LEUCOCYTIC CHANGES FOLLOWING THE INTRAVENOUS INJECTION OF PEPTONES.

by

D. G. COOPER, M.B., Ch.B.

Thesis for the Degree of M.D., 1926.
During the winter 1925-26 a number of patients who were suffering from Rheumatoid Arthritis were treated in Ward 25 of the Royal Infirmary, Edinburgh, by intravenous injections of peptone. The observations on which this thesis is based were made on these patients. To Professor Murray-Lyon I am grateful for permission to make the observations and for much help while the work was in progress.

The number of cases is small. Nevertheless, as the findings in the different series of observations agree so closely with each other and with related results obtained by other workers, they do provide data for a hypothesis.

The arrangement of this thesis will be:

1. A general survey of the method.
2. A statement of cases with tables and graphs.
3. A general description of the results of the observations made.
4. A comparison of these results with those of other observers.
5. A discussion of the meaning of the observations.
6. A summary.
7. A list of references.
GENERAL SURVEY OF THE METHOD.

Patients were given intravenous injections of peptone in increasing doses in accordance with the usual method for such treatment. After some of these injections examinations were made of the changes in the leucocyte picture and especially of the progressive changes in the numbers of neutrophil polymorphs when classified by Arneth's method.

The first two patients were only examined with a view to finding out whether a leucocytosis occurred, and to determining the nature of any increase in the white blood cells. It was found that a neutrophil polymorphonuclear leucocytosis did occur.

In subsequent cases this increase of polymorph leucocytes was analysed by means of Arneth's classification. In doing this I have followed the modification introduced by W.E. Cooke.

In each case a basal estimation was made immediately before the injection. (In some cases several estimations were made for a day or two before the injection. As they were found to agree in the main with the basal counts they have been omitted from the tables attached to the cases).

During the day of the injection from 3 - 7 observations were made at varying intervals. One was made on the following day. And in some cases further examinations/
examinations were made at intervals during the suc­ceeding week.

Each observation consisted of two parts:­

(a) a total white cell count.

(b) a differential count combined with an Arneth count.

(a) A Thoma Zeiss counting chamber was used for the total count in the first few cases and a Bürker for the rest.

(b) Blood smears were made after the blood had been taken for the total count. These smears were stained in various ways, some by Jenner’s, some by Leishman’s, and some by the combined Jenner-Giemsa method.

Combined differential and Arneth counts were made of the stained smears. In most cases 250 or 300 cells were counted to make up the differential count. Then more polymorph neutrophils were counted to bring the total polymorph numbers up to a convenient figure for calculating percentages. This figure varied from 150-300 in accordance with the numbers of the polymorphs. The low figure of 150 was only considered sufficient for slides taken during the period of leucopenia; and then only when the total of the leucocytes was below 4000 per com. As a rule 250 neutrophil polymorphs were counted.
Cooke's modification of Arneth's classification depends on the nature of the material linking or separating the several nodes of the polymorph nucleus. Some nuclei show no nodes at all. In those nuclei which do show lobulation, those segments are considered separate which are connected to the other portions of the nucleus by chromatin threads alone. If there is a distinct band of nuclear material with the chromatin filament the lobe so connected is not considered separate.

By this means polymorph neutrophils are divided into five classes.

Class I shows no separation into lobes, this includes those cells which show no nodes at all. In these the nuclear matter looks like a ribbon and is often S-shaped.

Class II shows two segments.

Class III shows three segments.

Class IV shows four segments.

Class V shows five or more segments.

The distinction between neutrophil myelocytes and cells of class one is a very fine one. When both kinds/
kinds of cells appear in the peripheral circulation one is often at a loss in distinguishing one from the other. As cells of Class I are the immediate successors of myelocytes, and as myelocytes or an increase in Class I cells both indicate bone marrow activity, I have included myelocytes in Class I. Only those cells have been classed as myelocytes which showed acidophil cytoplasm, neutrophil granules, and an approximately round nucleus. Though I have classified such cells as myelocytes, I have also added them to Class I of the polymorphs. Thus only a few myelocytes are noted and though percentages and total numbers are shown in the tables, these do not affect the rest of the figures.

The actual numbers of leucocytes in Class V are so insignificant that Classes IV and V have been added together.

In practice it often happens that the different segments of the nuclei are superimposed. In many cases the fine connecting strands can be seen, in other cases it is not possible to be sure of their presence or nature. This circumstance tends to swell the numbers of the cells with less complicated nuclei. In all doubtful cases the cell has been placed in the class with the more complicated nuclei.
By means of these observations each case has provided a series of figures obtained at different stages of the peptone reaction.

These figures have been made into tables, and a graph has been constructed to illustrate each table.

To attain simplicity I have combined the figures for Classes I and II together, and Classes III, IV and V together in making the graphs. This does no violence to their meaning. Classes I and II are the juvenile cells, Class III consists of middle aged cells, Classes IV and V of aged cells. This question of age is not settled; it will be discussed later. An increase of Classes I and II is the same as Arneth's shift to the left and indicates bone marrow activity.

The small and large mononuclears have also been added together.

**Peptone.** A 20% solution of Armour's ordinary peptone was used. This consists of Primary Proteoses (approximately 0.4%), Secondary Proteoses (approximately 2.2%) and Peptone (approximately 0.3%).
Case I. Mc D., male, aged 57. Suffering from Chronic Rheumatoid Arthritis.

This patient had had a series of injections which commenced on 9.10.25. Observations were made on him on 13.11.25 after an injection of 1.75 ccs. of Armour's Peptone.

9.30 a.m. Armour's Peptone. 1.75 ccs. intravenously.
9.50 a.m. W.B.C. 10,000
Polymorphs 63.5% = 6350
Small Mononuclears 17% = 1700
Large Mononuclears 11% = 1100
Eosinophils 2% = 200
Mast cells 1.5% = 150

10.30 a.m. W.B.C. 9,200.
12.20 p.m. W.B.C. 12,200.
2.50 p.m. W.B.C. 26,400.
4 p.m. W.B.C. 28,000.
5.10 p.m. W.B.C. 33,000
Polymorphs 93.5% = 31042
Small Mononuclears 3% = 996
Large Mononuclears 3% = 996
Eosinophils -
Mast Cells 0.5 = 166
As only two differential counts and no Arneth counts were made in this case, the figures have not been tabulated and no graphs have been constructed. But a graph of another kind has been made to show the general reaction and the relation of the curve showing leucocytosis to the curves of Temperature, Pulse-rate, and Basal Metabolic rate. - Graph I.

Case II. Miss E.M., aged 28. This patient suffered from Epileptiform Seizures. She was not being treated with peptone alone. She was given three injections while she was in hospital.

<table>
<thead>
<tr>
<th>Date</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.10.25</td>
<td>0.75 ccs.</td>
</tr>
<tr>
<td>9.11.25</td>
<td>1.2 ccs.</td>
</tr>
<tr>
<td>11.11.25</td>
<td>0.75 ccs.</td>
</tr>
</tbody>
</table>

Observations were made on one of these occasions. No Arneth count was made. On another occasion blood could not be obtained on account of a convulsion. A record is shown in Table I.

Case III. G.M., female, aged 24, suffered from chronic Rheumatoid Arthritis. She received ten injections. The amount of the first injection was 0.25 ccs. and of the biggest 1.3 ccs. of Armour's peptone.

She/
She left hospital greatly improved.

Observations were made on the 14th and 18th of December 1925 and the 8th and 14th of January 1926. The results are shown in Tables II, III, IV and V and the graphs of the same numbers.

In table II a considerable increase in mononuclears is shown at the height of the increase. This will be discussed later.

Case IV. J.B., male, age 56. Suffered from chronic Rheumatoid Arthritis. He was given injections of 0.25 ccs. of peptone on the 14th and 18th of December 1925, an injection of 0.75 ccs. on the 29th Dec. 1925, and one of 1.0 cc. on the 10th January 1926.

Records of the observations made on the 29th of December are shown in graph VI and table VI.

Case V. Mrs S., age 45. Suffered from Chronic Rheumatoid Arthritis. This patient received an injection of 0.25 ccs. of peptone on the 1st of March 1926, and an injection of 0.5 ccs. on the 10th of March 1926. Observations were made on the 1st, 2nd, 5th, 8th, 9th, 10th, 11th and 16th, so that a fairly complete record has been obtained for sixteen days, during which time two injections were/
were given. Tables VII and VIII and graphs VII and VIII show these results. Graph VIII and table VIII are continuous with their forerunners.

Case VI. J.S., female, age 18. Suffered from Lupus of the face. She was not treated with peptone but with injections of Sanocrysin. Observations were made on the 2nd and 3rd and the 8th and 9th of February, after intravenous injections of 1 gramme of Sanocrysin on each occasion. The reactions were so similar to the reactions of other patients after peptone that they have been incorporated in this thesis.

Tables IX and X and the graphs IX and X show the results.

The general reaction in this case was much less severe than the reaction in cases after peptone. She usually felt sick after an injection, and sometimes suffered from a rise of temperature and an increase in the pulse rate. But the degree of these was comparatively slight and she did not always need to go to bed after an injection.

Case VII. J.M., male, aged 21. This patient received a course of injections. Observations were made after an injection of/
of 0.25 ccs. of peptone on the 17th of February and after 0.5 ccs. of peptone on the 11th of March.

The results are shown in tables XI and XII and graphs XI and XII.
Chart to show the relations of:

Temperature
Pulse Rate
Basal Metabolic Rate
Leucocytosis

Leucocytes: Peptone 1.75 cc
3.500 0.16" 180 +60
3.000 0.18" 160 +50
2.500 0.14" 116 +40
2.000 0.10" 110 +30
1.500 0.10" 100 +20
1.000 0.09" 80 +10
0.500 0.09" 60 +0

Hours after injection: 0 1 2 3 4 5 6 7 8
### TABLE I

<table>
<thead>
<tr>
<th>Hours after injection</th>
<th>4(^{1}/_{2})</th>
<th>14(^{1}/_{2})</th>
<th>3(^{1}/_{2})</th>
<th>4(^{1}/_{2})</th>
<th>5(^{1}/_{2})</th>
<th>6(^{1}/_{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Total</td>
<td>% Total</td>
<td>% Total</td>
<td>% Total</td>
<td>% Total</td>
<td>% Total</td>
</tr>
<tr>
<td>Total Leucocytes</td>
<td>7600</td>
<td>8800</td>
<td>16600</td>
<td>27000</td>
<td>26000</td>
<td></td>
</tr>
<tr>
<td>Polymorphs.</td>
<td>49.5%</td>
<td>7.5%</td>
<td>87.5%</td>
<td>93%</td>
<td>91.5%</td>
<td>23790</td>
</tr>
<tr>
<td>Small Mononuclears</td>
<td>34</td>
<td>12.5%</td>
<td>1100</td>
<td>3</td>
<td>810</td>
<td>3.5%</td>
</tr>
<tr>
<td>Large Mononuclears</td>
<td>16</td>
<td>12.5%</td>
<td>1100</td>
<td>3</td>
<td>1080</td>
<td>4.5%</td>
</tr>
<tr>
<td>Eosinophils.</td>
<td>0.5</td>
<td>0.5</td>
<td>83</td>
<td>0.5</td>
<td>130</td>
<td>0.5</td>
</tr>
<tr>
<td>Mast.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>Time</td>
<td>9.30 a.m.</td>
<td>10.50 a.m.</td>
<td>1.55 p.m.</td>
<td>4.50 p.m.</td>
<td>5.55 p.m.</td>
<td>4.30 on 15.12.25</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
<td>------------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
<td>----------------</td>
</tr>
<tr>
<td>Hours after Injection</td>
<td>0</td>
<td>1 1/3</td>
<td>4 1/4</td>
<td>7 1/3</td>
<td>8 1/3</td>
<td>31</td>
</tr>
<tr>
<td>Total Leucocytes</td>
<td>8000</td>
<td>5800</td>
<td>15000</td>
<td>16400</td>
<td>14000</td>
<td>4700</td>
</tr>
<tr>
<td>Total Polymorphs</td>
<td>52.5</td>
<td>4200</td>
<td>73</td>
<td>13425</td>
<td>10824</td>
<td>91.5</td>
</tr>
<tr>
<td>I.</td>
<td>.7</td>
<td>294</td>
<td>12</td>
<td>19</td>
<td>16.5</td>
<td>20</td>
</tr>
<tr>
<td>II.</td>
<td>23.5</td>
<td>987</td>
<td>37</td>
<td>41</td>
<td>40</td>
<td>49</td>
</tr>
<tr>
<td>III.</td>
<td>46</td>
<td>1932</td>
<td>38</td>
<td>25</td>
<td>26.5</td>
<td>26.5</td>
</tr>
<tr>
<td>IV &amp; V.</td>
<td>23.5</td>
<td>987</td>
<td>13</td>
<td>15</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Total Mononuclears</td>
<td>46</td>
<td>3460</td>
<td>25</td>
<td>10.5</td>
<td>32.5</td>
<td>15.5</td>
</tr>
<tr>
<td>Eosinophil</td>
<td>1</td>
<td>80</td>
<td>1.5</td>
<td>84</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Mast</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.5</td>
<td>1</td>
</tr>
</tbody>
</table>

Peptone 1.0 cc. at 9.30 a.m.
**Graph II**


- Total Leucocytes
- Polymorphs
- Arpetli Classes I & II
- III, IV & V
- Mononuclears

Broken line indicates a long interval.

For an explanation of the lines made by question marks see the discussion on mononuclears.
### TABLE III.

**Peptone. 1.2 cc. at 9.30 a.m.**

<table>
<thead>
<tr>
<th>Time Hours after injection</th>
<th>9.30 a.m.</th>
<th>11.10 a.m.</th>
<th>3.10 p.m.</th>
<th>4.20 p.m.</th>
<th>7 p.m.</th>
<th>10.45 a.m.</th>
<th>19.12 25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Leucocytes</td>
<td>6200</td>
<td>4000</td>
<td>17000</td>
<td>16800</td>
<td>17500</td>
<td>11,000</td>
<td></td>
</tr>
<tr>
<td>Total Polymorphs</td>
<td>72</td>
<td>4464</td>
<td>59.6</td>
<td>94.4</td>
<td>16800</td>
<td>94</td>
<td>No differential</td>
</tr>
<tr>
<td>I</td>
<td>7.6</td>
<td>342</td>
<td>35.5</td>
<td>6200</td>
<td>34</td>
<td>5392</td>
<td>Count. 23 2050</td>
</tr>
<tr>
<td>II</td>
<td>31.2</td>
<td>1390</td>
<td>33.5</td>
<td>7030</td>
<td>44</td>
<td>6952</td>
<td>435 3880</td>
</tr>
<tr>
<td>III</td>
<td>46</td>
<td>2050</td>
<td>22.5</td>
<td>4200</td>
<td>19</td>
<td>3000</td>
<td>27.5 2450</td>
</tr>
<tr>
<td>IV &amp; V</td>
<td>15.2</td>
<td>854</td>
<td>3.5</td>
<td>336</td>
<td>3</td>
<td>474</td>
<td>6 538</td>
</tr>
<tr>
<td>Total Mononuclears</td>
<td>27</td>
<td>1924</td>
<td>39.6</td>
<td>1484</td>
<td>5.6</td>
<td>1000</td>
<td>10 1230</td>
</tr>
<tr>
<td>Eosinophil</td>
<td>1</td>
<td>62</td>
<td>0.4</td>
<td>16</td>
<td>1</td>
<td>170</td>
<td>1 110</td>
</tr>
<tr>
<td>Mast.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Total Leucocytes.
- Polymorphs
- Large Class XI & XII
- III, VIII
- Neutrophils.

Breaking line indicates a long interval.
No differential count was done at the 9th hour. The figures here are computed and indicated by guesswork marks.
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Time and Hours after injection</td>
<td>9.50 a.m.</td>
<td>10.35 a.m.</td>
<td>11.10 a.m.</td>
<td>12.30 p.m.</td>
<td>4 p.m.</td>
<td>5 p.m.</td>
<td>8 p.m.</td>
<td>8 p.m.</td>
<td>11 a.m.</td>
</tr>
<tr>
<td>Total Leucocytes</td>
<td>8400</td>
<td>8200</td>
<td>5600</td>
<td>7800</td>
<td>14600</td>
<td>14800</td>
<td>19000</td>
<td>10,000</td>
<td></td>
</tr>
<tr>
<td>Total Polymorphs</td>
<td>71</td>
<td>59.64</td>
<td>40.05</td>
<td>73.6</td>
<td>84.5</td>
<td>6591</td>
<td>92</td>
<td>13452</td>
<td>90</td>
</tr>
<tr>
<td>I</td>
<td>7.3</td>
<td>438</td>
<td>12</td>
<td>400</td>
<td>14</td>
<td>574</td>
<td>27</td>
<td>1782</td>
<td>24.6</td>
</tr>
<tr>
<td>II</td>
<td>21</td>
<td>1280</td>
<td>30</td>
<td>1200</td>
<td>41</td>
<td>1681</td>
<td>42.5</td>
<td>2805</td>
<td>43.4</td>
</tr>
<tr>
<td>III</td>
<td>46</td>
<td>2760</td>
<td>42</td>
<td>1680</td>
<td>37.5</td>
<td>1537</td>
<td>29</td>
<td>1914</td>
<td>26.4</td>
</tr>
<tr>
<td>IV &amp; V</td>
<td>25.6</td>
<td>1536</td>
<td>16</td>
<td>640</td>
<td>7.5</td>
<td>308</td>
<td>1.5</td>
<td>99</td>
<td>5.6</td>
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<tr>
<td>Mononuclears</td>
<td>27</td>
<td>2268</td>
<td>33.4</td>
<td>2071</td>
<td>26</td>
<td>1456</td>
<td>15.5</td>
<td>1209</td>
<td>8</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>1.5</td>
<td>128</td>
<td>2.0</td>
<td>124</td>
<td>0.4</td>
<td>22</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mast Cells</td>
<td>0.5</td>
<td>42</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
The coloured lines indicate the same classes as in the preceding diagrams.
<table>
<thead>
<tr>
<th>Date</th>
<th>7.1.26</th>
<th>14.1.26</th>
<th>14.1.26</th>
<th>14.1.26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time after injection</td>
<td>10 a.m.</td>
<td>11 a.m.</td>
<td>11 a.m.</td>
<td>11 a.m.</td>
</tr>
<tr>
<td>Totals</td>
<td>8400</td>
<td>12000</td>
<td>12000</td>
<td>12000</td>
</tr>
<tr>
<td>Arath I.</td>
<td>62.4</td>
<td>5208</td>
<td>71</td>
<td>54</td>
</tr>
<tr>
<td>Arath II.</td>
<td>25.2</td>
<td>1810</td>
<td>230</td>
<td>34.4</td>
</tr>
<tr>
<td>Arath III.</td>
<td>44.4</td>
<td>1310</td>
<td>52.4</td>
<td>27.8</td>
</tr>
<tr>
<td>Mononuclears</td>
<td>26</td>
<td>1560</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>1.1</td>
<td>1074</td>
<td>9.8</td>
<td>27.2</td>
</tr>
<tr>
<td>Mast Cells</td>
<td>0.3</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*In this case several normal counts had been done. As it happened no basal count was made on the day of injection so a previous day's normal count has been used.*
The various colours have the same meanings as in other diagrams.
**TABLE VI.**

**JAMES BROCKIE.** 29.12.25.

Peptone at 9.30 a.m.

<table>
<thead>
<tr>
<th>Time and Hours after injection</th>
<th>10 a.m.</th>
<th>11.10 a.m.</th>
<th>12.10 p.m.</th>
<th>2.50 p.m.</th>
<th>4.40 p.m.</th>
<th>2.30 p.m.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.5 hour</td>
<td>2 hours</td>
<td>2.5 hours</td>
<td>5.5 hours</td>
<td>7.5 hours</td>
<td>29 hours</td>
</tr>
<tr>
<td>Total Leucocytes</td>
<td>% 9800</td>
<td>% 9200</td>
<td>% 12000</td>
<td>% 14200</td>
<td>% 12800</td>
<td>% 8600</td>
</tr>
<tr>
<td>Total Polymorphs</td>
<td>78</td>
<td>7644</td>
<td>89.5</td>
<td>8284</td>
<td>90.8</td>
<td>10896</td>
</tr>
<tr>
<td>I</td>
<td>6.5</td>
<td>497</td>
<td>19</td>
<td>1560</td>
<td>23.2</td>
<td>2505</td>
</tr>
<tr>
<td>II</td>
<td>21.5</td>
<td>1641</td>
<td>35.5</td>
<td>3000</td>
<td>44</td>
<td>4800</td>
</tr>
<tr>
<td>III</td>
<td>53.5</td>
<td>4080</td>
<td>34</td>
<td>2780</td>
<td>25.6</td>
<td>2600</td>
</tr>
<tr>
<td>IV &amp; V.</td>
<td>18.5</td>
<td>1414</td>
<td>10.5</td>
<td>864</td>
<td>7.2</td>
<td>767</td>
</tr>
<tr>
<td>Mononuclears</td>
<td>21.2</td>
<td>2078</td>
<td>9.2</td>
<td>329</td>
<td>9.2</td>
<td>1104</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0.3</td>
<td>78</td>
<td>1.5</td>
<td>138</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mast</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Time and Hours after injection:
- 0.5 hour
- 2 hours
- 2.5 hours
- 5.5 hours
- 7.5 hours
- 29 hours

Total Leucocytes:
- % 9800
- % 9200
- % 12000
- % 14200
- % 12800
- % 8600

Total Polymorphs:
- 78
- 7644
- 89.5
- 8284
- 90.8
- 10896

Leucocytes and Polymorphs:
- 10 a.m.
- 11.10 a.m.
- 12.10 p.m.
- 2.50 p.m.
- 4.40 p.m.
- 2.30 p.m.

**Peptone at 9.30 a.m.**
VI

J.B. 19/12-25 - 30/12-26.

Broken lines indicate a long interval.
### TABLE VII.  
**MRS STEWART.**  
1.3.26  
**Armour's Peptone 0.25 at 11 a.m.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Time after injection</th>
<th>Total Leucocytes</th>
<th>Polymorphs</th>
<th>Arneht I</th>
<th>Arneht II</th>
<th>Arneht III</th>
<th>IV &amp; V</th>
<th>Mononuclear</th>
<th>Eosinophils</th>
<th>Mast Cells</th>
<th>Myelocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.3.26</td>
<td>10.50 a.m.</td>
<td>4900%</td>
<td>56.4</td>
<td>2807</td>
<td>51.5</td>
<td>1030</td>
<td>59.5</td>
<td>1726</td>
<td>33.7</td>
<td>337</td>
<td>22</td>
</tr>
<tr>
<td>1.3.26</td>
<td>11.50 a.m.</td>
<td>2000%</td>
<td>51.5</td>
<td>3030</td>
<td>33.7</td>
<td>2905</td>
<td>59.5</td>
<td>1726</td>
<td>33.7</td>
<td>337</td>
<td>22</td>
</tr>
<tr>
<td>1.3.26</td>
<td>12.50 p.m.</td>
<td>3500%</td>
<td>50.6</td>
<td>3589</td>
<td>33.7</td>
<td>3205</td>
<td>59.5</td>
<td>1726</td>
<td>33.7</td>
<td>337</td>
<td>22</td>
</tr>
<tr>
<td>1.3.26</td>
<td>3.20 p.m.</td>
<td>8360%</td>
<td>56.4</td>
<td>8360</td>
<td>56.4</td>
<td>8360</td>
<td>56.4</td>
<td>8360</td>
<td>56.4</td>
<td>8360</td>
<td>56.4</td>
</tr>
<tr>
<td>1.3.26</td>
<td>7.20 p.m.</td>
<td>14500%</td>
<td>50.6</td>
<td>14500</td>
<td>50.6</td>
<td>14500</td>
<td>50.6</td>
<td>14500</td>
<td>50.6</td>
<td>14500</td>
<td>50.6</td>
</tr>
<tr>
<td>1.3.26</td>
<td>11 a.m.</td>
<td>10000%</td>
<td>50.6</td>
<td>10000</td>
<td>50.6</td>
<td>10000</td>
<td>50.6</td>
<td>10000</td>
<td>50.6</td>
<td>10000</td>
<td>50.6</td>
</tr>
<tr>
<td>2.3.26</td>
<td>11 a.m.</td>
<td>8840%</td>
<td>50.6</td>
<td>8840</td>
<td>50.6</td>
<td>8840</td>
<td>50.6</td>
<td>8840</td>
<td>50.6</td>
<td>8840</td>
<td>50.6</td>
</tr>
<tr>
<td>3.3.26</td>
<td>11 a.m.</td>
<td>1600%</td>
<td>50.6</td>
<td>1600</td>
<td>50.6</td>
<td>1600</td>
<td>50.6</td>
<td>1600</td>
<td>50.6</td>
<td>1600</td>
<td>50.6</td>
</tr>
<tr>
<td>5.3.26</td>
<td>11 a.m.</td>
<td>4600%</td>
<td>50.6</td>
<td>4600</td>
<td>50.6</td>
<td>4600</td>
<td>50.6</td>
<td>4600</td>
<td>50.6</td>
<td>4600</td>
<td>50.6</td>
</tr>
<tr>
<td>8.3.26</td>
<td>11 a.m.</td>
<td>4500%</td>
<td>50.6</td>
<td>4500</td>
<td>50.6</td>
<td>4500</td>
<td>50.6</td>
<td>4500</td>
<td>50.6</td>
<td>4500</td>
<td>50.6</td>
</tr>
<tr>
<td>9.3.26</td>
<td>11 a.m.</td>
<td>6400%</td>
<td>50.6</td>
<td>6400</td>
<td>50.6</td>
<td>6400</td>
<td>50.6</td>
<td>6400</td>
<td>50.6</td>
<td>6400</td>
<td>50.6</td>
</tr>
</tbody>
</table>
Mrs S. 10-26 - 9-316.

Broken line indicates long intervals.

Reproduce
Injecting
0-25 C.C.S.

Arnell Classes III, IV, V

Total Measurements

Hours after Injection
### TABLE VIII. MRS STEWART. 10.3.26 - 16.3.26.

Peptone 0.5 cc. on 10.3.26 at 10.30.

<table>
<thead>
<tr>
<th>Date</th>
<th>10.3.26</th>
<th>10.3.26</th>
<th>10.3.26</th>
<th>10.3.26</th>
<th>10.3.26</th>
<th>11.3.26</th>
<th>16.3.26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>10.25 a.m.</td>
<td>11.30</td>
<td>12.30</td>
<td>3 p.m.</td>
<td>6 p.m.</td>
<td>10.30</td>
<td>10.30</td>
</tr>
<tr>
<td>Hours after Injection</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4½</td>
<td>7½</td>
<td>24</td>
<td>134</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>% Totals</th>
<th>% Totals</th>
<th>% Totals</th>
<th>% Totals</th>
<th>% Totals</th>
<th>% Totals</th>
<th>% Totals</th>
<th>% Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Leucocytes</td>
<td>5700</td>
<td>2900</td>
<td>5900</td>
<td>9100</td>
<td>15600</td>
<td>5700</td>
<td>4100</td>
<td></td>
</tr>
<tr>
<td>Polymorphs</td>
<td>54</td>
<td>3078</td>
<td>62.4</td>
<td>1810</td>
<td>82.1</td>
<td>4839</td>
<td>92</td>
<td>8370</td>
</tr>
<tr>
<td>Arthen I</td>
<td>24.5</td>
<td>780</td>
<td>50.5</td>
<td>909</td>
<td>56.1</td>
<td>2763</td>
<td>60.4</td>
<td>5074</td>
</tr>
<tr>
<td>Arthen II</td>
<td>36.5</td>
<td>1131</td>
<td>35</td>
<td>630</td>
<td>32.5</td>
<td>1560</td>
<td>27.6</td>
<td>2318</td>
</tr>
<tr>
<td>Arthen III</td>
<td>33</td>
<td>1025</td>
<td>14</td>
<td>252</td>
<td>7.5</td>
<td>380</td>
<td>10.8</td>
<td>807</td>
</tr>
<tr>
<td>&quot; IV &amp; V.</td>
<td>6.0</td>
<td>186</td>
<td>0.5</td>
<td>9</td>
<td>1.8</td>
<td>91</td>
<td>1.2</td>
<td>101</td>
</tr>
<tr>
<td>Mononuclears</td>
<td>42.8</td>
<td>2439</td>
<td>33.6</td>
<td>974</td>
<td>18</td>
<td>1062</td>
<td>8.0</td>
<td>730</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>3.2</td>
<td>183</td>
<td>4.0</td>
<td>118</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mast Cells.</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myelocytes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>which are included in P.M.</td>
<td>1</td>
<td>59</td>
<td>0.4</td>
<td>36</td>
<td>1.0</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
VIII

MS S. 10.3.26 — 16.3.26.

The broken lines indicate long intervals.

P.100/58
Injection
0-5 c.c.s.

[Graph with labeled lines representing data over time]
### TABLE IX.

**JESSIE STENHOUSE.  2.2.26.**

Sanocrysin gramma 1.0 at 11.40 a.m.

<table>
<thead>
<tr>
<th>Date</th>
<th>2.2.26</th>
<th>2.2.26</th>
<th>2.2.26</th>
<th>2.2.26</th>
<th>3.2.26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>11 a.m.</td>
<td>1.10 p.m.</td>
<td>3.15 p.m.</td>
<td>8 p.m.</td>
<td>11 a.m.</td>
</tr>
<tr>
<td>Hours after Injection</td>
<td>0</td>
<td>1½</td>
<td>3½</td>
<td>7½</td>
<td>25</td>
</tr>
<tr>
<td>% Totals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Leucocytes</td>
<td>6400</td>
<td>8200</td>
<td>10600</td>
<td>6000</td>
<td>5800</td>
</tr>
<tr>
<td>Total Polymorphs</td>
<td>70.8</td>
<td>4531</td>
<td>73.2</td>
<td>6005</td>
<td>75.2</td>
</tr>
<tr>
<td>Arneth I</td>
<td>18.</td>
<td>810</td>
<td>22.5</td>
<td>1710</td>
<td>24.8</td>
</tr>
<tr>
<td>&quot; II</td>
<td>32.5</td>
<td>1462</td>
<td>34.5</td>
<td>2070</td>
<td>40.4</td>
</tr>
<tr>
<td>&quot; III</td>
<td>36.5</td>
<td>1542</td>
<td>29.2</td>
<td>1740</td>
<td>25.2</td>
</tr>
<tr>
<td>&quot; IV &amp; V</td>
<td>13.0</td>
<td>584</td>
<td>8.0</td>
<td>480</td>
<td>9.6</td>
</tr>
<tr>
<td>Mononucleares</td>
<td>27.6</td>
<td>1765</td>
<td>25.2</td>
<td>2065</td>
<td>23.6</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0.8</td>
<td>51</td>
<td>0.4</td>
<td>32</td>
<td>0.8</td>
</tr>
<tr>
<td>Mast Cells</td>
<td>0.8</td>
<td>51</td>
<td>1.2</td>
<td>98</td>
<td>0.4</td>
</tr>
</tbody>
</table>
J. S. 2.2.26 - 3.2.26.

Broken lines indicate long intervals.

IX.

Sennacepin
1 Grammes.

Total Leucocytes

Total Polymorphs

Neutroph.Dil. & L. G. M.

Mononuclears

Hours after Injection: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 12, 24.
<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Hours after injection</th>
<th>Total Leucocytes</th>
<th>Total Polymorphs</th>
<th>Neutrophils</th>
<th>Eosinophils</th>
<th>Mast Cells</th>
<th>Myelocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.2.26</td>
<td>8.2.26 10.35</td>
<td>0</td>
<td>8000</td>
<td>70</td>
<td>20.2</td>
<td>31.2</td>
<td>3.4</td>
<td>2.9</td>
</tr>
<tr>
<td>8.2.26</td>
<td>8.2.26 3 p.m.</td>
<td>4</td>
<td>10200</td>
<td>74.5</td>
<td>26.5</td>
<td>32.6</td>
<td>4.2</td>
<td>2.9</td>
</tr>
<tr>
<td>8.2.26</td>
<td>8.2.26</td>
<td>11 a.m.</td>
<td>24</td>
<td>7000</td>
<td>4200</td>
<td>1940</td>
<td>1528</td>
<td>412</td>
</tr>
</tbody>
</table>

JESSIE STENHOUSE

Sanocrysin 1 gramme at 11 a.m.
Sanoepisil
1 Grammge.

Total Leucocytes.

Total Polymorphs.

Neutrophiles I. & II

Meroeblasts

Granular classes III, IV, & V

Hours after Injection

0 1 2 3 4 5 6 7 8 9 — — 24
<table>
<thead>
<tr>
<th>Date</th>
<th>Time after Injection</th>
<th>10 a.m.</th>
<th>1 p.m.</th>
<th>2.30 p.m.</th>
<th>4 p.m.</th>
<th>5.30 p.m.</th>
<th>7.5 p.m.</th>
<th>9 p.m.</th>
<th>11 p.m.</th>
<th>23rd</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.2.26</td>
<td></td>
<td>11,000</td>
<td>10,000</td>
<td>8400</td>
<td>8126</td>
<td>4937</td>
<td>3503</td>
<td>3023</td>
<td>1297</td>
<td>143.8</td>
<td>1188</td>
</tr>
<tr>
<td>18.2.26</td>
<td></td>
<td>11,000</td>
<td>10,000</td>
<td>8400</td>
<td>8126</td>
<td>4937</td>
<td>3503</td>
<td>3023</td>
<td>1297</td>
<td>143.8</td>
<td>1188</td>
</tr>
<tr>
<td>19.2.26</td>
<td></td>
<td>11,000</td>
<td>10,000</td>
<td>8400</td>
<td>8126</td>
<td>4937</td>
<td>3503</td>
<td>3023</td>
<td>1297</td>
<td>143.8</td>
<td>1188</td>
</tr>
</tbody>
</table>

**Polymorphs**

- Total: 1188
- Type I: 143.8
- Type II: 40
- Type III: 31
- Type IV & V: 15

**Artemia**

- Total: 1188
- Type I: 143.8
- Type II: 40
- Type III: 31
- Type IV: 15

**Monocytes**

- Total: 1188
- Type I: 143.8
- Type II: 40
- Type III: 31
- Type IV: 15

**Eosinophils**

- Total: 1188
- Type I: 143.8
- Type II: 40
- Type III: 31
- Type IV: 15

**Basophils**

- Total: 1188
- Type I: 143.8
- Type II: 40
- Type III: 31
- Type IV: 15

Total Leucocytes.

- Polymorphs.
- Arpeth Classes EC II
- Y"Y"Y
- Mononuclears.

Break line indicates a long interval.
<table>
<thead>
<tr>
<th>Date</th>
<th>11.3.26</th>
<th>11.3.26</th>
<th>11.3.26</th>
<th>11.3.26</th>
<th>12.3.26</th>
<th>13.3.26</th>
<th>16.3.26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>10.30</td>
<td>12 noon</td>
<td>3 p.m.</td>
<td>6 p.m.</td>
<td>10.30 a.m.</td>
<td>10.30 a.m.</td>
<td>12 noon</td>
</tr>
<tr>
<td>Hours after Injection</td>
<td>0</td>
<td>1½</td>
<td>3½</td>
<td>6½</td>
<td>24</td>
<td>48</td>
<td>97</td>
</tr>
<tr>
<td>% Totals</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Leucocytes</td>
<td>8000</td>
<td>6800</td>
<td>10560</td>
<td>20200</td>
<td>10680</td>
<td>7800</td>
<td>10,000</td>
</tr>
<tr>
<td>Polymorphs</td>
<td>64.4</td>
<td>5152</td>
<td>78.5</td>
<td>5338</td>
<td>94.8</td>
<td>9954</td>
<td>97.2</td>
</tr>
<tr>
<td>Arneith I</td>
<td>16</td>
<td>832</td>
<td>50.5</td>
<td>2676</td>
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<td>4920</td>
<td>49.4</td>
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<tr>
<td>&quot;</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot; IV &amp; V.</td>
<td>13.5</td>
<td>676</td>
<td>1.5</td>
<td>80</td>
<td>4.4</td>
<td>440</td>
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<td>Mononuclears</td>
<td>34.4</td>
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<td>20.5</td>
<td>1360</td>
<td>5.2</td>
<td>546</td>
<td>2.6</td>
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<td>1.2</td>
<td>96</td>
<td>1.5</td>
<td>102</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mast</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>-</td>
<td></td>
<td>0.8</td>
<td>84</td>
<td>1.0</td>
<td>202</td>
<td>0.4</td>
</tr>
</tbody>
</table>
GENERAL DESCRIPTION OF THE RESULTS OF PEPTONE INJECTIONS.

After a peptone injection a general reaction takes place. Part of this consists in activity of the bone-marrow and this is shown by changes in the leucocytes. Though these changes are part of the general body changes they will be described separately.

(A) GENERAL REACTION.

The degree of this reaction varies with the amount of the dose. The same dose may cause a greater or a less reaction in different patients. A dose of over 0.8 coms. will bring about a marked effect in most patients. Smaller doses may do the same for more susceptible individuals.

From fifteen minutes to half an hour after the injection the patient begins to feel cold. During this period of chill a headache begins to assert itself. A rigor generally occurs. The patient feels sick and often vomits. The temperature rises one or two degrees. The patient exhibits some degree of cyanosis and suffers respiratory discomfort. The basal metabolic rate is greatly increased. This stage lasts for a period of half an hour to an hour.
Next comes a stage of fever. The chill from which the patient has suffered gives place to a feeling of comfort which in turn is displaced by a sensation of excessive warmth and discomfort. The basal metabolic rate is reduced. The temperature rises to $103^\circ$ or $104^\circ$ Fahrenheit and the pulse rate becomes more rapid in proportion to the temperature. The patient may have pains in various parts of the body. Some have complained of great pain in the small of the back. The joints which are the seat of the Rheumatoid changes usually become more swollen and tender and lose some degree of flexion. This stage lasts for about three hours and ends with more or less profuse perspiration.

During the next few hours all the symptoms gradually abate and at the end of twelve hours the patient is generally as comfortable as he or she may have been before the injection. Sometimes the headache persists for a longer period. The joints which were tender become less so and more supple than they were before the injection. This improvement may not be equal in all the joints. It persists for a few days and succeeding injections increase the movement.

(B) CHANGES IN THE LEUCOCYTES.

(a) Leucopenia occurs during the period of chill. The total number of leucocytes in each cubic millimetre/
The degree of leucopenia seems to depend on the dose. The smaller doses may not cause any leucopenia or the decrease in number may be so slight and transient that it escapes notice.

(b) **Leucocytosis** follows the leucopenia. It commences shortly after the rise of temperature begins, and persists long after the temperature begins to fall. It may continue for as long as forty-eight hours. The greatest increase occurs between the sixth and ninth hours after injection. The rise is rapid and the fall gradual.

(c) The **Differential Leucocyte count** shows that the different varieties are unequally affected.

During the period of leucopenia all varieties are decreased in total number but there is not a very great change in the percentages. If the blood specimen is taken after the lowest point of the leucopenia a relative neutrophil increase may be seen because the leucocytosis has really commenced. Sometimes during the leucopenia there is a relative decrease in polymorphs as in the case of G.M. in table III and graph III.

**Neutrophil Polymorphs** make up the bulk of the leucocytosis. As the graphs and tables show there is a decided increase in the cells of Arneth Classes I/
I and II. This corresponds to a shift to the left.

The Eosinophils are decreased in numbers. As a rule they are only slightly diminished in numbers during the leucopenia. After that they are seldom found till the day after injection.

Mast Cells behave in the same way as the eosinophils.

Mononuclears decrease in number during the leucopenia. A further diminution in their numbers may occur during the leucocytosis. But when the total number of the white blood cells begins to decrease after the height of the increase the mononuclears increase in number both relatively and absolutely. At the end of the leucocytosis the total number of mononuclears may be greater than it was before the injection.

In one case (G.M. table II and graph II) the mononuclears show an increase during the height of the leucocytosis. This will be discussed later in connection with promyelocytes.

Neutrophil Myelocytes are found during the height of the leucocytosis.

Premyelocytes. Their appearance in the peripheral blood will be discussed later.
COMPARISON OF THE AFOREMENTIONED RESULTS WITH THOSE OF OTHER OBSERVERS.

(a) General Reaction.

Many investigators have recorded the results of intravenous injections of peptone and other allied protein substances, (such as those derived from bacteria) or of the intravenous injection of metallic preparations. Macfarlane and Barlow have used peptones in Asthma and Rheumatoid Arthritis; Auld has published the results of similar work. Scully has used Typhoid vaccine in Acute Articular Rheumatism, Chronic Rheumatoid Arthritis, and Lobar Pneumonia. Gay and Chickering have employed "a ground polyvalent vaccine that had been sensitised by Antityphoid serum, and then killed and precipitated with alcohol. From the ground culture the endotoxins were extracted by carbolated saline solution and the remaining sediment of bacterial bodies alone were used." Auld has also employed colloidal metals and found that the body reacts in the same way as when a protein derivative is injected.

These observers are in singular agreement with regard to the clinical and other phenomena which have occurred after their injections. And to state their findings would be to restate what has already been written earlier in this thesis. One worker may omit one/
Composite curve from 167 injections in 35 cases.
Typhoid Vaccine used by Scully.
Compiled from article by Scully.
Journal of the American Medical Association
1907 (Apr.), p. 20.
Small Lymphocytes show a slight rise during the chill followed by a fall after two to three hours; and then a gradual rise to the same percentage as before.

Eosinophils show an absolute and relative increase followed by an absolute and relative decrease.

Basophils show an absolute and relative increase followed by an absolute and relative decrease.

Most of the other observers are content to record a neutrophil leucocytosis.

My findings do not agree with Scully's with regard to the Basophils. They seem to me to follow the same numerical variations as the Eosinophils. They were sometimes present during the whole of the leucocytosis. On other occasions they were present at some period of the leucocytosis but their appearance at any particular period was inconstant.

In this my results agree with those of Gulland and Goodall, who, in describing a neutrophil leucocytosis state: "Eosinophils and Basophils are often absent or reduced to a minimum, especially in septic cases." So apparently the laws to which they conform are not yet discovered.

Auld, Elliot Smith and Fergusson & Thomas record the results of the injection of metallic and other preparations. Auld employed intravenous injections of colloids of platinum and of gold. Elliot Smith and/
and Fergusson & Thomas used intramuscular injections of one gramme of the Salicylate of Mercury, or 0.5 grammes of Quinine Bihydrochloride, or intravenous injections of Novarsenobilon.

Auld found that a similar general reaction and a similar neutrophil leucocytosis occurred. In the two instances in which I observed the results of intravenous Sanocrysin injections, the general disturbance was slight, and the neutrophil increase was not very marked. In this point I agree with Fergusson & Thomas who noted that in the leucocytosis following an intramuscular injection of the Salicylate of Mercury the variations in the differential count were within the normal limits.

One of my two counts after a Sanocrysin injection showed a polymorphonuclear percentage above seventy-five and then it was only seventy-nine. On this occasion no estimations were made between the periods of 3½ and 7½ hours after injection. It is possible that the height of the leucocytosis occurred in the interval for the polymorph percentage of 79 was found when the leucocytosis had passed off. (Table number IX). The observations are too few to permit of a general statement. They have been included for the sake of their agreement in the Arneth variations.
(c) Arneth's Classification.

As regards this classification I have not been able to find references to any series of counts made during the development of a neutrophil leucocytosis. The nearest related series of figures is that published by Cooke. He has made counts by this method in a variety of diseases such as Typhoid Fever, Measles, Scarlet Fever, Erysipelas, Diphtheria, Rubella, Chicken pox, Whooping Cough and Gonorrhoea. In each count there is a shift to the left. Rayevsky and others have shown a shift to the left in cases of Tubercular infection. Now some of these diseases show a neutrophil decrease, others show no marked change in total numbers, others show a neutrophil increase. This is in agreement with my records which show a shift to the left even during the period of leucopenia; also in the Sanocrysin cases in which the differential count does not show much variation from the normal; and in the counts in which there is a great neutrophil increase.

Cooke, Rayevsky, and Kramer (quoted by Rayevsky) are in general agreement with Arneth in regard to the percentages in which the various Arneth classes are to be found in normal individuals. An average of my basal counts which were made before the injections does not vary greatly from their figures.

I have also made a number of counts in such diseases/
diseases as Pneumonia, Endocarditis, Septicaemia, Acute Rheumatic Fever, and Broncho Pneumonia. These counts, as well as those made after the peptone injections, agree with Cooke's. Those made after peptone show a greater deviation to the left than any of Cooke's figures. Perhaps this is because the leucocytosis was more sudden and transitory. Cooke's estimations would be made after a more settled leucocytosis had been established.

The following are the normal averages in percentages as found by Arneth, Cooke, Rayevsky and Kramer, together with an average from my basal counts:

<table>
<thead>
<tr>
<th>Class</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
<th>Class V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arneth</td>
<td>5</td>
<td>35</td>
<td>41</td>
<td>17</td>
</tr>
<tr>
<td>Cooke</td>
<td>10.9</td>
<td>25</td>
<td>46.7</td>
<td>15.3</td>
</tr>
<tr>
<td>Rayevsky</td>
<td>5.33</td>
<td>34.74</td>
<td>42</td>
<td>15.5</td>
</tr>
<tr>
<td>Kramer</td>
<td>4</td>
<td>30</td>
<td>45</td>
<td>18</td>
</tr>
<tr>
<td>Average of my basal counts</td>
<td>10.4</td>
<td>28.5</td>
<td>43.6</td>
<td>14</td>
</tr>
</tbody>
</table>

This shows that the basal counts are very like the normal average. I have omitted two counts which showed such an obvious shift to the left that they could not be considered even approximately normal.

Cooke's/
Cooke's figures for various diseases are as follows:—

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
<th>Class V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typhoid Fever</td>
<td>43-54</td>
<td>31-33</td>
<td>13-22</td>
<td>0-5</td>
<td>0</td>
</tr>
<tr>
<td>Scarlet Fever</td>
<td>26-44</td>
<td>32-43</td>
<td>13-30</td>
<td>2-8</td>
<td>0-1</td>
</tr>
<tr>
<td>Measles</td>
<td>39-51</td>
<td>30-39</td>
<td>14-20</td>
<td>1-3</td>
<td>0-1</td>
</tr>
<tr>
<td>Erysipelas</td>
<td>44-59</td>
<td>30-40</td>
<td>6-19</td>
<td>0-1</td>
<td>0</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>21-60</td>
<td>32-48</td>
<td>8-32</td>
<td>0-5</td>
<td>0-1</td>
</tr>
<tr>
<td>Rubella</td>
<td>22-30</td>
<td>30-35</td>
<td>32-43</td>
<td>3-4</td>
<td>0-4</td>
</tr>
<tr>
<td>Chicken Pox</td>
<td>18-51</td>
<td>31-35</td>
<td>17-45</td>
<td>1-6</td>
<td>0</td>
</tr>
<tr>
<td>Whooping Cough</td>
<td>24-34</td>
<td>39-44</td>
<td>27-31</td>
<td>0-3</td>
<td>0</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>12-20</td>
<td>31-30</td>
<td>39-43</td>
<td>8-12</td>
<td>1</td>
</tr>
</tbody>
</table>

A DISCUSSION OF THE MEANING OF THESE OBSERVATIONS.

(A) The General Reaction.

This bears a strong resemblance to an attack of Malaria. In each case the typical sequence of events is a cold stage followed by fever which abates gradually.

The injection of a dose of peptone corresponds to/
to the process of sporulation in an attack of Malaria. In each case a feeling of discomfort follows. This develops into a chilly feeling which may end in a rigor. During this cold stage the skin temperature falls though the rectal temperature may be rising. The patient looks blue. The pulse is rapid, the peripheral arteries contracted. Nausea is present. Vomiting may occur at this stage or early in the next. In some cases of Malaria no cold stage occurs, and sometimes after injections of peptone too the period of fever is not ushered in by a chill or rigor. This stage lasts for twenty or thirty minutes.

A period of fever follows both in Malaria and after an injection of Peptone. Headache is common to the two conditions. The pulse becomes full and bounding and the pulse-pressure is reduced. During an attack of Malaria the patient may become delirious. Great mental distress sometimes occurs after a peptone injection.

After the fever has lasted for from three to five hours the patient begins to perspire. The temperature then begins to fall and all the symptoms abate. The headache often lasts longer than the fever.

If an acute infectious fever like Measles could be compressed into the space of a day, the resemblance would also be close. Many cases of Liver Abscess, atypical cases of Typhoid or Paratyphoid fever have days/
days in which a similar sequence of events occurs.

In each case a foreign substance has entered the body of the sufferer. There is the obvious difference that in the case of Malaria or of an infectious fever the foreign substance is a living one. Typhoid vaccine as used by Scully, and ground bacteria as used by Chickering and Gay provide links between the living plasmodia or bacteria and the protein derivatives which compose Armour's peptone.

Moreover the foreign substance or antigen in each case causes the reaction when it is in the bloodstream. The plasmodium of Malaria causes no fever until sporulation occurs. It is only then that the parasites are free in the blood. When they become attached to or penetrate erythrocytes, or suffer destruction from the attacks of leucocytes or quinine or fixed tissue cells, the fever begins to abate. Few observers have the temerity to describe the free forms of the plasmodium. When an object that looks like a merozoite is unattached to a red corpuscle there is always considerable doubt as to its identity. Nevertheless the young parasite must spend some time free in the bloodstream. And as fever only follows sporulation it is fair to conclude that there is a causal connection between this freedom of the merozoites and the pyrexia. In the case of bacteria general symptoms are produced when they or their toxins enter the/
the circulation. Tubercle bacilli when encysted in a fibrous capsule cause no symptoms. In the same way metals do not affect the body as a whole till they enter the circulation. A sterile metal plate fixed to a bone causes no symptoms; nor does an intramuscular injection of Mercury. Instances could easily be multiplied to support this contention. But for the purposes of this thesis it is enough to establish the fact that the intravenous injection of "peptone" produces a reaction that is very similar to those caused by living substances free in the blood stream.

The similarity of the reaction tempts one to consider the possibility that living parasites and bacteria only produce their effects when they disintegrate and that protein derivatives are the actual cause of the reaction. It is even possible to argue that metallic and other foreign substances act in the same way by causing the degeneration of tissue cells and so producing peptones. The lack of experimental evidence takes away the possible usefulness of such speculation though it is deeply concerned with the rationale of non-specific protein therapy.

In an earlier part of this thesis attention was called to the agreement of the various observers on matters of fact concerning the results of protein and other injections. This does not produce any unanimity with regard to the theories put forward to explain the/
the findings. Nor is there any agreement as to the manner in which the injections of vaccines, bacteria, protein derivatives and inorganic compounds help to cure or alleviate such a variety of diseases as Typhoid Fever (Gay and Chickering), Acute Rheumatic Fever, Lobar Pneumonia, Chronic Rheumatism (Scully), Asthma, Chronic Rheumatoid Arthritis (Macfarlane and Barlow) - and the list is not exhausted. Whatever be the mechanism, the symptoms, which have been described, are always present in some degree. They are produced during the body's attempt to attain immunity from a foreign substance, - that is - the body's attempt to absorb, confine, or extrude its unwelcome visitors.

This comparison of the effects of a peptone injection with Malaria and other conditions has been made to show that the similarity of symptoms suggests that the same mechanism carries on the struggle for immunity, whether the antigen is a living organism or is merely a chemical entity. This point needs to be kept in mind during the consideration of the leucocytic reaction.

B. Leucocytic Reaction.

The changes we have to consider are those stated in a previous section of this thesis. They may be summarised briefly as follows:-
(1) An initial leucopenia affects all varieties of cells.
(2) A Neutrophil leucocytosis follows.
(3) The Arneth Count shows a progressive shift to the left during the leucocytosis. This shift to the left is seen even during the period of leucopenia.
(4) The mononuclear cells decrease during the leucocytosis and increase gradually after the height of the leucocytosis. There is occasionally a mononuclear increase during the height of the leucocytosis.

The ages of the Cells in Arneth's Classes.

Arneth claims that polymorph cells of Class I are the youngest cells and those of Class V the oldest polymorphs. This has been disputed by observers who state that some of the cells of Class I with rounded nuclei are really degenerated forms. These conflicting views must be considered before the other leucocyte changes can be discussed.

Arneth's classification depends on the nuclei of the polymorphs so we will first consider it from the point of view of the development of the neutrophil nucleus. We do not need to go far back in its evolution. The neutrophil myelocyte is typically a cell with an oval kidney or horse shoe shaped nucleus. This horse shoe/
shoe shaped nucleus is the immediate precursor of the nucleus of the polymorph as we meet it in the peripheral circulation. The nuclei of cells in Arneth's Class I very closely resemble the horse shoe myelocyte nuclei. The most complicated nucleus of this class consists of a series of segments attached to each other by bands of nuclear matter. Transitional forms can be seen which link together all the members of the series of classes. In class I we find cells with nuclei like horse shoes, ribbon like nuclei with no nodes, twisted ribbons, ribbons with nodes on them. These are succeeded by the bilobed nuclei of class II, which in turn give place to classes III, IV and V. And it is not necessary to look at pathological specimens to find these cells; they are present in the blood of healthy individuals. The resemblance between those of the cells of class I which have the most simple nuclei and the myelocytes with horse shoe shaped nuclei is so close that it is a matter of difficulty to place the one in one category and the other in a different one. The gradual changes in the nuclei are shown more or less diagramatically below.

Myelocyte.

Class I

Class II
M. Heidenheim explains the development of the horse shoe shaped nucleus from the rounded form by a reference to the behaviour of the nucleus and centrosome. Embedded in the cytoplasm of a free cell are radii which proceed outwards from the centrosome. These radii tend to pull the centrosome to the centre of the cell. In so doing they displace the nucleus if the relative sizes of the cell and the nucleus allow of this. The nucleus is thus pushed to one side and deformed. Pappenheim explains the further development of a polymorph nucleus as a process of ripening. Gulland and Goodall suggest that this process is for the purpose of facilitating amoeboid movement. Pappenheim also considers that the changes in the nucleus are not reversible. Once a nucleus is divided into lobes it remains divided or can be still further segmented but it cannot again regain the/
the simple horse shoe shape. This means that cells of classes II, III, IV and V are, in that order, further removed from myelocytes than the cells of Class I.

It is possible that the nuclei of cells do not alter while the cells are in circulation and that they complete their lives in the state in which they first left the bone marrow. Such a view would make it possible for any class to contain cells of all ages. But such a view would not take any account of the time spent in development in the bone marrow. It is fair to assume that the cells of more advanced development take a longer time to ripen than those less advanced. The time taken for this preparation of the nucleus would need to be considered in determining the age of a cell. If Arneth's classification were considered from this point of view, it would be a differentiation of cells in accordance with the stage of development of their nuclei. There would be a distinction but no real difference between such a statement and Arneth's original one.

Before Pappenheim put forward his explanation of the form assumed by the Polymorph nucleus, the accepted theory was that the nucleus became deformed as the result of the cells amoeboid movements. This theory too is in favour of the less complicated nuclei marking the younger or, at any rate, the cells that had/
had shown least activity. The classification would then indicate intensity rather than length of life.

Carnegie Dickson in describing the development of the neutrophil polymorph states:— "As this transition from myelocyte to adult leucocyte takes place, the nucleus becomes progressively more and more convoluted and irregular in shape until it finally assumes the typical and familiar type found in the polymorphonuclear leucocyte". He was not contemplating Arneth's classification and so it is not fair to stretch his meaning. Nevertheless his description does describe a progress from a simple to a more complicated type of nucleus as being part of development.

I have not been able to find any reference to a neutrophil leucocytosis which failed to show a shift to the left. Nor have I examined any blood film taken during the course of a polymorph leucocytosis which did not show a drift to the left. Other observers, already quoted, have demonstrated its occurrence in many conditions.

The successive counts made during the development of a leucocytosis following a peptone injection show a progressive increase in percentages and absolute values of Classes I and II. The neutrophil increase is almost wholly made up of cells of these classes, as the graphs show. If we were to consider the cells of class I as degenerate forms then we would/
would have to go further and state that large numbers of degenerate forms are produced by the bone marrow for the purpose of combating toxic conditions. Or we would have to assume that a depot of veteran leucocytes is maintained for a leucocytosis. The first of these statements is not in accordance with the efficiency of the body machine nor even with the ability of a leucocytosis to achieve its purpose. The second assumes an arrangement which has no parallel in the body nor has any one described such stores of cells in the bone marrow. And there is no doubt that a neutrophil leucocytosis is the product of bone marrow activity.

We find then (1) that morphologically the nuclei of the cells of Class I more nearly resemble the nuclei of myelocytes than do those of Class II, and that classes III, IV and V show a progressively more distant likeness to the myelocyte; (2) that the segmentation of the nucleus is the result of development; (3) that the cells of Classes I and II represent the bulk of the result of bone marrow activity during a leucocytosis. Both facts and theory force us to agree with Arneth with regard to the ages of the cells in the different classes.

The Leucopenia that occurs shortly after the injection of peptones now has to be considered.

The leucopenia affects all types of cells.
What causes it?

Not all cases showed the initial leucopenia. It is possible that sometimes it did occur but was not found because the interval between the injection and the taking of the first specimen of blood was too lengthy. But that its occurrence is not invariable will be seen by reference to graphs X and XI. These were both made from the same patient on different occasions. On the first occasion the dose was only 0.25 ccs. of peptone and no leucopenia occurred. A count made half an hour after the injection showed the beginning of a leucocytosis. On the second occasion the dose was 0.8 ccs. of peptone and a leucopenia was found as long as one and a half hours after the injection. So the dose has something to do with the nature of the reaction and this is in conformity with the general observation that drugs which stimulate in small doses often depress if they are used in large doses. We will revert to this point after considering the causes of the leucopenia.

A leucopenia, as we know it, is a reduction in the number of white blood cells in the peripheral circulation. This does not of necessity mean that there is a reduction in the total number of cells in the body.

There are two possible ways in which a leucopenia may be brought about.

(1) It may be the result of a redistribution of corpuscles in the body.

(2)
These two possibilities must be considered in turn. Various observers have found that in health leucocytes are not evenly distributed throughout the body. The spleen, liver, kidneys and bone marrow have more, other internal organs and the central blood vessels have less than the proportion in the peripheral circulation. It is possible that a leucopenia is an exaggeration of this unequal distribution and that there is a concentration of cells in some of the internal organs.

Teale has published the results of some interesting experiments that have a bearing on this point. He injected sometimes virulent and at other times non-virulent bacteria or spores into a vein of an immune or a susceptible animal. A minute after the injection he drew blood from another vein and after culture counted the colonies recovered. He repeated the drawing of blood and making cultures at intervals for a period of 48 hours. The number of colonies recovered 1 minute after injection varied from 50,000 to 200,000; after an hour only, 300 to 3000 were recovered; after four hours the numbers varied from 40 to 600; after 48 hours, if the animal survived as long, no colonies were recovered. The result was the same whether he used immune animals or not, whether the
the bacteria were virulent or harmless. Even spores were removed from the peripheral circulation with the same speed. Now though the organisms could not be found in the circulation they could be demonstrated in the capillaries of the lungs, liver, spleen and bone marrow. Phagocytosis took place in those sites by means of leucocytes and also by means of the local fixed tissue cells. The disappearance of the bacteria did not depend upon antibodies for it took place with the same rapidity in immune and susceptible animals. The bacteria were found in clumps entangled in masses of blood platelets and gelatinous material which he considered might have been incipient fibrin.

Any foreign substance injected into a vein has to follow the direction of the blood stream in the same way as the bacteria of Teale's experiments. Such substances proceed through the right side of the heart to the lungs and on to the left side of the heart. Thence they complete the circuit through the body. This goes on over and over until the peptones are excreted, hydrolysed or neutralized in some way.

After a meal containing protein, amino-acids enter the blood stream and give rise to no untoward symptoms. If peptones injected into the blood stream were further hydrolysed they would be rendered innocuous. Halliburton refers to some experiments by Mendell and Rockwood. They injected foreign food proteins/
proteins intravenously and intraperitoneally. These proteins were apparently used in the body. In some cases small quantities of proteoses were found in the urine. They concluded that the proteins had been broken down by tissue cells. The enzymes in these cells are capable of doing the work of Trypsin and Erepsin.

Is it possible that the peptone molecules are detained in the lungs, liver, spleen and bone marrow in the same way as the bacteria of Teale's experiments? And do they lodge in the damaged tissues of the affected joints in Rheumatoid Arthritis? The experiments of Mendell and Rockwood show that the peptone must lodge somewhere to be split up by the tissue cells. Normally the liver deals with the excess of the amino-acids of digestion. The same organ may deal with the more complex peptones. We do know that the bone marrow is stimulated, and that the heat regulating centres are affected. So we may conclude that the peptone molecule forms chemical combinations or becomes attached to cells in various parts of the body. If so, would they cause local hyperaemia and leucocytosis and so produce a leucopenia in the Peripheral blood? It is probable that they do. Dale states that the leucopenia is due to leucocytes adhering to the walls of capillaries. As a result they are not found in the circulation. (I have not been able/
able to verify the reference so I am not able to state whether Dale was referring to capillaries in general or to those of any particular organ. Nor have I been able to find references to any animal experiments on this point).

The second possibility is that the leucopenia is caused by the destruction of leucocytes. We have to explain the deficiency in the number of leucocytes during the initial leucopenia and also the more gradual reduction of much larger numbers when the leucocytosis ends and a restoration to normal takes place.

During health leucocytes like other body cells are formed, employed, and destroyed. My conception of the life of leucocytes is that some enter the circulation as cells of Arneth's class I, some of class II. In the circulation they develop into cells of the other classes. Not all the cells reach full maturity, many are expended or killed before full ripeness is attained. During the course of a day many slight infections and small doses of toxin have to be neutralised. The normal number of leucocytes is sufficient for this. Those that are destroyed during the wear and tear of the day are replaced by freshly formed cells. If some such gradual destruction did not take place the various Arneth classes would contain approximately equal numbers of cells.
The comparison of this age distribution to that of a normal human population has already been made. We can complete it by suggesting that it is produced by a similar method of elimination. Cells and men at the extremes of life have a greater expectation of death.

If this is so, then during the return to normal conditions at the end of a leucocytosis cells of classes I and II would be developing into cells of classes III, IV and V, but this would not account for all the cells that disappear from the circulation. Are these young cells more delicate than those of the more developed classes, and are they destroyed more quickly? The restoration to normal is very gradual, so no sudden holocaust has to be assumed. Dale's statement that leucocytes adhere to the walls of capillaries is certainly not against the possibility of destruction. There must be some alteration in the endothelium of the capillaries, or in the cell membrane of the leucocytes, or in both to cause such an adherence.

In favour of the possibility of the destruction of leucocytes is the theory that ferments and antibodies are produced by the disintegration of leucocytes. This is not yet proven. Wright's first case of immuno-transfusion proves that antibodies (or some substances of an allied nature) are manufactured in the/
the blood and are independent of fixed tissue cells. In this case a vaccine was added to a litre of the donor's blood which was stored in a suitable paraffin coated vessel. After this had been allowed to incubate for some hours it was transfused into the patient who recovered from a very critical condition. No record was made of the condition of the leucocytes at any stage of the process; so that, though the production of opsonins, ferments or antibodies is proved, no evidence is brought forward to show that the leucocytes broke down to manufacture them. However there is a strong presumption that the only cells present in the blood must have been the causal agents.

Another point in favour of the destruction of leucocytes during leucopenia is the shift to the left reported by Cooke in cases of Typhoid Fever. The shift to the left indicates that the bone marrow is producing fresh polymorphs. In spite of this the leucopenia in Typhoid fever mainly affects the polymorphs. What is happening to these polymorphs? Destruction or redistribution are both possible. The severity of the disease, its long course, the loss of the patient's weight, the parenchymatous degeneration in organs like the liver and kidney, all incline one to think that destruction is taking place.

The evidence is not conclusive, and the question must/
must be left open. Probably both processes are in action at the same time, a redistribution of cells takes place, and great numbers of cells are destroyed.

**THE PERIOD OF LEUCOCYTOSIS.**

A leucocytosis is an increase in the number of white blood corpuscles. In practice we only estimate the number of the white blood cells in the peripheral circulation and take no account of a possible redistribution of cells. As we have seen in the occurrence of a leucopenia this has to be borne in mind. Gulland & Goodall point out that sometimes when an abundant polymorph leucocytosis occurs before death no signs of it are present in the bone marrow. They suggest that this is due to a terminal sweeping out of the cells in the marrow. A possible additional explanation is a redistribution of cells due to other organs like the liver, spleen, and kidneys as well as the marrow giving up the leucocytes that were concentrated in them. But such a condition is exceptional. It is not sufficient to make us doubt that a polymorph leucocytosis indicates bone marrow activity.

But does the measure of a leucocytosis represent the whole of the activity of the marrow? As we have seen an initial leucopenia occurs and this is caused by/
by a redistribution or destruction of leucocytes or a combination of these processes. Redistribution is due to the positive chemiotaxis of the peptone which is concentrated in the liver or spleen or bone marrow, or in all these organs. If we favour the theory of destruction we must assume that it is caused by the peptone that has been introduced into the circulation. In either case we must grant that the process of redistribution or destruction will continue as long as the peptone is not neutralized, and the body has not gained immunity.

One of the signs that an antigen is taking effect is the general reaction. In the case of a patient suffering from Pneumonia or other disease due to bacteria the reaction goes on for days because there is a continued production of toxins. In the case of a single peptone injection the pyrexia only continues for a few hours because the peptone is rapidly neutralised and the dose is limited. Vaughan has shown that by repeated daily injections protein fever can be continued for weeks and that the temperature curve in such a case is indistinguishable from that of Typhoid Fever. With the limited doses which are generally used the fever abates as soon as the body gains immunity. But the leucocytosis continues and even increases while the temperature is falling. And not only does the leucocytosis increase but the shift/
shift to the left in Arneth's count becomes more marked until the fall in the number of white blood cells commences.

Does this mean that the bone marrow is unable to cease its activity as rapidly as the other mechanisms of the body are able to settle down after their disturbance? Or does it mean that the clinical symptoms require a greater minimal stimulus than the bone marrow? The latter is probably the true explanation. That a variable minimum quantity of a drug or a toxin or bacteria is required to evoke a general reaction is well recognised. That the continuance of the symptoms depends on the continued presence of a minimum quantity of the stimulant is also well known. In describing the crisis of Pneumonia, Osler & Macrae write:—

"The crisis, the most remarkable phenomenon of pneumonia, appears to represent the stage of active immunity to the toxin of the pneumococcus. The fever, dyspnoea, and general symptoms disappear when the immunity reaches a certain stage". After the crisis in Pneumonia the bacteria are still present in the lung. They may even cause complications later. The point is that at the time of the crisis, the concentration of toxins is below that necessary for the continuance of the fever. So too after a peptone injection the subsidence of the general symptoms means that the remaining quantity of peptone is too small to evoke them. This fact does not provide sufficient foundation/
foundation for the assertion that the leucocytosis is continued to complete the victory over the peptone. But we may say that such an arrangement is very probable.

We can now return to the question as to whether a leucocytosis as measured in the ordinary way represents the whole of the bone marrow activity? Most assuredly it does not. As we have seen Leucopenia is caused by the redistribution or destruction of leucocytes by the action of peptone. Let us connect this with the other fact that the general symptoms of fever and its accompaniments indicate the active stage of the peptone. We can then state that the process of redistribution or destruction or the combination of the two must continue as long as the general symptoms last. Therefore, in spite of the increase in the number of leucocytes in the peripheral circulation, large numbers of white blood cells are being destroyed or concentrated in certain organs of the body. That this is true can be shown from a comparison of the well known facts of pneumonia. In this disease we know that there is an enormous concentration of leucocytes in the affected part of the lung and in spite of this the number of polymorphs in the peripheral circulation is increased.

In this connection further evidence is offered by the Arneth count. The shift to the left is evident even during the initial leucopenia. This shift/
shift to the left, as we have seen, indicates increased bone marrow activity. In other words the leucocytosis has commenced but is not evident because it is masked by the leucopenia. It only becomes evident after the increase of white cells is in excess of the decrease that has occurred.

From a consideration of these arguments we may conclude that the leucocytosis which can be measured in the peripheral circulation only represents part of what is occurring. A great number of the fresh cells that are being produced by the bone marrow are being used to deal with the peptone in the liver, lungs, kidneys and spleen. The two processes of production and concentration or destruction are going on at the same time. The measured leucocytosis only represents the difference between the total product of the bone marrow and that proportion which is being expended in neutralizing the antigen.

If then a leucocytosis is very high, it means that though the marrow is very active the toxins to be combated are present in large quantities or are very intense in their virulence.

If we get the combination of a slight leucocytosis or a leucopenia with severe general symptoms and a marked shift to the left of the Arneil count, we may conclude that the bone marrow is acting vigorously, but that the processes of redistribution or destruction are more active still. This is shown in Cooke's figures.
figures for Typhoid Fever which are given in another part of this thesis.

The practical result of such a view is that in such cases we need to neutralize the toxins in some way. Chickering & Gay* have used vaccines to produce a leucocytosis in Typhoid Fever. They claim that distinct benefit resulted in 66% of their cases but their figures are not very convincing. Possibly this is because they were whipping a tired horse. Theoretically some such procedure as immuno-transfusion would be more efficacious. Such a method would reduce the load against which the bone marrow was working, instead of stimulating the marrow to make greater efforts.

THE ARNETH COUNT IN PROGNOSIS.

The following remarks only arise out of what has gone before in this thesis. As I have no actual experience of the use of the Arneth Count in disease, my suggestions are only theoretical.

Arneth claims that the degree of the shift to the left indicates the degree of the patient's resistance. The various graphs illustrating the shift to the left show that it is parallel to the degree of leucocytosis/
leucocytosis except during the period of leucopenia.

An isolated count, taken at the beginning of a leuco-
cytosis might show only a slight shift, but to give
a good prognosis on that would be erroneous as the
patient's troubles would be all to come.

An isolated count at the beginning of a fall in
leucocytosis would show a marked shift to the left
and if this were to prompt a bad prognosis, the
opinion would again be erroneous. Such isolated
counts only indicate that the bone-marrow is or has
recently been active.

In an acute condition a succession of counts
would show whether the bone-marrow was increasing or
decreasing its efforts. But an ordinary white cell
count would show that with greater accuracy, except
in those cases in which no great increase of leucocytes
occurred. One of my cases gives an instance of this.
In table III the total count at 3.10 p.m. was slightly
greater than that which was found at 4.20 p.m.
I thought that the height of the leucocytosis was over,
but a count done at 7 p.m. showed I was wrong.
The Arneth count at 4.20 p.m. showed a greater shift
to the left than that at 3.10 p.m. I did not appreciate
the significance of this at the time and made no dif-
ferential count in the 7 p.m. film.

In conditions like chronic tubercular cases
Arneth counts are, as one would expect, very valuable.
In/
In these cases the leucocyte increase is slight or absent. An Arneth Count would show whether new cells were being produced. Arneth claims that a shift to the left indicates the patient's power of resistance. In a sense it does, because it shows in these cases that though the bone marrow is active the number of leucocytes is not increasing. Earlier in this part of the thesis I have tried to show that this means that the cells are being expended as fast or faster than they are being produced. Hence if successive counts are made, with an interval of a few days between them, an increase of the dislocation to the left would be a bad sign. A decrease would be a good sign.

Arneth states that the younger cells are less able to combat infection than the old and that therefore a shift to the left indicates the patient's power of resistance. The conclusion seems correct, but I am not so confident about the reason alleged. My figures seem to suggest that the young cells must be quite efficient. For if every leucocytosis is like that which is produced after peptone, (and this seems likely) then, if young cells could not combat infection the work would have to be done by a diminishing number of old ones. More counts need to be done in series in a large number of different conditions before a definite opinion can be formed on this point.

MONONUCLEARS.
MONONUCLEARS.

The work I have done was for the purpose of examining the neutrophil variations, and I am not prepared to hazard any opinion with regard to the mononuclears. And yet their variations are so constant that I feel that they deserve much more study. The gradual decrease in numbers during the growth of a neutrophil leucocytosis suggests:

(1) That mononuclears are destroyed or redistributed in the same manner as the neutrophils.

(2) That their regeneration is not so rapid or not so necessary as the neutrophils. This is in agreement with Carnegie Dickson's findings that the bone marrow reactions specialize in particular types of cells though reactions affecting one class to the exclusion of all others is rare.

The increase of mononuclears during the fall of a neutrophil leucocytosis suggests that these cells have some function in connection with reconstruction. They may be scavengers. These are only tentative hypotheses and are not settled opinions. The data are insufficient. In dealing with the neutrophils the observations of others were able to fill up the deficiencies in my own, but this has not been the case with regard to the mononuclears.

Some explanation is necessary in connection with the/
the sudden marked mononuclear increase at the height of the leucocytosis in Graph II, Table II. In this case, as in all the others, I had duplicate films, but in neither set had I succeeded in getting the granules well stained. In other films, from this and other patients, neutrophil promyelocytes were seen. They were few in number and did not affect the percentages to any material extent. It is possible that in this case an unusual increase had occurred and that owing to the staining the neutrophil promyelocytes could not be distinguished from lymphocytes. It is the only explanation that I can offer.

Cabot has published the records of a few cases in which lymphocytosis seems to have taken the place of a neutrophil leucocytosis. But I do not think his findings have a bearing on this case, in which the increase of lymphocytes apparently only existed for an hour or two.

The variations in the numbers of mononuclears need more study.
SUMMARY.

(1) In certain cases of Rheumatoid Arthritis which were being treated by intravenous peptone injections, total and differential leucocyte counts and Arneth counts were made in series.

(2) These observations showed:

(a) An initial Leucopenia, which was succeeded by

(b) A Neutrophil Leucocytosis, which showed

(c) A shift to the left in Arneth's Count.

(d) The Mononuclear leucocytes showed a constant variation in numbers.

(3) Each of these findings has been compared with the published work of other observers.

(4) Arneth's claim that his classification divides the polymorphs in accordance with their ages is discussed and found correct.

(5) The Leucopenia is due to a redistribution or destruction of white blood corpuscles or a combination of the two processes.

(6) The same processes continue throughout the leucocytosis which really commences during the leucopenia. The numbers of leucocytes in the peripheral blood only represent a fraction of the numbers/
numbers which are produced by the bone marrow. Large numbers of leucocytes are used up in the process of attaining immunity against the peptone. These do not appear in the peripheral blood stream and so are not counted.

(7) Certain practical suggestions are offered as a result of this.

(8) Comments are offered on the use of Arneth's classification as an aid to prognosis.

(9) The variations in numbers of the mononuclear cells has been briefly discussed.
REFERENCES.


