pathology other than tuberculous in origin.

Pathological studies of the appendices removed showed concomitant tuberculous disease in seven cases. This is difficult to explain on more than a coincidental basis. It was noted that while the pyogenic infection was usually diffuse throughout all layers of the appendiceal wall, the tuberculous infection frequently involved only the outer layers. We can only assume, therefore, that these cases represent a low grade peritoneal involvement by tuberculosis, and that if biopsies had been taken from other peritoneal surfaces as well, a similar type of infection would have been found. In any event it would be hazardous to state that such cases represented primary tuberculous disease of the appendix alone.

This critique should in no manner be construed as a condemnation of pneumoperitoneum as a therapeutic measure. Although a relatively new procedure, its value as an adjunct to other forms of tuberculosis therapy has already been proven. Our intention has been to point out some of the pitfalls for which the clinician must be ever alert in the management of a relatively common but potentially dangerous condition. There may be other far-reaching effects of pneumoperitoneum of which we are as yet unaware. In the light of our present knowledge, however, if the clinician remains cognizant of its masking effect upon abdominal symptomatology, there is no reason why it cannot be used with comparative safety and with benefit to many.

**SUMMARY**

Pneumoperitoneum is an effective form of collapse therapy in the treatment of pulmonary tuberculosis, but presents certain hazards, foremost among which is the masking of the clinical picture in acute appendicitis.

The incidence of acute appendicitis among patients receiving pneumoperitoneum appears higher than among individuals receiving other forms of therapy for tuberculosis. This fact cannot be satisfactorily explained.

The onset of acute appendicitis does not always conform to the characteristic clinical syndrome, but abdominal pain is by far the most consistent symptom.

Tenderness to direct pressure is the most constant physical finding; rebound tenderness, rigidity, muscle guarding, etc., being conspicuously absent.

In any case of suspected appendicitis, aspiration of the intraperitoneal air is recommended as a preoperative as well as a diagnostic measure.

Due to diminished intraperitoneal defense against infection, appendicitis and/or peritonitis is a much more dangerous condition.

It is therefore imperative to operate when the diagnosis is equivocal, in view of the disastrous results of conservatism.
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CERVICAL CYSTS AND FISTULAE OF THYROGLOSSAL TRACT ORIGIN*

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DEVELOPMENTAL anomalies of the thyroglossal system form an important group among the congenital defects encountered in the cervical region. These lesions may present as cystic masses in the anterior midline of the neck from the thyroid area to the base of the tongue, as sinuses in the anterior neck which are the site of recurring abscess formation and/or drainage, or rarely, as complete fistulae which may discharge foul material into the mouth. Proper diagnosis and treatment is essential because of the disfigurement and recurring infection and discharge which may be the result of incomplete therapy.

The incidence of patients presenting with complaints due to lesions of the thyroglossal system is not high. Sistrunk in 1920 reported 31 cases in 86,000 patients examined at the Mayo Clinic. The incidence in patients presenting with neck masses is also low; Clute and Cattell in 1930 reporting 74 cases in 6582 patients with goiter, and McClintock in 1936 reporting nine cases in 2500 patients seen with complaints of midline neck swelling. Presented in this paper are 90 cases of thyroglossal cysts, sinuses and fistulae from the years 1932 to 1951, inclusive.

Extensive study of the embryology of the thyroid gland and the subsequent relation of the persistent remnants which produce these midline cysts and fistulae may be found in the reports of Wenglowski, Norris, and Meyer. In brief, it may be stated that the thyroid anlage appears in the 2.0 to 2.5 mm. embryo as a midline structure, projecting downward from the pharynx between the first and second branchial arches. This point of origin corresponds to the foramen cecum in adult life. The midline thyroid anlage then descends in the course of development to its position in the anterior neck. In the normal course of events, any connection between the cervical thyroid and its point of origin at the base of the tongue is obliterated and disappears. However, in certain instances, remnants of the strand of tissue connecting these points may remain, along with portions of the epithelial lining of the mouth cavity which have been dragged downward as the thyroid descends, to persist as definite structures and form cysts, sinuses and fistulae found in later life.

The hyoid bone, formed mainly from the second arch, appears in the embryo following the descent of the thyroid. There has been much discussion concerning the exact relationship of the thyroglossal remnant to this structure, but it is sufficient to state that the two structures become intimately associated. The hyoid, growing from behind forward, divides the tract into an infrahyoid and suprathyroid portion, with the intervening tissue appearing to pass anteriorly, posteriorly, or through the substance of the bone. The difficulty in determining this relationship at operation makes it mandatory to remove a portion of the hyoid bone to assure complete removal of the tract.

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Pathologically, cysts and sinuses of thyroglossal origin show mixed epithelial lining, composed of pseudostratified ciliated or non-ciliated columnar cells, and occasionally with stratified squamous cells. The lining may be smooth, but not uncommonly there are small, slit-like or irregularly branched side pockets extending for various distances into the surrounding tissue. Mucous glands may also be seen. Sinuses which have been the site of recurring inflammation may show little or no remaining epithelial lining. Subepithelially, there may be found varying degrees of acute or chronic inflammatory infiltration with neutrophils, plasma cells and lymphocytes, and deep to this the tissue is dense and fibrous.

Thyroid tissue has been found microscopically on occasion, and this finding was present in three cases in the present series. In one of these the cyst was attached to the upper pole of the pyramidal lobe of the thyroid gland when exposed at operation.

Sections of the central portion of the hyoid bone may show an irregular or branching epithelially lined tract piercing the bone or its periosteum. These areas often are undetectable grossly. Also, microscopic sections of the area above the hyoid bone and deep to the grossly detectable cyst or sinus often show epithelially lined remnants not suspected by visualization or probing, which may form the basis for recurrence if an incomplete operation is performed.

This series is made up of 90 patients treated during the years 1932 through 1951. Of these 90 patients, 49, or 54.4 per cent, were male, and 41, or 45.6 per cent, female. Pemberton and Stalker, in reviewing 293 cases at the Mayo Clinic from 1920 to 1938, found a sex incidence of two males to one female. Gross and Connerley, reviewing 198 cases in children, found a slightly higher percentage in females.

The presenting complaint in 55 patients was that of swelling or mass in the anterior neck, while 35 patients presented with draining sinuses. Eight of this latter group also complained of a mass at the time of admission. One patient, presenting with a mass and a sinus opening, complained of a bitter taste in the mouth on pressure over the mass, and at operation was found to have a cyst plus a complete fistula. Past experience has been much the same in series including patients of all ages. Clute and Cattell, in 58 patients reviewed, found 41 cysts, 18 sinuses, and one fistula. However, Gross and Connerley, in their series of children noted 85 per cent cysts and 15 per cent sinuses. Gross,* in a recent report of 188 cases, found cysts in 65 per cent.

It is thus seen that the commonest abnormality of the thyroglossal remnant is an anterior midline cyst. These masses may be found anywhere in the midline cervical structures from the base of the tongue down to the suprasternal notch. The size of the mass may vary considerably, the average in the present series being 3.0 cm., with the largest measuring 10 cm. in diameter. They are usually smooth and well defined, and unless infection has been present, or surgical drainage performed, are not attached to the overlying skin. The smaller cysts may be quite mobile over the deep tissues, although some degree of fixation to the hyoid bone may be noted, and often a cord-like tract may be palpable in this area. Movement with deglutition may be elicited. No tenderness is present unless there is superimposed infection. In the rare instances of complete internal tracts it may be possible, by pressure over the cyst, to express fluid into the pharynx. This finding was present in one case in the series of Clute and Cattell, and in one instance in the present series.

Sinuses of the thyroglossal duct have their opening in the anterior neck from the suprasternal notch to the region of the
hyoid bone. It is generally considered that
the sinus opening is secondary to sponta-
neous rupture of an infected cyst or to sur-
gical drainage of inflammation or abscess.
It is to be noted that although most
sinus openings are in the midline, the
opening may be some distance laterally
due to lateral pointing of the underlying
infection. The cutaneous openings are usu-
ally 1 to 3 mm. in diameter, and show mod-
erate to marked acute or chronic inflam-
matory changes in the surrounding skin.
Droplets of mucoid, clear, or purulent fluid
may be expressed from this opening, and it
is often possible, by careful palpation, to
outline a tract running from the skin lesion
upward to the hyoid bone.

The diagnosis of lesions of the thyroglos-
sal duct may usually be made on the find-
ing of a midline cystic swelling or sinus,
generally in the region of the hyoid bone,
which may move with deglutition, and
deep to which may be palpated a cord-like
tract. Submental adenitis may usually be
differentiated if infection in the teeth, lips,
or chin is found, and is usually more an-
teriorly placed than cysts of the thyroglos-
sal duct. Discrete tuberculous adenopathy
in this region may be difficult or impossible
to differentiate, however. Developmental
anomalies of the branchial or pharyngo-
thymic variety occupy a lateral position in
the neck and should not be confused for
that reason. Sinuses in the region below
the isthmus of the thyroid may be sec-
ondary to suppurative lesions in the medi-
astinum, and a chest roentgenogram should
be taken in these cases. Lipomata of the
neck are uncommon, are usually slightly
lobulated, and not as spherical as thyro-
glossal lesions. Dermoids and sebaceous
cysts may usually be differentiated by their
superficial position and fixation to the skin;
however, several dermoids lying deep to
the platysma have been encountered which
could not be differentiated preoperatively.

Confusion with lesions of the thyroid
gland is possible. Clute and Cattell reported two patients operated upon for thy-
roid adenoma in whom the lesion subse-
quently proved to be a thyroglossal cyst.
This diagnosis was made in one patient in
the present series and a thyroglossal cyst
attached to the pyramidal lobe of the thy-
roid was found at operation. The micro-
scopic examination subsequently showed
thyroid tissue in the wall of an otherwise
typical thyroglossal cyst. Thyroid gland
ectopia may occur, and in rare cases may
constitute all the functioning thyroid tissue
in the individual. Gross has pointed this
out, and cites one case in which an ectopic
thyroid gland was removed, the child sub-
sequently developing myxedema, necessi-
tating thyroid therapy. As a safeguard, he
advocates opening any cyst in this location
which contains solid material, and if thy-
roid tissue is found, exploring the neck to
determine the presence of a normal thyroid
gland.

Gross has also reported two cases of
midline cervical cleft, presumably due to
failure of fusion of the anterior extrem-
ities of the branchial arches, which may be
confused with a thyroglossal sinus.

Abnormalities of the thyroglossal duct
may be seen at any age, but predominantly
are found in the younger age groups. The
average age at the time of operation in the
cases here reported was 24 years, the
youngest patient being 19 months of age
and the oldest 60 years. In the 88 cases in
which definite information was available,
the average duration of symptoms prior to
hospital entry was four and a half years,
one patient presenting himself only one
week following the discovery of a mass,
while the longest interval occurred in a
patient who had been aware of a neck mass
for over 40 years.

The age of the patient at the onset of
symptoms was determined in 88 cases. In
five cases, a mass in the neck was noted to
be present at birth, and in 48 cases, or 55
per cent, symptoms were present prior to the age of ten years. This is in accord with previously reported series, Ward and Hendrick\textsuperscript{15} reporting 60 per cent of their cases as having noted the onset of symptoms prior to ten years. Gross and Connerley,\textsuperscript{5} in their series in children, noted 29 per cent of the lesions as present at birth, and 76 per cent present before the age of six. It is indeed true, however, that infrequently these lesions may present themselves later in life; Clute and Cattell\textsuperscript{2} reporting one case noting initial symptoms at the age of 71 years.

In the series of cases here reported, 36, or 40 per cent, had undergone some form of surgical treatment prior to their admission. Of these, 18 had had previous excision of a neck mass, 13 had had incision and drainage, and five had had multiple procedures involving both excision and surgical drainage. Pemberton and Stalker\textsuperscript{11} reported 63.6 per cent of their cases as having had unsuccessful surgical treatment prior to their initial visit.

It has been amply shown that the treatment of choice in dealing with lesions of the thyroglossal system, whether cyst, sinus or fistula, consists of complete removal of the tract to the foramen cecum, with resection of the central portion of the hyoid bone. Schlange\textsuperscript{12} in 1893, and Durham\textsuperscript{3} in 1894, advocated removal of a portion of the hyoid bone in order to facilitate exposure and to insure removal of all portions of the tract. However, it was not until Sistrunk,\textsuperscript{13, 14} in 1920, described in detail the radical removal of the tract and the central portion of the hyoid bone, that the procedure gained wide acceptance. Many reported series since that time have shown that although limited excision of a thyroglossal cyst may occasionally effect a cure, the recurrence rate following incomplete operation is sufficiently high to warrant the use of the radical procedure in all cases, as originally advocated by Sistrunk. Gross and Connerley\textsuperscript{2} reported no recurrence in 91 cases treated by the complete operation, while 50 per cent of 12 cases treated by excision needed further surgery. In a later report, Gross\textsuperscript{4} found seven recurrences in 188 cases treated by the radical method. Clute and Cattell\textsuperscript{2} reported no recurrence in 51 cases with radical operation. Pemberton and Stalker\textsuperscript{11} reported four recurrent sinus in a series of 261 cases treated by the radical procedure. Ward and Hendrick\textsuperscript{15} reported a recurrence rate of 6 per cent following radical extirpation, while 25.6 per cent recurred when lesser procedures were employed.

In this series of 90 cases, operations have been performed by many members of the attending and resident staff. The radical operation was performed in 78 cases, or 86.7 per cent, while in 12 cases simple excision was done. There have been eight known recurrences in this series. Of these, six occurred in patients on whom the complete operation had been performed, giving a recurrence rate of 7.7 per cent, while two cases in the limited excision group recurred for a rate of 16.6 per cent. It is interesting to note that all of the recurrences following the radical procedure were discovered in less than one year following operation, the length of time varying from two weeks to ten months. Five of these cases were reoperated upon by the radical method with cure, while the sixth case required six subsequent procedures, and has remained well for the past nine years. Recurrences in the excision group took place nine months and three years following operation, and both were cured by the radical procedure.

The radical operation performed in this series has been essentially that described by Sistrunk\textsuperscript{15} in 1920. It has not been found necessary to inject dye or marking fluid into the tract in the great majority of cases. The patient is positioned as for thyroidec- tomy, supine, with the neck extended to
expose the hyoid area. Endotracheal inhalation anesthesia has been the agent of choice in recent years. A transverse incision, 3 to 4 cm. in length, is made in the skin crease of the neck over the presenting mass if the lesion is a cyst. If a sinus opening is present, or if there are scars of previous operations, these are removed by a transverse elliptical incision.

The incision is then deepened through subcutaneous fat and platysma muscle, isolating the cyst or sinus from these tissues by sharp dissection. Some dissection of the upper and lower skin and platysma flap may be necessary at this point if the cyst is large or lies low in the neck. Slight traction is then made on the cyst or sinus, facilitating the dissection of the deep fascia from the tract. At this point, it is possible to divide, in a vertical plane, any deep tissue overlying the deeper layer of muscles, and so expose the oblique fibers of the mylohyoid in the upper aspect of the wound, and the vertical fibers of the sternohyoid in the lower aspect. The thyroglossal tract will then be seen to course upward to the hyoid bone, which lies at the junction of these two muscle groups.

Sharp dissection then frees the upper and lower borders of the central 1.0 to 1.5 cm. of the hyoid bone from its muscular attachments. The hyoid may then be grasped with an Allis clamp just to one side of the midline and pulled forward. Division of the bone is then made, using a scalpel or heavy scissors in younger children, and bone cutting forceps in older children and adults. The opposite side is then divided in similar manner. A core of muscular tissue and tract is then dissected from the surrounding muscles down to the thyrohyoid membrane and mucous membrane of the pharynx. This step is facilitated by having the anesthetist or assistant place a forefinger in the mouth and exert outward pressure over the region of the foramen cecum, thus bringing this tissue up from the depths of the wound. The thyrohyoid membrane may usually be identified by its smooth, grey-yellow appearance, and the muscular tissues are divided to this depth with the dissecting scissors to completely isolate the tract. At this point, the tract may be cut across, and the specimen removed.

Following careful hemostasis, the mylohyoid muscle and strap muscles are approximated with several interrupted sutures. It is not necessary to unite the ends of the hyoid bone unless they seem to fall together without tension, as no disability will result. The subcutaneous tissues and platysma are then brought together with interrupted sutures, and the skin edges carefully approximated with fine interrupted sutures. Non-absorbable suture material is used throughout. One small rubber tissue drain may be left down to the thyrohyoid muscle if desired, to be removed in 24 hours. Skin sutures are removed in 48 hours, and the incision supported by one strip of adhesive tape. Disability following operation is usually minimal, and oral intake may be commenced following full awakening from anesthesia.

**SUMMARY**

Developmental anomalies of thyroglossal origin have been reviewed in embryologic, pathologic and clinical aspects. The findings and results of treatment in a series of 90 patients presenting lesions of the thyroglossal system have been reported. These lesions are found predominantly in the younger age groups, but may occur at any age. The diagnosis in the majority of cases should present little difficulty. The results in this series bear out the generally accepted teaching that the treatment of choice in all lesions of thyroglossal origin is the radical operation, with removal of a portion of the hyoid bone and complete excision of the tract to the foramen cecum.
STAHL AND LYALL

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