STUDIES ON GLANDULAR FEVER (DRUESENFIEBER PFEIFFER) WITH LYMPHOID REACTION

Report of the First Cases from the Tropics

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History

Though Filatow mentioned a peculiar non-inflammatory enlargement of lymph glands in children it was not until Pfeiffer that this clinical entity of lymph adenopathy was described as “Druesenfieber” and well defined. A number of papers were published during the following years all picturing with considerable detail a febrile and apparently infectious condition.
with enlargement of the lymphatic nodes and often the spleen also. None of the early references in literature, however, allude to the blood-picture.

In 1907 Tuerk described 3 cases with adenopathy and a blood-picture strongly resembling lymphatic leukemia but with recovery. Since that time considerable interest has focussed on these febrile conditions where the differential white cell count shows rather the picture of lymphatic leukemia and where a general enlargement of lymph glands is present. The striking difference to leukemia, however, is the complete recovery, no death reported so far.

Since Sprunt and Evans—though they do not mention the painstaking endeavours of these early authors—a general conception has gained foothold to consider this symptom complex as a whole and to include as identical the observations described by Pfeiffer and Tuerk, as long as the etiologic agent remains unknown and, consequently, the postulate of Koch cannot be established.

A considerable amount of evidence points to the existence of rather clear cut, uniform clinical features with typical lymphatic leukemia-like changes in the white blood-picture sufficient to warrant the adoption of a distinct clinical entity. In setting apart the typical cases of "glandular fever with lymphoid reaction" from other similar clinical features we are doing so with the idea of further study and research. It must be borne in mind, however, that a number of individual cases will always remain questionable as to their classification in this column or their exclusion therefrom, pending the settlement of the question of a disease sui generis, i.e. a nosologic entity, or a peculiar lymphoid reaction of the individual toward one or several "Noxes."

This major problem will be dealt with in this paper based on studies of our own cases as well as those in recent medical literature. The outcome will touch and, eventually, upset our present conception of lymphoid reactions and leukemia, this dread disease.

Nomenclature

Considerable confusion exists in literature as to the different terms of this clinical entity. It is nowadays generally conceded that Pfeiffer's "Druesenfieber" and Tuerk's "sublympho-phaemische Lymphomatose" are one and the same condition.
Glandular Fever

It is beyond the scope of this paper to discuss in detail the different views of clinicians who have made their contributions to this material elsewhere in the literature.

For the sake of avoiding any misunderstanding and in order to eliminate unnecessary designations of the same clinical entity, priority should be given to the first authors. It is unfortunate that Pfeiffer's term does not call particular attention to the lymphocytotic blood-picture. It seems to us that for this reason the designation of "Infectious Mononucleosis" suggested by Sprunt and Evans would be more accurate were it not for the entirely misleading word "mononucleosis," as this expression suggests an increase of monocytes. The question of sharp distinction between monocytes and lymphocytes which aroused considerable discussion in European literature has, quite unduly, failed to attract sufficient notice in the American medical journals, notwithstanding the paramount importance of the monocytes for the clinician and practitioner particularly in the tropics. In a further section something will be said about this matter.

Other designations in current medical papers comprise: "acute lymphádenosis" (Downey and McKinlay) "lymphocytosis of sepsis" (Cabot), "acute lymphatic leukemia ending in recovery" (Hall), "acute lymphatic leukemia with apparent cure" (Ireland and Ruhrah), "acute benign lymphoblastosis" (Bloedorn and Houghton), "acute benign leukemia" (Cross), "akute, infektioese stammzellenvermehrung in blute mit heilung" (Hopmann), "l'adénolymphoïdite aiguë bénigne avec hyper-leucocytose modérée et forte mononucléose" (Chevalier).

German authors like Deussing and W. Schultz, whose contributions to this difficult problem are outstanding, dissented for some time from this conception of a clinical entity and considered the associated angina as an essential part. This was adhered to until further research (E. Schwarz) proved with high probability the identity of "Glandular Fever (Pfeiffer)," "Infectious Mononucleosis (Sprunt and Evans)" and "Angina mit lymphatischer reaktion (Deussing)" or "Monozytenangina (Schultz)" respectively. In a more recent paper, however, Schultz abandons his first term "Monozytenangina" but still emphasizes the occasional inflammation of the fauces in his "Plasmazellulaere-lymphoidzellige Angina."
Definition

Glandular fever with lymphoid reaction is a disease of the fixed lymphatic tissue with clinical symptoms of fever, adenopathy and increase of lymphoid cells in the peripheral blood stream. Mostly, a number of lymph nodes are involved, though occasionally the involvement of a single group may be paramount. The relative and the absolute number of lymphatic blood cells is more or less increased. The total number of the white blood cells is normal or moderately increased. The character of the lymphoid elements however, may be most unusual showing quite bizarre and often totally immature forms which suggest a leukemic condition alone, apart from the increased number of lymphoid cells. The clinical course, invariably ending in recovery with the unimpaired of the bone-marrow which still responds to certain stimulations with the usual increase in granulocytes, distinguishes the disease from leukemia.

Observations made on the mode of infection and the occurrence of epidemics suggest the infectious nature of this disease beyond reasonable doubt.

Our first case of glandular fever with lymphoid reaction resembled in its detection and its surrounding circumstances surprisingly the first case of Tuerk which started a new era. Like Tuerk we felt surprised and alarmed to find a leukemic-like blood-picture with quite atypical and, presumably, unripe lymphoid elements. Like Tuerk also we considered the prognosis as most pessimistic but had to correct ourselves later.

Report of Cases

Case 1. *Girl L. H., 4 years old, American, never seriously ill before. No history of serum or foreign protein injection. Since about ½ year the child had occasional intermittent fever up to 39°C. (about 102.2°F.), without other clinical symptoms except a very few convulsions. The reflexes and peripheral nerves had been normal and no paretic signs

*The author diagnosed this case and made the blood studies only as a consultant. Thanks are due to the attending physicians, Dr. Margarete Hasselmann-Kahlert and Dr. Lindsay Z. Fletcher, who called upon the author for the hematological examinations and were kind enough to help in preparing the clinical report of this case.
observed. Blood was repeatedly negative for malaria. Nevertheless quinine was given over a long period in the daily amount of about 5 grains but without any effect.

On February 22nd, 1930, the girl was admitted to the hospital on account of high fever and a disseminated rash all over the body. Itching was very pronounced. The rash consisted of papular efflorescences but slightly elevated above the surface of the skin. The size of these papules varied from that of a pinhead to the size of a dime though most of them were about the size of a pea. The colour of these micropapular exanthematous spots was a very bright red strongly resembling the colour of scarlatina though in marked contrast to scarlet fever no confluence could be found, but all efflorescences remained distinctly separated from each other. Practically the entire skin of the body was affected. The mucous membranes in the mouth and the fauces appeared bright red.

The blood-picture revealed a most striking increase in mononuclear elements as shown in the following table.

<table>
<thead>
<tr>
<th></th>
<th>February, 22nd.</th>
<th>24th.</th>
<th>March, 13th.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total count of leucocytes</td>
<td>12,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of granulocytes excluding eosinophiles</td>
<td>14</td>
<td>15.5</td>
<td>78</td>
</tr>
<tr>
<td>Percentage of lymphoid blood cells excluding true monocytes</td>
<td>84</td>
<td>82</td>
<td>22</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Non-segmented polymorphonuclears</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Segmented polymorphonuclears</td>
<td>10</td>
<td>9.5</td>
<td>76</td>
</tr>
<tr>
<td>Eosinophiles</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Basophiles</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Monocytes</td>
<td>1</td>
<td>1.5</td>
<td>0</td>
</tr>
<tr>
<td>Small lymphocytes</td>
<td>18.5</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Large lymphocytes</td>
<td>5.5</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Plasma cells</td>
<td>1</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>&quot;Atypical lymphoid cells&quot;</td>
<td>55</td>
<td>56.5</td>
<td>1</td>
</tr>
<tr>
<td>&quot;Smudged&quot; lymphocytes (&quot;Kernschatten&quot;)</td>
<td>9</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

Liver and spleen were considerably enlarged, the latter reaching to the umbilicus. The lymphatic nodes of the neck, axilla and elbow, under the jaw and in inguinal region were all much swollen but indolent. No other physical symptoms could be found. Soreness of the throat or angina was never noticed except the already mentioned enanthem of the mucous membranes. The tonsils were big but without any sign of pseudo-membranes, ulcerations or pus-pockets.
A few days later, however, fever set in again. Three grains of quinine had been administered at bedtime the day before, March 12th. The following day the child was seen with convulsions of the clonic type lasting up to 15 minutes. Fever up to 39.5°C. (103°F.) was present as shown in chart (figure 2). At the same time a micropapular rash of the same appearance was observed but not quite so extensive and not of such a bright red colour as before. The rash subsided after 2 days and defervescence set in.
Glandular Fever

It was most noteworthy that the white cells were, this time, normal in appearance and percentage as shown in table 1.

The girl was taken a few weeks later to the United States and returned to the Philippines some months ago. No other attack of glandular fever with lymphoid reaction recurred. The grandmother, however, became ill at about the same time as the child reached the U. S. with "acute leukemia" as the parents told us, but recovered after X-Ray treatment of the spleen. In view of this scant information we have to refrain from discussing the possibility that this might have been lymphoid reaction also. In this event the question of a hereditary disposition for lymphoid reactions might naturally arise.

Discussion

The occurrence of a rash during fever and following twice at short intervals the administration of quinine, must, necessarily, prima vista, point towards the drug as the possible cause. The appearance of skin eruptions, however, after 4 weeks continuous medication would be most unusual. In the presence of all other characteristics of glandular fever with lymphoid reaction it would be more reasonable to consider the rash as that frequently observed in the course of this illness. But even so, we feel inclined to admit the quinine as the possible though not probable cause for the second eruption for lack of any other plausible explanation. The first illness, even if preceded by quinine medication, must be diagnosed as true "glandular fever with lymphoid reaction" on account of the uniform adenopathy, including enlargement of the liver and spleen, the typical increase of most bizarre and unripe mononuclear blood elements and the entire clinical course followed by restitutio ad integrum. The absence of tonsillitis or any signs of Plaut-Vincent's angina is of particular significance and, as will be discussed in a following section in conformity with other authors.

Since the white blood-picture did not show any increase of lymphoid cells during the recurrence of fever and papular skin eruptions, the second attack cannot be reasonably considered as a relapse. We refrain from a definite diagnosis of quinine idiosyncrasy—though it would be an acquired one—or one of these climatic fevers which cannot so far be properly classified.

Quinine in Glandular Fever

Only a few references could be found by us to quinine in glandular fever. Glanzmann gave chininum tannicum success-
fully in the case of a 2 year old boy with glandular fever for the diarrheic condition:

"On May 15, 1929 a 2 year old boy became sick with 40° C. fever and continued severe vomiting. The stool was green like grass. I found upon examination a rubeola-like rash of slightly pinkish macules over the head and trunk. Granular conjunctivitis on the right eye. The posterior cervical glands were tender, their size that of a bean. Later on the axillary and inguinal glands became involved, too. No splenomegaly. The gastro-intestinal symptoms cleared up in a few days after chininum tannicum and proper diet.

On July 11, 1929, I was called again to the boy. He had severe abdominal pains. The abdomen was slightly distended and tender. No signs of appendicitis. The blood picture pointed to a relapse of glandular fever of the abdominal type. Final recovery."

**TABLE 2.**

<table>
<thead>
<tr>
<th>Blood pictures</th>
<th>May 15th</th>
<th>May 23rd</th>
<th>July 11th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basophiles</td>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Eosinophiles</td>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Non-segmented polymorph</td>
<td></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Segmented polymorph</td>
<td></td>
<td>41</td>
<td>12</td>
</tr>
<tr>
<td>Large lymphocytes</td>
<td></td>
<td>23</td>
<td>40</td>
</tr>
<tr>
<td>&quot;Plasma-cell-like&quot;</td>
<td></td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Small lymphocytes</td>
<td></td>
<td>15</td>
<td>44</td>
</tr>
<tr>
<td>Large monocytes</td>
<td></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Monocytoides</td>
<td></td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Plasma cells</td>
<td></td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

The same author gave quinine suppositories in a case which will be mentioned later on account of its striking similarity to so-called "Monozytenangina (Schultz)" during a relapse followed by the typical polymorphonucleosis at a time when a lymphatic gland became suppurative.

**Case 2.** Clinical and hematological observations made on our first case led to the discovery of a second case a few months later.

A 28 year old American male who was under treatment for prostatitis following Neisserian infection was complaining of stomach and gas pains after intravenous injections of gonorrhoeal vaccine. X-Ray examinations both by fluoroscope and series of pictures revealed no pathological changes except a pyloric spasm disappearing after atropine.

About the middle of June slight fever with general malaise set in. The fever never reached more than 38.5° C. (101.3° F.) as shown in chart
Nausea and occasionally vomiting were the chief complaints. After a few days slight adenopathy of the axillary lymph glands with marked tenderness was noticed. The blood picture showed a total white cell count of 5800 with very pronounced increase in mononuclear elements up to 78 per cent as will be shown in table 3. The majority of these cells were typical small lymphocytes. Atypical lymphoid elements were few, only 8.5 per cent. Quite a number of lymphocytes, between 10 and 12 per cent, were “smudged.” They could not be properly classified owing to the fact that the continuity of the cytoplasm was broken down and the nuclei only recognizable by their dark violet stained chromatin. This phenomenon, as is generally known, is only occasionally observed in ordinary smears on glass slides near the edges of the blood film. These so-called “Kernschtatten” occur in about the same percentage as broken down granulocytes. It is, however, most unusual in those blood films made on cover glasses as will be described in the section on technique. If this change occurs in the middle of a thin smear properly made after the cover glass method it invariably means unripeness of the corresponding lymphocytes.

In both of our cases, this comparatively high amount of over 10 per cent “smudged” lymphocytes is most noteworthy. We are surprised, indeed, that only Tuerk and Sprunt and Evans have particularly stressed this phenomenon.

Recovery was complete and quick in the course of one week. The dominating blood changes are given in table 3.

In these two cases we did not find any particular increase in the percentage of the small lymphocytes parallel to convalescence as found by Deussing in his case.
Table 3.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total count of erythrocytes</td>
<td>4,200,000</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total count of leucocytes</td>
<td>5,800</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Percentage of granulocytes excluding eosinophiles</td>
<td>18</td>
<td>22</td>
<td>50</td>
</tr>
<tr>
<td>Percentage of lymphoid cells excl. true monocytes</td>
<td>77.5</td>
<td>72.5</td>
<td>44.5</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Non-segmented polymorphonuclears</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Segmentated polymorphonuclears</td>
<td>17</td>
<td>21</td>
<td>48</td>
</tr>
<tr>
<td>Eosinophiles</td>
<td>2</td>
<td>2.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Basophiles</td>
<td>0</td>
<td>0</td>
<td>1.2</td>
</tr>
<tr>
<td>Monocytes</td>
<td>2.5</td>
<td>3</td>
<td>2.8</td>
</tr>
<tr>
<td>Small lymphocytes</td>
<td>48</td>
<td>41.5</td>
<td>33.5</td>
</tr>
<tr>
<td>Large lymphocytes</td>
<td>9</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Plasma cells</td>
<td>2</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>&quot;Atypical lymphoid cells&quot;</td>
<td>8.5</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>&quot;Smudged&quot; lymphocytes (&quot;Kernschatten&quot;)</td>
<td>10</td>
<td>12</td>
<td>3</td>
</tr>
</tbody>
</table>

Case 3. Our third case was a 3 year old American boy. No history of any illness except dengue. For a few days he had had swollen lymphatic glands in the right posterior cervical region. At the same time the fauces and tonsils showed a slight redness but without any pseudomembranes or ulcerations whatever. Temperature 37.4°C. (about 99.3°F.).

About 1 week later the boy had slight temperatures which never ran more than 38.1°C. (about 101.5°F.). He started to complain of pains in the inguinal region. At this time the redness in the pharynx had nearly completely disappeared but the lymph glands in the neck and inguinal region were all slightly tender, enlarged to the size of a small cherry. The axillary and epitrochlear lymphatic glands were likewise enlarged but indolent. All lymph nodes remained distinctly separated from each other and no confluency could be felt among the different nodes in the respective regions. The spleen could be palpated but seemed not particularly involved. The blood picture on February, 2nd, 1931 is shown in table 4.

Two days later the temperature was only 36.8°C. (about 98.3°F.) and the boy started to cough. These spells reminded one of whooping-cough though they were not typical. Examination of the lungs revealed but a very few bronchial rales hardly in proportion to the severity of the cough.
Glandular Fever

The adenopathy subsided very slowly and remained present for weeks. A dry spasmodic cough, likewise, persisted for some weeks. Otherwise convalescence was uneventful.

**Table 4.**

<table>
<thead>
<tr>
<th>Blood cells</th>
<th>February, 2nd</th>
<th>February, 16th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total count of erythrocytes</td>
<td>4,820,000</td>
<td>—</td>
</tr>
<tr>
<td>Total count of leucocytes</td>
<td>11,700</td>
<td>—</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>0 %</td>
<td>0,5 %</td>
</tr>
<tr>
<td>Non-segmented polymorphonuclears</td>
<td>1</td>
<td>2,5</td>
</tr>
<tr>
<td>Segmented polymorphonuclears</td>
<td>20,5</td>
<td>30,5</td>
</tr>
<tr>
<td>Eosinophiles</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Basophiles</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Monocytes</td>
<td>3</td>
<td>3,5</td>
</tr>
<tr>
<td>Large lymphocytes</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Small lymphocytes</td>
<td>42,5</td>
<td>43,5</td>
</tr>
<tr>
<td>Plasma cells</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>&quot;Atypical lymphoid cells&quot;</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>&quot;Smudged&quot; lymphocytes (&quot;Kernschatten&quot;)</td>
<td>7</td>
<td>3,5</td>
</tr>
<tr>
<td>Percentage of granulocytes excluding eosinophiles</td>
<td>22,5</td>
<td>33,5</td>
</tr>
<tr>
<td>Percentage of lymphoid cells excl. true monocytes</td>
<td>69,5</td>
<td>55</td>
</tr>
</tbody>
</table>

In this latter case a marked increase in the proportion of small, ripe lymphocytes to all lymphoid blood cells could be noticed parallel with convalescence as described by Deussing in his cases.

**Symptomatology and Clinical Characteristics**

Reviewing the numerous papers in current literature dealing with the clinical aspects at the beginning of the illness it seems to us rather unnecessary and may even cause confusion if this one time happily accepted clinical entity should be divided up into several forms of onset. Suffice it to state that the clinical characteristics are fever, general enlargement of lymphatic glands including, mostly, splenomegaly, lymphocytosis and, though not necessarily, a sore throat.
The onset is associated with the common symptoms of an infectious disease. Prodromal symptoms may or may not occur. Fever sets in often rather suddenly, occasionally accompanied by chills. Pyrexia is either of the septic type or more or less continuous. The fever may last from a few days to 3 weeks; it reaches, generally, not more than 103°F. (39.5°C.). Defervescence is by lysis rather than by crisis. *Herpes labialis* occurs not infrequently.

The pulse rate varies from normal up to 110. The blood-pressure seems not to be particularly affected. The amplitude between the systolic and the diastolic minimum remains unchanged without any sign of myocardial insufficiency. Longcope found frequent premature ventricular contractions in a case of a 12 year old girl with a history of frequent attacks of febrile tonsilitis but no previous evidence of rheumatic fever.

In the typical cases the patients complain of headache, general malaise, sore throat, occasionally of abdominal pains and nausea. This complaint was paramount in our second case.

*Rhinitis sicca* may be one of the early symptoms. If deeper parts of the respiratory tract are affected, bronchitis with even whooping-cough-like attacks may result, as found in our third case.

Conjunctivitis with marked swelling of the follicles has been described. Glanzmann claims this to be an early sign which enabled him to make a diagnosis at the onset of the high fever before even any adenopathy could be detected.

Usually the lymphatic glands become enlarged and tender during the first week of the disease. It is generally agreed that no relationship exists whatsoever between the type and course of the fever and the degree of lymphadenopathy. The lymph nodes remain palpable in most cases for a considerable time after recovery. Periodical appearance followed by disappearance has been recorded. The tenderness of the lymph nodes may subside long before the normal size is again reached.

Glanzmann claims that fever and adenopathy mostly start together, but that adenopathy may even anticipate the febrile
Glandular Fever

stage for weeks. Concerning the usual conception of fever followed by adenopathy he says:

There are, however, according to my observations cases, also where the lymph nodes do not become distinctly apparent until some days after the onset of fever.

Some observers point out that there is a predilection to the involvement of the fixed lymphatic tissue in certain regions. Very often the adenopathy starts in the left cervical region. Lehndorff stresses the fact that not the superficial but the deep lymph nodes, under the sternocleidomastoid muscle, are mainly affected, and that other groups become involved later. In our second case the tenderness of the axillary lymph nodes was the dominating feature though by palpation they seemed but little enlarged. However, Baldridge et al, found glands that were removed always larger than had been anticipated. This is very likely because of their rather soft consistency.

Glanzmann stresses the point that the lymphatic nodes are seldom confluent but remain separated from each other even if enlarged. We could confirm this observation in all our cases also.

The fact that the different observers in current medical literature differ somewhat in their opinion over those lymph glands which get principally involved seems to point out that nearly any lymphatic group can be first and chiefly affected.

Considering the affection of the whole fixed lymphatic tissue we agree with Lehndorff that perhaps quite a number of cases in medical literature with retrosternal pains and pseudoappendicitis, “grippe with lymphatic reaction” and others might be included in this class. It is only just to presume that the tracheo-bronchial and mesenteric lymph nodes and even those of the hepatic hilus may also become involved. This would account for the abdominal symptoms.

Tidy and Daniel have described the case of a 9 year old child with fever and dullness over both lower lobes of the lungs together with intensive pains in the right upper abdomen. The younger brother suddenly got adenopathy of the left cervical lymphatic nodes which made the authors believe that the girl's illness was really an affection of bronchial nodes around the hilus. Since then, Feer and others have recorded cases with
similar symptoms of broncho-pneumonia associated with increased total white blood cells and lymphocytosis up to 72 per cent.

It is generally conceded that attacks of whooping-cough are caused by the involvement of bronchial and peribronchial lymphatic nodes, though conclusive evidence, either through X-ray or autopsy, is still lacking. As will be noted in another section, pertussis does not in general show such a pronounced increase of lymphocytes. Furthermore, the lymphocytoid elements in glandular fever may be of distinctly unripe character with abnormal features.

However, as Czerny pointed out, whooping-cough belongs to these infections with a marked lymphocytoid reaction. The lymphotropism of the *B. pertussis* is very characteristic though no generalized adenopathy results. The lymphocytosis caused by whooping-cough, though mostly only moderate in character and degree, may occasionally be identical with the type met with in glandular fever as in the case of a 5 month old baby with pneumonia after whooping-cough described by M. Frank.

Pfeiffer has mentioned the presence of abdominal pains mostly between the umbilicus and symphysis pubis. He considered the swelling of mesenteric lymph nodes as the cause. Spasmodic attacks might occur at the beginning of the disease with regular intervals. Liver enlargement and splenomegaly are mostly present. These abdominal symptoms may be confused with appendicitis. However, the enlargement of liver and spleen together with the lack of acute abdominal signs, the only slightly increased pulse rate and its good quality will guide the careful examiner.

The abdominal form is accompanied in a number of cases by diarrheic conditions which are, however, free from any inflammatory process and are easily distinguishable from typhoid fever or other enteritic conditions.

Jaundice in the course of glandular fever with infectious mononucleosis was first described by Markey and Wackefield and confirmed by other observers. Swelling of lymphatic glands in the neighbourhood of the hepatic hilus is considered to be responsible for this icterus which would be then of the obstructive form. The strongly positive reaction of urobilinogen
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in the urine, on the other hand, shows that some kind of a hepatotropia with impairment of the proper function must also exist.

Splenomegaly is generally present. The enlargement of the spleen is in some instances quite characteristically recognised by the patients as griping or stinging sensations, similar to malaria. The percentage of hepatic enlargement differs among the authors. Whereas some do not even mention it, others like E. Glanzmann found it in from 1/3 to 1/2 of his cases.

The spleen, may or may not remain palpable for quite some time after clinical recovery. Baldridge et al, report a persistent splenomegaly even up to 7 years.

Benign nephritis with considerable hematuria has been observed in a number of cases. Hislop and Tidy and Daniel estimate its frequency at about 6 per cent. The type of nephritis judged by the clinical course seems to be an acute glomerulo-nephritis, though no autopsy findings are recorded in literature owing to the consistent recovery of the patients.

The most striking feature in glandular fever with lymphoid reaction is the marked increase in percentage of mononuclear blood elements. The type and proper designation of these cells will be fully discussed in a later section.

The granulocytes show nothing unusual. The polymorphonuclear leucocytes, the eosinophiles and the basophiles are normal both in appearance and relative number. Eosinophiles may or may not be present during the height of the fever.

The erythropoetic system shows, likewise, no changes. The red blood corpuscles are normal in number, amount of hemoglobin and morphological appearance.

Though at the onset of the illness a passing increase of granulocytes may be observed, the percentage of lymphoid cells is soon more or less increased. The systemic reaction on the part of the lymphatic tissues is so constant and so pronounced that it suggests a highly lymphotropic virus whatever nature the virus may yet have.

There is no relationship between the clinical symptoms and the course of the disease on one hand and the type of mononuclear elements on the other. Neither is the total amount
of leucocytes of diagnostic value. Cases recorded in current medical literature differ widely in the total number of white blood cells and type of leucocytes with but one nucleus.

The lymphocytosis disappears only gradually after defervescence. Numerous cases are mentioned where after several years a marked lymphocytosis was still present. Abnormal lymphoid cells—which will be amply discussed in a later section—may likewise remain in the peripheral blood even for years. (Baldridge et al.).

Skin symptoms have been described in great variety from rubeola-like rash with typical erythematous mottling to scarlatiniform erythema and urticarial wheals and even pustules. The general conception seems to be that the rash in glandular fever, if present, resembles German measles in the majority of the cases. It is to be deplored that in a number of descriptions the proper dermatological designation is not adhered to. Glanzmann, whose work is, perhaps, one of the most painstaking in other respects, speaks of "macules slightly elevated." For the sake of proper recognition and to facilitate the diagnosis and the understanding of following observers, a spade should be called a spade and a papule a papule. Inflammatory changes in the corium of more than merely hyperemic congestion, but with cell infiltration to such an extent as to raise the surface of the skin thus giving the clinical impression of an elevated area deserve the proper term of "papules."

Moderate hemorrhage into the mucous membranes and skin has been occasionally noticed (Downey and McKinlay). Nelken examined a papular and hemorrhagic exanthem histologically and found inflammatory infiltration of polymorphonuclear and round cells together with adventitia cells in the papillae. Perivascular infiltration showed a fair number of polymorphonuclear cells besides round cells and the usual adventitia elements. The histological picture, therefore, is not purely lymphoma-like, but has to be considered as a true inflammatory one.

The clinical course of the disease is sometimes complicated by relapses. Scheer speaks of fever with weekly periods. Glanzmann names the 9th to the 16th, the 13th to the 14th and the 19th to the 24th day. Since Baldridge, Rohner and Hansmann, Chevalier and Glanzmann have observed relapses
even up to several times the question of resistance arises. Very little attention, so far, has been given to this problem in current literature. Some authors claim that a chronic infection occurs. It was Lehnhartz who first pointed out the possibility of the disease developing into chronic lymphatic leukemia.

This, however, can be discussed only on the understanding that leukemia is caused by some kind of an infection. It is not in the scope of this paper to discuss this fundamental question which is perhaps one of the most interesting ones in the diseases of the blood system. It is noteworthy that Naegeli, hitherto known as a dogmatic defender of the theory that leukemia must be considered as a disease of the organism itself (“Systemerkrankung”) without any infectious agents whatsoever, has recently published through his assistant Gloor the report of a case of myeloblastic leukemia ending in *restitutio ad integrum* with the conclusion that this case does not fit in with his conception but seems to point to a possible infectious cause for leukemia.

Reports of recurrence after months and years as well as of repeated attacks during 3 consecutive years (Baldridge *et al.*) seem to prove that in these cases no resistance has developed. In view of our limited knowledge about this clinical entity we refrain from using the term immunity as this expression ought to be reserved for a disease entity with Koch's postulate experimentally established. These relapses, however, bring up again the question whether glandular fever is or is not related to leukemia.

At the present time, glandular fever has been classified as a clinical entity involving a well defined clinical, pathological and hematological symptom-complex. In the years to come, perhaps, as our knowledge of the lymphatic system, its diseases and their causative agents advances filling one more nosological gap, it may be decided to which disease entity “glandular fever with lymphoid reaction” belongs or if it is a distinct one of its own.

**Prognosis**

It is generally admitted that final recovery is always certain. Tidey and Morley mention 4 cases in literature with lethal outcome. Even these 4 cases, and especially one of them, are not
beyond doubt so far as the causal connection with glandular fever is concerned.

Quite another question and a problem still to solve is whether glandular fever is or is not a forerunner or only a mild form of lymphatic leukemia. As already mentioned Lenhartz pointed out this possibility. Still taken from another angle: if glandular fever and lymphatic leukemia are only the same response from the fixed lymphatic tissue and differ but in degree, then this would imply that deaths are recorded in lymphatic leukemia only.

A case of Glanzmann's points at least in this direction. A man 34 years old succumbed in 3 months to what for over two months was considered glandular fever. Not until 3 weeks before death had the blood picture changed to one which the author believed to be more typical of leukemia, accompanied by a gradual change for the worse in the general state.

A number of borderline cases with fatal ending remain uncertain, as their proper classification is doubtful. Strong resemblance to either classical leukemia or lymphadenoma may exist so that it seems unwise to adhere to any too sharp boundary line. Poynton and Moncrieff, therefore, start anew on the assumption that in their fatal cases infective processes produced reactions of a most unusual kind.

Epidemiology

Numerous papers are found in literature on glandular fever in epidemic forms. Since the mild cases remain often unrecognized by the patients themselves it is apparent that possibly many small epidemics have never come to our attention. The occurrence of epidemics in communities suggests the possibility of an infectious, perhaps of a contagious, agent. Observations made on an epidemic recently by Scheer seem to point that the possible virus is not air-borne but that the infection rather spreads from bed to bed.

The youngest case, 4 months old, seems to be that recorded by Schaeffer. Persons over 30 years are affected very seldom, if at all. This is construed by some observers as a sign that active lymphatic tissue with reactibility is an integral point. The larger epidemics, as far as known, seem to have been more
among males than females. Medical students make up a comparatively large contingent. It is our belief, however, that this will be easily explained by the fuller knowledge and more careful observation which medical people employ.

The incubation period seems to be between 5 and 9 days, even though 2—3 weeks are occasionally mentioned. Such long periods might, perhaps, indicate that the infectious stage lasts for a longer time and also that it is not always the first exposure that necessarily results in transmitting the disease.

The largest epidemic outbreak recorded so far seems to be in America with over 300 cases, described by Guthrie and Pessel. In Europe, Scheer reports an epidemic of 45 cases in a “Kinderheim.” It is difficult to explain the discrepancy in observations made on this material in the United States and in Europe. Some believe that the different type of education with its numerous “colleges” in America would be sufficient to explain the more numerous reports of epidemic forms in the United States. With the careful medical supervision of school children as exercised by European physicians however larger outbreaks or even frequent sporadic cases would, doubtless, not have remained unnoticed. We refrain from offering a definite and plausible explanation, but want to remind the medical fraternity that the old *Genius Epidemicus*—at one time scoffed at and banished under the shining glamour and unrestrained worship of bacteriology, parasitology and hygiene—rose again from its ashes as modern Loimology teaching the dominating importance of the “Seuchengrund” (soil of contagion) (Sticker) for the reasonable explanation of epidemic waves and periods of contagious spread, otherwise inexplicable by laboratory investigation alone.

The fact, however, remains that glandular fever in epidemic form has been rarely observed in Europe to such extent as in the United States. This, undoubtedly, accounts for the fact that European authors have focussed their interest rather upon the accompanying pharyngitis than upon the contagious peculiarity of the disease and the mononuclear phase in its blood morphology. For a long time this onesided conception threw the limelight on to the “angina” and gave to the all-important lymphocytoid reaction its share only as an attribute (“Monozytenangina” Schultz). Since the work of Evans and Sprunt, however, it
has been generally conceded that these features belong to the same distinct disease entity.

It is a noteworthy feature that the percentage of mononuclear elements among the white blood cells averages considerably higher in the recorded sporadic cases than in the recorded epidemic cases. We venture to say that probably this difference is explained by the "Fehler der kleinen Zahl" (error of small numbers).

Modus of Infection

As already pointed out the modus of infection might be through the upper respiratory tract on account of its early implication and the predominance of adenopathy in the cervical region. Chevalier and Glanzmann however report a striking adenopathy of the inguinal lymph nodes which might point to the mucous membranes of the genital organs as a possible portal of entry.

The susceptibility of one and the same person seems to vary in the same way as for instance in the case of rubeola as found by M. Hasselmann-Kahlert. The first exposure might not necessarily result in infection but a second contact might be followed by it.

Infection through the intestines is claimed by some observers to be not infrequent, and they attribute to this route of infection the early involvement chiefly of the left cervical lymph nodes to which the ductus thoracicus may carry first the causative agent from the bowels.

Pathology

Histological examination of swollen lymph nodes show a non-specific lymphadenitis.

Sprunt and Evans found congestion of the sinus with lymphoid cells, Downey and McKinlay hyperplasia of the follicles, Longcope a picture resembling Hodgkins disease, Hartwich catarrh of the sinus with hyperplasia.

This picture of a non-specific lymphadenitis hyperplastica is quite commonly encountered in any inflammatory process where products of metabolism from the inflamed area are carried away and are passing through the lymphatic nodes.
Bacteriological and serological blood examinations give no further evidence as to the cause of this disease.

**Blood Picture**

During the first week of the disease and coincident with the enlargement of the lymphatic glands the total amount of white cells is increased in the majority of cases. However, even a slight leucocytosis need not necessarily be present. The absolute increase of white blood cells may last from a few days to several weeks. This leucocytosis is due to both an absolute and relative increase of blood cells with but one nucleus and the corresponding decrease, both absolute and relative, too, of polymorphonuclear granulocytes. At the onset, however, a passing increase in polymorphonuclears may be present.

In a later section this most important question of proper classification and designation of the white cells with but one nucleus will be fully considered.

The highest percentage of lymphoid elements without regard to the date of the illness is reported by Ireland, Baetjer and Ruhrau with 97.5% lymphoid cells among a total number of 20,000 white blood cells. The highest total count is reported with 36,000 white cells of which 84% were lymphoid cells and 16% granulocytes in a case of P. E. W. Smith. On the other hand, Glanzmann observed a case with but 3,000 white cells of which 73% were lymphoid elements and 25% granulocytes.

The first author, Tuerk himself, directs particular attention to the fact that the lymphoid cells are exceedingly liable to break up (enorme Zerreisslichkeit) though the granulocytes are only very seldom broken in their cytoplasmatic continuity in the blood smear. In our 3 cases we met with this condition in 'about 10 per cent and record it in the column as "smudged lymphocytes." We are surprised that we could not find references to this in the literature since Tuerk's observation particularly mentioning this very noticeable fact, except by Sprunt and Evans.

With recovery the granular elements gradually increase with a corresponding reduction of mononuclear elements. Often, though not necessarily, the normal proportions of the different white cells are finally reached before the adenopathy has subsided.
Technique of Making and Staining Blood Smears

A properly made blood smear is indispensable for any kind of studies on blood pictures. In former papers (Hasselmann) the method giving the best percentage of the different cells equally distributed on a slide has been fully discussed. On the average it will be always a distinct advantage to employ the method of Naegeli in the use of cover glasses. A small droplet of blood is taken directly from the pricked finger (preferably from the dorsal side next to the nail) on a cover glass. By putting a second cover glass over, the droplet is allowed to spread between the two cover glasses which are quickly but gently removed. By examining this smear it will be invariably found that a more even distribution of the different blood elements has been obtained, compared with the usual spreading of a droplet on a glass slide by drawing or carrying the droplet along the edge of another slide. Though this latter procedure has the advantage of easier staining and transporting, and likewise, for photographing the thin blood smear specimen, the distribution of polymorphonuclears and lymphocytes is uneven and irregular. The difference in viscosity of these two important cell types causes the accumulation of the polymorphonuclears along the border of the smear whereas the lymphoid elements predominate in the central parts. By using the so-called Meander-field counting the error can be only partly corrected. Naegeli's cover-glass method avoids this interference of diverse viscosity through not allowing viscosity to interfere and a more even distribution of all types of white blood cells results. The disadvantage of the procedure is the more difficult handling of the thin and easily breakable cover glasses compared with the comparatively less fragile slides. For the usual routine examination, particularly if a thick blood film for malaria is made on the same slide, the common thin smear is sufficiently satisfactory. For detailed morphological studies on blood cells, however, the cover glass method is more accurate and superior to the slide.

The second imperative condition for proper classification of blood elements is the stain. In former publications (C. M. Hasselmann) the advantage of Giemsa stain has been stressed. We were never able to detect the details and finesses of protoplasm and nucleus with any of the other common stains.
Particularly in the tropics where climatic and water conditions are often highly unsatisfactory, Giemsa stain has proven to be superior to all other modifications. This, however, applies to the original Giemsa stain only obtained in the original bottles from Gruebler. We feel obliged to make this elaborate statement—even with the risk of being accused of advertising a certain manufactured brand—as this stain gave us the only reliable results in dealing with the delicate question into what group certain lymphoid blood cells could reasonably be included. All other stains—Wright, Wilson, Giemsa stain in other than the original brand from Gruebler—have not given the same satisfactory results.

The count of white blood cells is always made in total numbers and the percentage is given for each type. It is entirely unnecessary to add the total number of each type. We are at a loss to understand why figuring out of the absolute numbers of each leucocyte type could be considered of any importance, nor why their graphic curve should be claimed to show better the changes in blood pictures. As the absolute number of each type can only be obtained from the relative count, it is, indeed, only a matter of custom as how to read a chart, be it the presentation of blood cells, or, for example, of the body’s temperature. Nobody would dare to imply that any difference is to be found in charting this in Centigrade or in Fahrenheit. It is just the same in giving the blood pictures in percentage numbers of the different types, instead of complicating this routine, long since adopted by hematologists, and again dividing the total count by the percentage figures for the mere purpose of obtaining a new curve in a published chart. There is absolutely no need to sidetrack the old and proved methods of Pappenheim, Naegeli, Arneth, V. Schilling, a.o. The so-called “lymphocytic index” of Jones and Crocker is entirely misleading.

**Classification of so-called Atypical Lymphoid Blood Cells**

In recording our own blood pictures we chose to record in the first place the typical monocytes. We consider these as “typical” if they have a broad band of cytoplasm with distinctly dust-like azurophile granulation. The cytoplasm is slightly besophilic but with a grayish note. Frequently small vacuoles
and plasmosomes are encountered. There is never a perinuclear bright zone present. The nucleus has less chromatin than that of lymphocytes. Consequently, the nucleus of monocytes appears not very deeply stained, with rather irregular dispersion of chromatin. A rather eccentric position is typical. The outline of the nucleus varies very much, being oval, bean, kidney or horse-shoe shaped and even irregularly lobulated. The surface is never smooth but shows nuclear protrusions in more or less marked degree. If some of these features were not typical or others present which would interfere with the proper ranging of the cells in question as "monocytes," we preferred to include them as "atypical lymphoid cells." We have no grounds either to admit or dispute that in a number of instances some among them might still be "monocytes."

Typical lymphocytes show a clear, blue cytoplasm without any azurophilic granulation whatsoever but occasionally with a small number of larger azurophilic granules, not to be mixed up with the dust-like azurophilic granulation of the cytoplasm in monocytes. The lymphocytes show generally a marked bright perinuclear zone. The nucleus consists of dark stained chromatin which is made up of irregular bands and threads with a rather wavy appearance. The outline of the nuclei is rather uniform and round or slightly oval. The edges are smooth and not indented. Very typical is the proportion of nucleus to cytoplasm in so far, as the size of the nucleus in lymphocytes is relatively very large compared with the small amount of cytoplasm whereas in monocytes there is much less discrepancy. Consequently, the nucleus of lymphocytes appears very seldom to be eccentric but seems to have a more central position.

Plasma cells are recorded separately without discussing their close relationship to lymphocytes. They are still deeper stained than lymphocytes, both cytoplasm and nucleus. The latter shows fairly regular shaped dots of condensation of chromatin, giving a clock faced appearance. Plasma cells show a very marked bright and almost hyaline zone in the cytoplasm at one side of the nucleus. The outline of the latter may be round with often a slight notch. The pachychromatic structure contains condensed, dark angular blocks radiating from the center of the nucleus.
Typical "ATYPICAL LYMPHOID CELL" with a broad, blueish band of smooth, pale hyoplasm containing a few, large, azurophilic granules. The leptochromatic nucleus has the shape of a mushroom and a rather wavy appearance but still with irregular shaped dots of condensation of chromatin.

Two "smudged lymphocytes" ("Kernschatten") where the continuity of the cytoplasm is broken up. The two other cells are "atypical lymphoid cells" with an excentrically placed, leptochromatic nucleus. The shape, particularly of one of these cells, is quite bizarre.
Two typical lymphocytes of nearly normal appearance both in regard to the pachychromatic nucleus with the marked bright perinuclear zone and the clear blueish cytoplasm, show already a nucleus with a slight notch and a surface occasionally with a few nuclear protrusions.
The Dominance of Atypical Lymphoid Blood Elements, only with difficulty classified and placed in one of these common Groups, thus becomes Characteristic for "Glandular Fever with Lymphoid Reaction" as seen particularly in our first case.

We are in agreement with such early American observers as Longcope who not only states that these forms predominate but who simply distinguishes three different lymphoid blood elements:

(1) A small mononuclear leucocyte identical with the small lymphocyte seen in normal blood.

(2) Large mononuclear cells identical in appearance with the large mononuclear and transitional cells of normal blood.

(3) Mononuclear cells of a type not usually encountered in normal blood.

In this connection we desire to point out that in American literature on blood pictures the line between atypical large lymphocytes and monocytes is not always sharply drawn, in our opinion perhaps due to the impossibility of identifying the differences in Wright, Goodpasture or Wilson stained smears which are mostly used in America. In a number of cases there are no illustrations accompanying the papers. Consequently it is not possible to pass judgment on the mononuclear cells described. Furthermore, as has been already mentioned, the terms "mononucleosis" is most inconsistent and entirely misleading, for "mononuclears include myelocytes and nucleated younger forms of the red cells, as well as monocytes and lymphocytes. On the other hand, monocytes or transient cells with a nucleus distinctly divided into two fractions would lose their rightful places. The terms "mononuclears" and "mononucleosis," therefore, should be dropped and always be replaced by the accurate and proper terms "monocytes" and "lymphocytes," respectively, for the sake of avoiding any misunderstanding and false interpretation. This erroneous designation has already given rise to considerable misunderstanding which would have been avoided if proper and uniform terms had been accepted (H. P. Schenck and O. H. Perry, Pepper, W. Schultz and F. Mirich).
Not infrequently—well illustrated in our first case of glandular fever as will be seen in the accompanying microphotographs—a large percentage of lymphocytes are made up of almost all conceivable varieties of abnormal lymphoid elements. Indeed their type is frequently so atypical and bizarre as to make their identification presumptuous if not impossible. In view of the uncertainty of classifying these cells, as their origin is questionable, we have chosen the term “atypical lymphoid cells.” A number of these forms show an eccentrically placed nucleus and basophilic protoplasm though generally not quite so deeply stained as the stimulation form of Tuerk. The nuclei are sometimes notched or even horse-shoe-like. It is this bizarre appearance which resulted in confusion with monocytes and, indeed, there are quite a number of forms which even experienced hematologists will be always at a loss to classify beyond doubt.

A number of lymphocytes are typical “Rieder” forms with deeply indented nuclei. Tuerk, as already stated, stressed the fact that quite a number of lymphoid cells are exceedingly fragile, continuity of the cytoplasm being easily broken up. In one of our cases a large percentage of these highly fragile forms were encountered which look “dissolved” and smudged (so-called “Kernschatten”).

Naegeli speaks of “lymphoblastic plasma-cells.” This latter term, however, might be constructed as misleading as to their origin or incorrect and either excluding the other so far as the structure of the nucleus is concerned. Plasma cells, as is generally conceded, are either traced back to “Gewebewanderzellen” or are representing particular functional types of lymphocytes. Lymphoblasts show a very marked cloudy chromatin structure in the nucleus with only a few white or slightly bluish vacuoles, an appearance quite characteristic and not confusable with the compact dark nucleus of plasma cells in properly Giemsa-stained specimens.

The term “vascular endothelial cell” has been chosen by McJunkin. These atypical lymphocytes have, doubtless, many features in common with endothelial cells: the long shape, often with tailshaped extended protoplasm and the typical oval nucleus of fine chromatin structure. However, we do not feel sure that their endothelial nature is beyond reasonable doubt nor
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could other cells be reasonably included in this column though also not coming under the simple description of lymphocytes.

Deussing, one of the earliest German observers, points particularly to the plasma-cell-like appearance of a number of lymphocytes, apart from the typical plasma-cells, both as regards the dark staining quality of the cytoplasm and the satellite-like shape of the nucleus chromatin. In our cases, however, these features were not very noticeable.

We cannot approve the classification of “abnormal mononuclears” by Longcope as this term would prejudice the case and be misleading.

In order to simplify the classification of atypical lymphoid cells Schultz and Mirich suggest the adoption of the system of Arneth. Arneth classifies all mononuclear cells according to the shape and number of nuclei, holding that monocytes and transitional cells are nothing but later stages of the large lymphocytes. This means abandoning the trialistic standpoint of V. Schilling and others which, doubtless, has its merits and meets a number of hematological conditions which otherwise would conflict with certain principles of pathogenesis. Without entering into any discussion over this problem of general pathology as this is without our present scope, we must admit that the adoption of such a simple classification based mainly on morphological features of the nucleus and the number of nuclei in the mononuclear blood elements has unquestionable advantages. It must be recalled that Pappenheim, on the other hand, takes the opposite standpoint advocating that the monocytes are younger, somewhat indifferent stem cells, the antecedents of normal lymphocytes and with the possibility of developing either into the lymphatic or myelocytic stage.

The oxydase reaction is always, in these questionable atypical cells, negative. Furthermore this staining test alone where even typical monocytes may show no bluish or only a very faint colorization of the cytoplasmatic parts will never be considered by anybody familiar with finer blood studies as of imperative value in the differential diagnosis of the blood cells if the other features, as described before, are either lacking or confusing.

Supravital staining with neutral red and Janus green for the identification of the larger lymphoid cells has been strongly
advocated by J. A. McLean who claims that these cells are typical lymphoid cells ("lymphendotheliocytes") apparently formed by proliferation of the reticulo-endothelium of lymphatic vessels in glands and spleen. This is in perfect accord with all other reasonable explanations based on our present knowledge of this clinical entity. K. Lorentz found, however, that both neutral red with Janus green and brillant-resyl-blue will not give uniform results as the appearance and staining qualities of the respective granulations is vague and uncertain in otherwise typical cell types. This author considers the staining qualities of the granules dependent on their function and age and has warned against the over-estimation of this supravital staining method for drawing any definite conclusions in regard to the origin of mononuclear blood cells. As stated above, it seems more appropriate to admit courageously that a certain number of white blood cells, even in properly stained films, cannot be reasonably classified in these atypical blood pictures. We agree with the above mentioned hematologists, particularly with V. Schilling, that it is wise to include them in a special column. So long as the discussion as to whether the oxydase reaction is positive or negative even in true monocytes of normal blood pictures remains open, we are at a loss to understand why a questionable staining procedure should be regarded as a final appeal in this difficult question of classifying the atypical mononuclear cells of glandular fever. This applies to all modifications of the oxydase method. Even Baader, strongly advocating the non-lymphocyte descent of the mononuclear elements in the "Monozytenangina," admits:

"It must be, however, stated, that obviously regular transitions seem to exist from lymphocytes to monocytes in the oxydase treated preparation, just as like difficulties are met with in Giemsa stained films as to differentiating lymphocytes from monocytes."

It is not within the scope of this paper to discuss the difficult question as to the relationship of typical monocytes to lymphocytes, as encountered in normal blood pictures, or in other words the merits of the trialists and dualists concerning mononuclear blood elements. We want to direct attention, here, to the most striking pictures of all transient stages between simple lymphocytes and typical monocytes as given in the publication of Schultz and Mirich. We have seen like forms in perhaps even greater variety in our cases.
We see little value in overemphasising the possible detection of some true "myeloblasts" among these atypical lymphoid cells, nor do we detect the resemblance of the sometimes extremely fine net-work of the chromatin with nucleoli and distinct parachromatin to the immature, leptochromatic structure of those antecedents of the normal lymphatic cells. We also have seen among these atypical lymphoid cells various transitional forms to the coarse, pachychromatic ripe nucleus characteristic of lymphocytes in the peripheral blood stream.

Most of the authors with the possible exception of Downey and McKinlay stress the fact that the majority of the atypical lymphocytes show the above described features of immature, leptochromatic nuclei and a cytoplasm showing pale smooth hyoplasm rather than dark blue, foamy spongioplasm. As to their number in proportion to the ripe lymphocytes they may or may not outnumber the latter ones. Our three cases show very clearly the two possible extremes. Whereas the first case had, among 83% lymphoid cells, only 20% typical ripe lymphocytes reasonably recognizable as such, the majority of lymph cells in our second case, about 59%, were of the usual ripe type and only 18.5% showed immature and atypical features. In the second case this predominance of typical, mature, small lymphocytes, as in the case of Ireland et al., suggested rather a marked sameness in the blood-picture.

For clinical reasons and to facilitate the differentiation of clearly distinguishable white blood cells we follow the very practical scheme of V. Schilling. The scheme of Arneth's is doubtless more exact but too minute in its elaborateness for practical routine and but little would be gained of paramount importance to warrant its adoption. Furthermore it would, as pointed out, prejudice the problem of relationship between lymphocytes and monocytes. The tabular classification after V. Schilling is accurate to a satisfactory degree and gives in its outlines a certain pattern easy to read and to interpret.

We find help in our difficulty of definitely settling the questionable classification of these blood elements from such an expert hematologist as Schilling who admits that under certain conditions where greater changes of the lymphoid elements are met with it will be impossible to distinguish definitely between these elements especially where even younger monocytes,
micromyeloblasts and very young forms of erythroblasts occasionally look quite similar to lymphocytes. In all these cases of pathological blood-pictures we follow his suggestion to add another column for the atypical forms.

There is no reason why monocytes should not be called monocytes, provided they have beyond reasonable doubt the usual features of typical monocytes. But a sharp line must be drawn against other forms which, in our opinion, are better called “lymphocytoids” or “lymphoid cells” and no effort be made to force them into a range where their right might be questioned. Therefore, all blood cells of the mononuclear type, which could not be reasonably included in one of the outlined classifications, are recorded either as “atypical lymphoid cells” or in a column “smudged lymphocytes” (“Kernschatten”). This expression is self-explanatory. In all of our cases a fairly large number of obviously lymphoid elements showed a dissolved cytoplasm and the nucleus as a chromatin patch so rendering any classification futile.

In one of these two columns therefore, are placed those cells which other authors describe as “monocytoides,” “plasma-cell-like.” We are, furthermore, not able to agree with those writers who refrain from any attempt at all to classify the different forms with but one nucleus and who simply speak of “mononuclears.”

In making this statement we again want to make it clear that we refrain from any judgment whatsoever whether (Arneth) or not (V. Schilling) the monocytes may possibly represent but an advanced state of large lymphocytes, notwithstanding the dust-like azurophile granulation of the protoplasm.

As to the origin of the atypical elements in glandular fever we consider their lymphoid nature as certain. We follow in this respect Baldridge, Rohner and Hansmann who state:

“1. Histologically the greatest activity in the lymph nodes is in the germinal centers and lymphatic cords.

2. Cells resembling in size and shape the abnormal circulating elements are present in the germinal centers of the hyperplastic lymph glands, as well as in the lymph sinuses.

3. The greatest and most consistent apparent pathologic change of the disease is in the lymph glands.
4. Many of the circulating cells have the staining characteristics, the nuclear structure and the azure granules of lymphocytes.

5. A very marked scarcity of normal circulating small lymphocytes is often an outstanding feature of the blood picture."

This latter statement, however, does not apply to all cases. Our second patient showed, quite to the contrary, 51 per cent and, a few days later, 42.5 per cent of small lymphocytes with the usual mature features.

We may add that at the present time, it seems to us an unnecessary task to give paramount space to the differential diagnosis between these most atypical mononuclear cells, so long as the pathogenesis of the disease remains in the dark. Suffice it to say that glandular fever is a shaking up of the normal distribution and perhaps genesis, also, of the leucopoetic system. The entire mesenchymatous tissue obviously is affected by some kind of stimulation. It is only to be expected that according to the degree and respective site, varieties of white blood corpuscles respond from their different sources of origin. This has to be considered as systemic reaction of the possible lymphotropic virus.

Accompanying Angina

Soreness of the throat at the onset of the disease or right after it has been noticed in most cases. This type of pharyngitis may be a hyperplasia of the follicles in the pharyngeal wall with a peculiar translucent appearance (Baldridge et al.).

Considerable discussion and confusion started over the importance of this throat affection. Severe cases of pseudomembranous angina—with dirty gray membranes over either tonsils, pillars, buccal and pharyngeal walls—were prima vista taken for diphtheria and, the culture being negative, even new designations were coined putting forth this striking feature of throat affection. In a preceding section it has been pointed out that a number of facts led European observers to over-emphasise this throat trouble and to unduly neglect adenopathy and blood morphology.

Tidy and Morley in England have already pointed out that only in little more than half of the cases does the throat become affected. In a subsequent paper Tidy and Daniel found, in an epidemic of 24 cases, no instance of any exudation on the tonsils
whatever. We are in conformity with Lehndorff who stresses the fact that in many instances the angina sets in only after the onset of the adenopathy and without any relationship between the extent and severity of both. It seems beyond reasonable doubt that the angina—if present—cannot be considered as the primary lesion. It is quite another problem whether the specific virus gains entrance through the pharynx or the tonsils considering the invariable adenopathy in the cervical region and the early and quite frequent implication of the upper respiratory tract. But even so, we cannot follow the custom of some authors in calling the pharyngitis a secondary stage and comparing it to the secondary stage (Glanzmann) of syphilis. It must not be forgotten that these terms are reserved for syphilis only where a clear separation in different stages is clinically and morphologically present as a matter of course. But even in the secondary treponematous infection, in yaws, these stages become indistinct and without a clear-cut boundary line. In other diseases it will be even more useful to refrain from too far reaching analogies.

Affections of the oral and buccal mucous membranes like stomatitis aphthosa are recorded by Glanzmann.

Taking into consideration all these different observations about streptococcal infections met with in ulcerative conditions of the oral cavity and followed by lymphatic reaction in the peripheral blood, we believe that any infection of the mucous membranes in the mouth leading to ulcerations may be followed by a lymphatic reaction in the peripheral blood. We consider this rather as the result than the cause. It is, perhaps, a lymphatic answer either to a lymphotrophic virus, yet unknown, or to other microorganisms well known to be found in these lesions (Streptococci, fusiform bacilli and spirilla).

Relationship to Plaut-Vincent's Angina

The severe cases of angina with pseudomembranes were taken occasionally for the Plaut-Vincent type of angina though, however, in our first case as well as in those of other observers already quoted, a general dark red congestion of the pharyngeal walls with marked oedematous swelling was present without any of the typical ulcerations of Plaut-Vincent's disease. Smears from the gum margins, pharynx and inflamed tonsils show not
infrequently spirochaetes and fusiform bacilli mostly in but small numbers as in many forms of throat infections. It would be highly improper to attach any significance to this common finding in view of the total absence of the typical ulcerative patches of Plaut-Vincent's angina and the entirely different morphological appearance of the sore throat. In this connection it is well to remember that Baldridge, Rohner and Hansmann who found out of 29 smears of their patients with glandular fever 27 to be positive for organisms of Plaut-Vincent's angina also found 41 positives out of 50 general medical patients who had neither enlarged glands nor any mononuclear increase in the blood whatsoever.

Naturally, a typical Plaut-Vincent's angina might occur, though very rarely, following an attack of glandular fever, but, as A. Vogl pointed out, during the well developed clinical picture of the disease with all syndroms present, no signs of Plaut-Vincent's angina exist and therefore the latter must be ruled out as the causative agent.

On the other hand a certain reciprocity seems to exist between the predominance of mononuclear elements in the blood and the disappearance of polymorphonuclear granulocytes from it. The mucous membranes of the cavum oris show a unique predisposition for the well known dirty yellowish patches and ulcers ranging from the classical Plaut-Vincent's disease to the terminal feature of so-called noma. We refrain from speculations as to whether this uniform clinical response is primarily caused by the virus, as discussed above, or by the lack of granulocytes in the blood. The decrease of granulocytes in the peripheral blood seems, apparently, to facilitate necrosis, particularly of the mucous membranes, followed by extensive growth of fusiform bacilli together with spirochaetes on the ulcerated spots. Spirochaetes, at least, are more likely to be only incidental and not causative agents as similar conditions of Plaut-Vincent's angina have been observed during antisyphilitic treatment with salvarsan (R. E. Jameson). At any rate, if the clinical appearance and the predominance of fusiform bacilli together with spirilla are found in a smear it is mostly so after the acme of the disease. Vogl observed it on the 11th day after the onset of fever and lymphadenopathy. Landon expressly states that in his case only a congestion of the pharynx
with no abnormal tonsils existed on the 4th day of the illness
and it was not before the 22nd day after the onset of the disease
that a membrane formed on both tonsils with the appearance
of Plaut-Vincent’s angina.

**Relationship to so-called “Monozytenangina”**

Considerable confusion exists in current literature about
all diseases where the increase of monocytes in the peripheral
blood seem to be a dominant feature to such an extent as to be
exalted to a criterion for the existence of a new disease entity.
Without viewing in this paper the merits of the still disputed
“Monozytenangina” (Reschad and Schilling), the overestimation
of purely morphological characteristics of blood cells for the
establishment of new disease entities is evident in so-called
“Monozytenangina” which caused for some time quite a little
confusion in medical literature. It complicated at the same time
the problem of infectious mononucleosis to which these cases
possibly belong.

In 1922 A. W. Schultz demonstrated as “Monozytenangina”
a case of angina with fever, splenomegaly and a blood picture
with 78 per cent blood cells with the appearance of monocytes.
The author stressed the fact that in his observations protracted
defervescence—over 38 days—liability to relapses, persistence
of the typical blood changes, distinct enlargement of liver and
spleen were most frequently encountered. All these symptoms
are, likewise, typical and, furthermore, pathognomonic of the
condition of glandular fever with lymphoid reaction as described
by the overwhelming majority of other observers.

In a recent paper, however, Schultz admits that in check­
ing up a number of blood pictures of his early cases he could not
reasonably maintain any longer that the atypical mononuclear
cells were all monocytes. He therefore abandons his first
statement and adopts the term “lymphoidzellige angina.”
Though he still overemphazises, in the opinion of most of the
other observers and ourselves, the localisation in the pharynx,
which may or may not be present in glandular fever. He also
takes up the systematical scheme of Arneth which is purely
morphological and has, as already mentioned, doubtless a prac­
tical side. Again, we must refrain from discussing the merits
of this dualistic over the trialistic standpoint (V. Schilling).
We venture to believe that quite a number of cases of so-called "Monozytenangina" in current medical literature may be possibly nothing else than glandular fever with accompanying angina where atypical lymphoid cells have been confused with monocytes.

With this recent paper of Schultz and Mirich it seems to us that the term "Monozytenangina" is about to disappear for the sake of simplification and terminology, as no evidence exists to warrant any separation from glandular fever with lymphoid reaction.

**Relationship to so-called "Agranulocytosis"**

Tuerk has described a septic condition with but one polymorphonuclear granulocyte among more than 532 white blood cells and a total count of 940, of which 95.6 per cent were lymphocytes. Schultz reported in 1922 what he called "gangrenous processes and defect of the granulocytic system." (Gangraeneszierende Prozesse und Defekt des Granulozytensystems) which must still be considered as a distinct disease entity so long as it cannot be otherwise classified. Though the considerable decrease and even the complete absence of polymorphonuclear and eosinophile blood elements reminds us of "infectious mononucleosis," the striking feature in blood morphology is the absolute decrease of white blood cells. The total count of white cells may sometimes yield not more than a few hundred in the cubic millimeter. This, on the other hand, constitutes an important difference from leukemic conditions to which the disposition for gangrenous ulcerations and necrosis gives it a strong resemblance. Another most characteristic difference from leukemia is the unimpairment of the whole erythropoetic system in agranulocytosis.

Whereas Schultz in his first publication stresses the fact that the disease affects mainly adult females, that necrotic ulcerations in the mouth and pharynx are constantly met with and that death always occurred, reports of diseased males and children as well as recovery have since then been made which have been confirmed in a recent paper by this author himself.

Considerable discussion has been focussed upon the accompanying necrotic ulcerations and their localization in the oral mucous membranes. We fully agree with Reye that necrotic
ulcerations are not necessarily limited to the mucous membranes of the mouth and pharynx but may appear in areas either of skin or mucous membranes other than those of the oral cavity. Two cases of Reye's illustrate this well. In the first case an agranulocytotic blood picture was found before any necrotic ulcers in the pharynx appeared. The second case showed the agranulocytotic blood features together with necrotic ulcerations over two fingers and on the skin and mucous membrane around the anus but no changes in the oral cavity whatever.

The pathogenesis and therapy of agranulocytosis are unknown and are still under discussion. An infectious agent most likely causes the intoxication of the myeloid system. The possibility of a congenital disposition and underfunction of the myeloid tissues is remote. The above mentioned case of Reye is, perhaps, quite noteworthy in this line as the agranulocytosis was discovered in the patient following a slight attack of angina but without any necrotic ulcers in the mouth. The patient continued to live with the agranulocytotic blood picture for about 2 1/2 months more with comparatively little complaint until all of a sudden a change for the worse set in and death occurred in the course of a few days.

The pathological changes in agranulocytosis are quite different from those encountered in simple septic conditions though clinical symptoms strongly resemble sepsis (Schultz, Lindemann, a.o.).

A most painstaking observation was made by Roberts and Kracke which may reflect much light upon the pathogenesis of this dysfunction and finally complete loss of function of the bone marrow, so far as the production of granulocytes is concerned. The authors were able to follow up a case with daily blood counts over nearly 8 weeks. The blood stream onset preceded for a few days the clinical onset with the symptoms of septicemia. Abscess formation occurred with apparent complete granular cell regeneration. After a stage of recovery a second attack set in followed by death. "The sepsis follows the agranulocytosis rather than precedes it." This would mean that sepsis is not the cause as considered by Schultz and Stocké, which the latter author advocates again recently in a very noteworthy paper to which reference must be made for particulars. Another case with an interval of even two years between the
first and the second lethal attack of agranulocytosis has been described by Franke.

No therapy has proven of much value against agranulocytosis so far, though some authors claim neosalvarsan, blood transfusion, antistreptococcal serum, gold preparations or X-ray application to the long bones (Friedemann) to be effective.

In this connection it is very interesting to note that quite a number of agranulocytotic white blood cell conditions have been met with in syphilis after specific treatment. In the majority of these cases, however, the red blood cells were affected also. For this as well as for pathogenic reasons these conditions ought to be clearly differentiated from agranulocytosis as pointed out by Steinert, to whose painstaking paper reference must be made for details.

Nature of Lymphoid Reaction

The question now arises if such an extensive lymphoid reaction is limited—apart from true lymphatic leukemia—to conditions of glandular fever only or if this form of lymphoid reaction is met with in essentially differing clinical entities.

In this latter case it would be possible that either the diseased body is bound to respond to infections with the characteristic lymphocytoid blood picture owing to constitutional conditions, or it might be that a particular lymphotropic virus causes the pseudoleukemic changes without any influence from the patient’s constitution at all.

In this respect, Deussing’s observation is interesting that in glandular fever with lymphoid reaction the intravenous injection of collargol produced not only temporary but even permanent increase of granulocytes in the peripheral blood. According to the author a similar observation was made by Hopmann with intramuscular injection of milk in a patient convalescent from glandular fever. The total count rose from 5,300 to 13,800, the lymphocytes dropped from 39 per cent to 16 per cent and the polymorphonuclears rose from 52 per cent to 80 per cent 8 hours after injection at the height of the resulting fever. Eight days later the respective figures were 7,200, 50 per cent lymphocytes and 40 per cent polymorphonuclears.
The second case of Vogl of glandular fever with a lymphocytosis up to 81 per cent and a total count of only 12,000 came, 1½ years later, again under observation after an attack of appendicitis with a total count of 13,500 white cells of which only 15 per cent were lymphocytes. This shows that in this case, at least, the same individual may respond with the usual increase of polymorphonuclear cells to a simple pyogenic infection.

Sprunt and Evans likewise reported a case where a perfectly normal polymorphonuclear response was observed three months after an attack of glandular fever.

All these observations prove that the tissues manufacturing granulocytes were still able to respond to a definite stimulus.

Other authors have likewise reported streptococcic septicemic conditions with leucopenia and highly increased lymphocytes together with an early impairment of the erythropoetic system (Marchand).

Cabot saw one case with an infection of an unknown organism with a total number always less than 20,000 white blood cells of which 70 per cent were lymphocytes, and another case suffering from persistent boils with 3,400 white blood cells of which 82 per cent were lymphocytes.

On the other hand Benedict observed a case of a 62 year old woman who had pneumonia twice with an interval of one year. During the first attack a lymphocytosis up to 81 per cent occurred. The second time 97.5 per cent lymphoid cells were counted of which 85.5 were atypical. The total count was 4,000 to 5,000.

These cases suggest very strongly that such high lymphocytosis may result in conditions where glandular fever and any lymphtropic virus must be ruled out. The rather vague conception of constitution cannot but revive if the same individual responds twice in the same manner. Benedict himself considers this lymphatic reaction as a biological though unspecific reaction comparable to eosinophilia or the increase of macrophages of the monocyte type.

Lymphocytosis following the administration of certain drugs and biological substances has long been known (thyroid
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injection, tuberculin, arsphenamin, pilocarpin, tetrachloromethane poisoning). Feer saw agranulocytitic blood pictures with a lymphocytosis up to 96.5 per cent and a total white count of only 1970 after nirvanol in a 10 year old boy suffering from chorea minor. Lymphocytosis is also observed after X-ray treatment to the extent of 40 per cent (Klövekorn).

The conception of a particular lymphatic reactibility was for a while associated with so-called status thymolymphaticus. Since this condition—though doubtless clinically well defined and not to be missed—is in its conception limited more or less to children and since status thymolymphaticus is one of the most flexible and least understood conditions in constitutional pathology, it should not be associated with a disease which has only one feature in common, namely the predominance of lymphoid elements in the blood picture.

The relationship of “glandular fever with lymphoid reaction” to true leukemia will be elucidated through future studies. Its relationship to “agranulocytosis” must likewise be determined. Not a few symptoms are in common, though agranulocytosis following sepsis is apparently a destruction of myelogenic parenchym. The lymphoid reaction of glandular fever, on the other hand, looks more like a proliferation of lymphoid elements caused by irritation of lymphatic tissues. It must remain unsettled where the boundary line must be drawn. Over-irritation finally ends in exhaustive destruction and death.

Differential Diagnosis

At the onset of glandular fever with lymphoid reaction a number of other diseases have to be ruled out. The differential diagnosis may be difficult particularly if one or the other symptoms seems to dominate the whole clinical aspect.

True leukemia is nearly impossible to rule out at the beginning of the illness. We are in accord with Tuerk, Naegeli and the majority of the hematologists that in the beginning of the disease the blood picture, very often, is entirely that of leukemia and that all forms characteristic both for acute and chronic lymphatic leukemia may be present in a given case. If Downey and McKinlay think they are able to make a differential diagnosis from the appearance of the lymphoid cells alone—though the reproduction of the different lymphoid cells in their
paper is such that nothing can be reasonably differentiated—it is to be assumed that their cases, both of glandular fever and true leukemia, did not show the variety so common in most cases of these diseases.

The high percentage of most atypical lymphocytoid elements, as in one of our cases is by no means a criterion either pro or contra. The comparatively high number of very fragile, "dissolved" cells in one of our cases has been so far considered quite pathognomonic for leukemia. As in glandular fever epistaxis has been, though rarely, seen, the tendency to hemorrhage in leukemia cannot be reasonably construed as a distinguishing feature.

Early impairment of the erythropoetic system with anemia and cachexia together with the whole course of the disease will point soon to the acute form of leukemia. The chronic form, however, is even more difficult to eliminate. Low leucocytosis or even leucopenia (Landon, Hislop), disappearance of lymphatic swellings and appearance in other regions points more towards lymphatic reaction.

**Lymphosarcoma and leucosarcoma**—without discussing in this place the differentiation of both and the occurrence of microscopically similar destructive malignant infiltrations in both diseases—can be ruled out by the clinical course very soon, even if associated with an increase of lymphocytes of the ripe type. Again may we draw attention to our clinical observation that the ripeness or unripeness of the lymphocytes is by no means any indication pro or contra either of true leukemia or "glandular fever with lymphoid reaction."

Adenopathic conditions in simple leukemia show mostly marked tendency to infiltrate adjacent tissues and organs, sometimes to such a degree that malignancy is even macroscopically evident. Whereas Paltauf and Sternberg advocate a clear separation between cases showing only microscopical changes of infiltrative growth and those leukemic conditions where early breaking down of neighboring barriers and consecutive malignant invasion are met with, others, like Hirschfeld, desire to reserve the term leucosarcomatosis apart from leukemia only to such cases as can be proved to have originated in one strictly localized area of lymphatic glands.
In this connection it may be mentioned that Gottron and Jacobi observed lymphocytosis of 51 per cent with adenopathy and spleen enlargement 1/2 year after Herpes zoster. Subcutaneous infiltrations at the sites of the former vesicles histologically examined showed lymphadenosis cutis.

Grippe may be very difficult to rule out. We even venture to say that grippe, mostly accompanied by lymphocytosis and sometimes with some form of adenopathy, must not infrequently be left to the physician's tact and discretion to diagnose and separate from glandular fever and vice versa, provided it is a borderline case. The observation of Cornelia de Lange is a very illustrating example of this uncertainty.

In tropical countries Dengue can be difficult of differentiation from glandular fever. Dengue, too, may not infrequently involve glandular enlargement. In the classical monography on dengue fever P. C. Riley calls it even a most constant symptom. He found constantly enlarged the post-cervical, epitrochlear and inguinal glands. They were frequently tender, and in some of the cases, with a prolonged subfebrile temperature, the glands have been noted to continue palpable. Enlargement of the spleen and liver is in our own experience, however, rarely observed here in the Philippines, though not entirely absent. Riley saw but two cases. We ourselves have recently observed a case of dengue fever with the typical clinical symptoms including the characteristic rash and a lymphocytosis of 59% among a total count of 6,000 white blood cells.

This affection of fixed lymphatic tissue in dengue fever together with lymphocytosis up to 59% can easily lead to confusion in the absence of marked leucopenia. We have seen many cases of dengue fever where this quite unduly stressed symptom of decreased number of leucocytes has never been present, and even the extreme number of over 30,000 leucocytes without any secondary infection whatsoever had been counted.

The appearance of a rash, if one happens to exist, together with a marked lymphocytosis might be mistaken for rubeola. The presence of a greater percentage of typical plasma cells, the comparatively little adenopathy of other regions than the posterior neck and further observation of the clinical course will soon help to exclude glandular fever.
Scarlet fever may be suspected by the flush sometimes observed in glandular fever. However, the blood picture will guide the careful clinician in the first days after onset, as scarlet fever produces in the beginning a polynucleosis and not until the 2nd week is there a rise in lymphocytes (Fileston and Locke).

If angina with pseudomembranes is already present when the physician is called in, Diphtheria is, doubtless, the most urgent question to ascertain or to rule out. The bacteriological examination, both in a smear and by culture, will definitely settle any doubt. In the meantime, however, the blood picture and the smell, easily noticed and of a particular sweet kind and characteristic for diphtheria, may guide the clinician.

Whooping-cough might be suspected in those cases where attacks of spastic cough are present. Whether these coughing spells are caused by an enlargement and inflammation of bronchial and peribronchial lymph glands remains to be definitely proven; though it seems to be the general conception, it still lacks definite proof. Neither through X-ray nor autopsy findings has this theory been verified so far. The diagnosis must be founded on those symptoms described in a preceding section. During the prodromium of whooping-cough and before even the onset of any clinical symptoms pointing towards pertussis, the blood-picture may show a similar percentage to that of acute leukemia as Opitz has demonstrated. More recently Wolff mentioned a very illustrative case of a one year old boy with febrile bronchial catarrh and a total leucocyte count of 75,000 of which 86 per cent were lymphocytes and only 8 per cent granulocytes. Not until a few days later did a classical whooping cough set in. The lymphocytosis with 63 per cent and a total count of 12,800 were still present 4 weeks after the onset of the cough and 3 days before the last attack.

The very early onset of the spasmodic coughs, in fact much too early for true pertussis, together with the possible enlargement of other fixed lymphatic tissue accompanied by high fever and very marked lymphocytosis with perhaps abnormal, unripe lymphoid elements, both unusual in such a degree for pertussis, may help to rule out whooping cough. The early disappearance of coughing attacks, furthermore, will decide the diagnosis against pertussis.
Mumps might be mistaken for glandular fever if the submaxillar and pre-auricular glands or the parotid itself become enlarged. Curschmann describes such a case. If a true parotitis happens to exist at the same time, the blood picture will, in the long run, reveal the participation of the lymphatic system by the percentage and, eventually, unripeness of lymphoid blood elements.

Tuberculosis has long been known to be accompanied by an increased number of lymphocytes in the peripheral blood. Miliary tuberculosis has been considered by Lubarsch and Wiechmann to be able to exert such a destructive action upon the leucopoietic system as to induce myeloblastic leukemia. It will mostly be distinguishable from glandular fever through the proper differentiation of the blood picture alone. It must be very exceptional for clinical symptoms and the differential white cell count to be such as to be mistaken for glandular fever with lymphoid reaction. Landon, however, describes a typical case: 16 year old colored girl suffering from pain in the upper abdomen for eight months, for two days sore throat. The examination showed an ordinary tonsillitis, indolent and palpable cervical and axillary lymph nodes. Heart, lungs and abdomen negative. X-ray examination showed a large node at the left hilus but nothing else abnormal. Sputum negative. The blood count showed during the following five weeks a minimum of 8,400 and a maximum of 36,800 white cells with between 80 and 97 per cent mononuclear forms. The patient had a persistent and increasing temperature and progressively lost flesh and strength. No other physical signs were found. Death occurred five weeks later. The autopsy revealed tuberculous bronchopneumonia of the tracheal and bronchial lymph nodes. Miliary tubercles were scattered through both lungs, the liver and the spleen. The marrow, studied both by smears and sections, showed no pronounced abnormality.

These rare cases will always remain impossible to diagnose in the absence of physical signs and Koch's bacilli until they come before the supreme court of the morgue.

Intermittent fever of the quotidian or tertian type may simulate malaria. The absence of parasites together with the early predominance of lymphoid elements in the peripheral blood stream will soon point to glandular fever.
Cerebral symptoms like intense headaches, photophobia, vomiting, rigidity and retraction of the neck, Kernig's sign and increased reflexes occur seldom but might be taken for meningitis at the onset.

Appendicitis in some cases, may be ruled out only with difficulty if griping sensations and défense musculaire are present, particularly in the ileo-cecal region. The presence of an enlarged liver with palpable spleen and the lack of the typical facies abdominalis together with the comparatively fair general condition will point more towards glandular fever of the abdominal type. The rate and quality of the pulse furthermore, points in this direction.

Blood picture, bacteriological and serological examination together with the whole clinical course will help to rule out other febrile diseases like typhoid fever, sepsis, tularaemia, undulant fever and others.

Disease symptoms with fever, adenopathy and splenomegaly respectively, have been reported from the tropics from time to time but all fail to show the indispensable features of a striking increase in lymphoid blood elements. Since Baldwin has, recently, proven that the one time "Endemic glandular fever as an acute disease characterized by an irregular remittent fever" of O. Smithson, Clarke and Breinl, Priestley and Fielding, occurring in the Mossman district of North Queensland, is nothing but either pyocyanus infection or typhus fever, respectively, this misleading term is no longer entitled to a place in medical literature.

Norrie reports a case of painful lymphadenopathy with fever in a patient from Bengal (British India) occurring two days after hunting in the jungle. As neither blood pictures nor counts were made, it is impossible to reach any definite diagnosis at all.

Our cases, therefore, are the first cases of "glandular fever with lymphoid reaction" which have been observed, diagnosed and reported from the tropics.
SUMMARY.

(1). "Druesenfieber" first described by Pfeiffer, and adenopathy with a blood picture strongly resembling leukemia as described by Tuerk are one and the same clinical entity "Glandular fever with lymphoid reaction."

(2). The first cases observed in the Tropics are reported, studied and discussed.

(3). Epidemiology, modus of infection, pathology and clinical symptoms are discussed.

(4). The most dominating features are adenopathy, fever and an increase of blood cells with but one nucleus.

(5). Though the type of these mononuclear blood cells may in the majority be the usual lymphatic cells, the percentage of lymphoid cells may be made up to a high degree of most bizarre and unripe lymphatic elements and this is characteristic of the disease.

(6). Differential diagnosis, particularly from true lymphatic leukemia, may be difficult at the onset.

(7). "Glandular fever with lymphoid reaction" affects the whole mesenchymatous tissue. According to the degree of this stimulation a disordered response calls forth a variety of lymphatic blood elements. This seems to point rather to a systemic reaction upon a possible lymphotropic virus.

(8). Two of our three cases of "glandular fever with lymphoid reaction" show the two possible extremes: the first case had among 12,000 white blood cells only 20% mature, typical lymphocytes whereas 64% showed a wild variation of unripe lymphoid blood elements of nearly all conceivable forms.

(9). The blood picture of the second case showed among 5,800 leucocytes a certain monotony with but 18.5% unripe and atypical lymphoid cells and 59% typical lymphocytes.

(10). Our third case had a total white cell count of 11,700 with 49% mature, typical lymphoid cells and 23% unripe, atypical lymphoid blood elements.

(11). The percentage of granulocytes exclusive of eosinophiles were 14, 19 and 23 respectively. The percentages of lymphoid blood elements, exclusive of typical true monocytes were 84, 77.5 and 69, respectively.
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The ideal of dentistry doubtlessly is the prevention of disease in the mouth.

The problem is of so vast and elusive a nature, that it would scarcely adapt itself to a general and final definition. From the viewpoint of a bacteriologist, it would be the control of bacterial activity in the mouth. A biologist or a chemist would say that the source of the truth is to be found in the methods of nutrition. A clinician looks at proper technical achievements, at the curing of defects in the mouth in good time. And, above all, is heard the voice of hygiene, which claims a continual and thorough care of the mouth.

Prevention in dentistry is therefore nothing special, nor anything essentially limited. It comprises the entire domain of dentistry from the viewpoint of medical science and hygiene.

It differs only in one respect, which up to recent times has been very much overlooked and which refers to the degree or intensity of need in prevention.

If, in respect of health in general, a cure of a disease in most occasions means real cure, it is far from being so with the restoration of oral defects. An extracted tooth, especially in youth, is a loss for ever, and an irreparable one, notwithstanding the best artificial fittings. A pulpless tooth, though properly treated, is occasionally a permanent source of infection and a danger to health. Pyorrhea, though thoroughly eliminated, cannot be considered as cured, unless the systemic reason from which it originated has been discovered and overcome.

Thus, speaking technically, there is no real "cure" in our profession, but only the ameliorating of a wrong to the best of human ability. Prevention of this wrong is therefore of primary necessity.

Preventive dentistry together with the theory of correlation between oral diseases and systemic conditions constitute in our days, the main object of mouth hygiene propaganda throughout the world and especially in the United States, where the work is done with a quite unprecedented enthusiasm. There
is practically no single issue of the leading medical and dental journals, where one or several articles devoted to these questions cannot be found. The American Dental Association comprises a special Bureau of Dental Health Education, whose work is reported in each number of the Association's Journal.

Preventive dentistry being not so much a scientific term as one of behaviour in life, its application is as wide as life. Measures of real prevention, and the most efficient ones, should be taken at the time of **Pregnancy**, long before the future subject of prevention in the dentists chair has been born.

Years ago the general belief prevailed that a woman in pregnancy should avoid dentists, as well as all other sources of trouble, pain and nervous irritation. While this fear seems quite justifiable in respect of certain oral operations, inclusive of extraction, as a rule, it is just the opposite that is to be recommended. The theory of the leading medical authorities is that every expectant mother should visit her dentist at least at monthly intervals, and all kinds of oral defects be carefully treated.

The second phase of preventive dentistry is to be found in the proper care of the **Deciduous Teeth**, which make their gradual appearance during the first two years. It is a great error and unpardonable neglect to admit that, because deciduous teeth are bound to disappear, they should not be treated, but just left to their own transitory fate.

The deciduous teeth form the basis of the permanent ones. What happens to the first during their temporary stay, is directly reflected in the formation of the others. It should be well remembered that the period of growth of deciduous teeth corresponds to the time when the individuality of the oral cavity is formed, and when, on the other hand, the bony structure of the jaws is most sensitive. The loss of even one of the deciduous teeth, caused by decay or consequent upon extraction exerts a direct effect on the growth of the jaws and the drifting of all the other teeth. Irregularity in the permanent set and malocclusion are thus bound to ensue.

Caries, once started in deciduous teeth, develops very fast. In most cases its origin is of a systemic nature, chiefly due to an insufficient or wrong diet,
Decay causes toothache and promptly affects the nerve substance with serious complications and consequences. With deciduous teeth in disorder, the baby is unable to properly masticate its food. It acquires the habit of swallowing unchewed food and indigestion follows. Moreover, due to the difficulties of treatment of greatly spoiled teeth in a baby's mouth, especially when accompanied by abscess formations, there only remains the extraction of such diseased teeth, with the alternative of upsetting the entire foundation for the coming permanent set.

The leading authorities on child dentistry are unanimous in insisting that a child should make his first appearance at a dentist's when 2½ to 3 years old, and from then on, he should visit the dentist not less than once every six months.

As, unfortunately, it is very rare to see a baby being shown to a dentist, and as, on the other hand, comparatively few of the expectant mothers and also those who have given birth are able to procure food containing all the requisites, not only on account of lack of means, but chiefly because of complete ignorance of what is right and what is wrong, it results that, when the permanent teeth come together, they appear in the great majority of cases in a disorderly state, with wrong occlusion, and all technical predisposition for mutual encroachment, stagnation of food, caries and gingivitis.

The third phase of preventive dentistry refers to School Dental Education. Children of school age are the most powerful agents in spreading the science of mouth hygiene. Once the ideals of oral cleanliness have been impressed on them, they will flourish. If only the directors of different schools could plainly see for themselves the tremendous moral, mental and physical detriment to the personality and the work of a pupil, caused by neglect of teeth and also the irreparable loss to the life and activities of the future citizen, they would be the first to enrol as dental hygiene apostles.

The first measure to be undertaken would be to ascertain the real state of oral health of these hundreds of young children who, from their outward appearances look normal—studying or seeming to study when they are in class, playing or seeming to play when the bell has sounded for recreation, and improving, though slowly, in every respect.
Were a dentist allowed to visit this virgin soil, he would doubtlessly discover ten in a hundred children with teeth in pretty good condition, but the rest unsatisfactory, and in the midst of these latter, at least 50 who are in need of immediate care.

Only after having listened to the report of the dentist and seen the card-report for each case, would the director begin to realize why one of his pupils, although capable, is slowly progressing, why another is so weak, a third shows so poor a mentality, a fourth is so nervous, and most of them are so unhealthy looking. From this moment, the mind of the pedagogue if a man of conscience, will become disturbed. He will surely doubt the perfection of his establishment and endeavour to interrupt the process of dental decay which is a clear impediment to the process of the mental and physical development of those under his care.

The fourth field for preventive dentistry, an extensive but rather poor ground, is to be found with the Public at Large, the mass of adult people, parents or otherwise, young or old, male or female, educated or uneducated, rich or poor.

Preventive dentistry in the midst of adult persons means a twofold thing: Good home care of the teeth, with regular brushing at least twice a day, and periodical visits to a dentist for so called prophylactic treatment, which means regular examination of the oral cavity by a dentist, accompanied by a thorough cleaning and overcoming of the first signs of decay at the very moment of their commencement. Thus true prophylaxis is an essentially preventive work.

If a new disciple of a mouth hygiene creed decides to desert his blind habit of germ breeding in his mouth, and of swallowing together with carefully balanced meals, a very unhealthy stuff bearing the disgusting name of "pus," — the first thing which this blessed newcomer would have to do is to have an X-ray picture taken of both sets of his or her teeth, or at least of those which are painful or suspected. These pictures will serve the dentist as a basis, and the only true basis, for judgment.

The fourth and most intensive phase of preventive dentistry is to be found with Dentists, and of course, physicians. They are equally the source of scientific research and knowledge, and
the active agents of curing for prevention and of prevention for cure.

Preventive dentistry, so far as direct work of the practising dentists is concerned, lies in the quality of their work, which means a certain harmony between character and knowledge.

A generous man, imbued with most altruistic principles, kind and patient but poor in scientific knowledge or capacity to carry deductive conclusions from his own practice, makes a helpless agent of prevention. Neither will a man of superior mentality, capable of grasping and developing the knowledge of principles on which human health is founded, but lacking in attention, care and conscientiousness create a source of prevention.

A capable technician who would excel in artificial dental appliances, porcelain jacket crowns or fillings, but would show no taste for deep analysis of the phenomena he remarks in the mouth of his patient in relation to his systemic conditions, may be considered as an excellent and precious preventive agent within the limits of the mouth cavity and by interrupting the action of oral infection on the general health, but would not constitute a source of prevention in the broad meaning of the term.

No longer can we examine the oral cavity and make our diagnosis on the basis of mechanics alone: we must solve the problem from the standpoint of biologic findings, and consider the whole body rather than the oral cavity.

The modern dentist must have the eye of his mind everywhere and a very sharp eye it should be. Through the health of an expectant mother, he perceives her systemic conditions, and either prescribes her a diet, if it is a question of deficient mineral salts in the system, or in more complicated cases, reports her to a physician. Through the mother in pregnancy, he foresees the dental conditions of the expected child and can advise measures of ensuring them. Through the state of deciduous teeth he will determine what may be expected for the permanent ones and undertake the necessary measures of prevention. Through the newly appeared permanent teeth of a baby, he foresees the perils of malocclusion, and may profit by
the still young and flexible bony tissues, for correction. Through the oral cavity of a school child, he begins to realize the truth of the systemic conditions of the future adult. He may understand the character of the child in a more precise and scientific way than does the best intentioned and most devoted pedagogue, because he can discover the physical conditions in the body which in a considerable degree determine the psychology of children.

With adults, the work is still more complicated, because the dentist, having properly examined the condition of the mouth disorder shown by the X-ray pictures, is usually placed in a dilemma. His expected role does not only consists in a "repairing" of the wrong he remarks, but he is bound to help out his patient, within the limits of his profession, from the plight of ill health or a systemic tendency to the same. Thus the modern dentist in the way of bringing a real and preventive help to this patient, performs to same mental work as does the physician, which is known as diagnosis.

This would not mean that the dentist enters the field of systemic healing and oversteps the prerogatives of the physician. The result of a proper diagnosis has, before all, to enlighten the dentist within the limits of his own professional activities, guiding him in the choice of his undertaking and opening before his eyes the remote horizons of well understood prevention.

Dentists "diagnosis," being of capital importance as the solution of the internal health problems by their visible oral manifestations, is, par excellence, "preventive dentistry." It is to be applied to all stages of human life, from infancy to old age.

Then dealing with children a great responsible diagnosti- cal work must be exercised in determining what has to be done from the view point of systemic immunity to dental decay, based on heredity or other factors. On diagnosis depends the entire future of the oral condition. Are tiny pits and slight fissures on a baby's teeth to be filled or not? Is a pulpless tooth to be extracted or should it remain? What kind of filling material should be used and at what period of resorption of the deciduous root and appearance of the permanent one?
Should an exposed pulp organ of a baby's tooth be preserved and what would be the method in each particular case?

With adults, what is the degree of immunity in a patient's mouth and by what means may this immunity be increased? In case of marked susceptibility, what constitutes its underlying reason and what is the remedy? In case of advanced pyorrhea extraction or treatment? With pulpless teeth—extraction or treatment? Thus many other questions bearing marks of systemic relationship, and many others of a purely local and technical nature, which are the source of prevention or a loss to prevention, are dependent on the degree of care, attention, enthusiasm and knowledge of the dentist.

The dentist's "diagnosis," as a source of prevention in pathology at large, together with a proper treatment, local and systemic, as much as the conditions of the oral cavity are concerned, are accompanied by a third function of preventive dentistry which is the upkeeping of mouth hygiene. This factor, though not absolute, because we occasionally see perfect teeth in a neglected mouth, and also teeth in hopeless decay notwithstanding a permanent and very conscientious care of them, still taken at large, is the very primary cause and source of dental decay and health.

The dentist is obviously the most natural and powerful source of general education in respect of mouth hygiene, beginning by advising and lecturing his patients when operating on them in his office, and devoting work and time to lecturing in public.

There is one more most important role to be expected from dentists in the field of prevention. This is to carry preventive dentistry to its further development, namely, to promote an efficient and direct interest in this movement by the State Authorities, the Municipalities and other official institutions.

Here lies the sixth phase of our problem and one which, I am glad to state, is no longer a dream of enthusiasm, but begins to become a reality.
The Problem of Preventive Dentistry undoubtedly is of Nation-Wide Bearing and Importance.

Healthy mothers produce healthy children, who, in their turn, create a healthy atmosphere of thought, effective system of work, and a powerful army.

With the advent into the domain of preventive dentistry of the State, or its public equivalents, such as the Municipalities or powerful establishments of official standing, such as the Red Cross Society,—it might be thought that the phases of our problem are completed and there is nothing more to say or to endeavour.

But no,—far from that. There is the seventh, and possibly, the mightiest source of sanitary prevention.

It is life itself,—A High Standard of Culture and Civilization.

This will make the Sunday of rather a "prevented" than "preventive" dentistry.

It will appear, when, in the centres of social life the sun shall dominate our activities and not the electric lights that illuminate our sleepless nights, when life shall get brighter, when the precious gifts of nature, such as fruits and vegetables, shall no longer be destroyed in order to maintain certain price levels, when the science of proper diet of which modern humanity is utterly ignorant, shall proclaim its definite laws.

Will this Sunday ever appear? None can guess.

Progress is a sequence of infinitely small acts and efforts, but an idea of what we have to attain through the ages should continually vibrate in our minds.

Now, after having wandered so far from the contents of our subject, let us return to our laborious six-day week, and firmly keep in mind, never to put off until tomorrow what can be done today.
Pseudo-Dextrocardia

PSEUDO-DEXTROCARDIA DUE TO CHILDHOOD PULMONARY TUBERCULOSIS

Report of A Case

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Sometime ago the writer recorded a case of congenital dextrocardia with visceral transposition (see C.M.J. 44:942, Sept., 1930). Since then he has seen in consultation another case of apparently similar nature, but on further investigation, the malposition of the heart was found to be due to pulmonary tuberculosis in childhood. In view of some interest in the diagnosis of the case, it may be worth reporting.

History. Y.C.C., a first year junior middle school boy, 17 years old, came to the Medical Clinic of the Woosung Health Station on account of the location of his heart in the right side of his chest, as found by a physician during the entrance physical examination in the Woosung Middle School. The family history was negative for tuberculosis or congenital deformities. Father was a blacksmith, strong and robust; mother was living and well. The boy had measles at age of 3 years. He began to go to school at age of 7 years; but, one year later, he was ill (probably with his chest condition), and had to stay at home for two years. At age of ten, he had a sprain of his right ankle which was treated in St. Luke’s Hospital, Shanghai. At the time of examination, he felt quite well. No cough, hemoptysis, or marked loss of weight. No dyspnea on slight exertion, palpitation of heart, or precordial pain.

Physical Examination revealed a moderately undernourished boy (weight 47 kg., height 164 cm.) with slight mental dulness. Eyes, ears and nose were normal. Tonsils were hypertrophied, and cervical glands palpable. The right side of the chest showed a striking deformity and contraction with some scoliosis of the back. In comparison with its corresponding side, the right lung had a very poor expansion, and an increase of dulness, and of tactile and vocal fremitus. However, no definite râles were heard. The cardiac impulse was visible and palpable in the 4th right interspace within the midclavicular line.
The right border of the heart was 6 cm. to the right of the midsternal line in the 4th interspace, and left border was about 1 cm. from the left border of the sternum. The heart sounds were indistinct on the left side of the chest, but clearly audible on the right side, best heard just within the right nipple. They were regular and of fair quality. No murmurs or thrills. Blood pressure (Tycos) was 120 systolic, and 60 diastolic.

Neither liver nor spleen was palpable. Liver dulness began in the 6th right interspace in the mid-axillary line. Genitalia were negative. Right ankle had chronic osteomyelitis with a sinus discharging yellowish fluid. The boy was right-handed.

Laboratory findings: Sputum negative for acid-fast organisms. Urine negative for albumen and sugar. Blood count: Hemoglobin 85% (Talliquist); Red cells 5,190,000; White cells 7,200; Polymorphonuclears 75%, Small lymphocytes 21%, Large lymphocytes 2%, and Eosinophiles 2%. Kahn test for syphilis negative. Tuberculin (0.01 mgm) ++ + strongly positive (Mantoux).

Roentgenological examination of the chest was kindly made by Dr. M. H. Chien of the Chinese Red Cross General Hospital with the following report:

“Both the trachea and heart are displaced to the right side of the chest, which shows a marked deformity and contraction, and an increase of density. At the base of the same side, there is a triangular area, 4 by 2 cm. of probably calcified pleura. The left side of the chest is clear and compensatorily enlarged, and has a calcified cervical lymph node.

“Diagnosis. Chronic pulmonary tuberculosis of the right lung with a displacement of the heart and trachea.”

Comment. Without careful history, physical and X-ray examinations of the chest, pseudo-dextrocardia secondary to some other cause may be easily mistaken for true congenital dextrocardia. As a matter of fact, the diagnosis of the latter condition was made on our case before we had made a thorough physical examination, and received the X-ray report of the chest. In some difficult cases, electrocardiogram and X-ray of the gastro-intestinal tract offer considerable help.
PHOTOGRAPH showing the outline of the heart on the right side of the chest, with the sign X at the maximal cardiac impulse.
X-RAY OF THE CHEST showing chronic pulmonary tuberculosis of the right lung with a displacement of the trachea and heart.
Summary. By means of careful history, thorough physical examination, X-ray of the chest, and tuberculin test, a case of pseudo-dextrocardia due to pulmonary tuberculosis in childhood was found in a 17 year-old junior middle school boy suffering from undernutrition and slight mental dulness.

The writer wishes to thank Dr. C. L. Kao for his helpful suggestions in preparing this report.

THE PHARMACY SCHOOL AT CHEELOO UNIVERSITY

W. P. Pailing, Ph.C., M.P.S., B.D. (Lond)

During the past several decades, while much has been done in China by Christian Missions for the training of doctors, there has been very little effort put forward to educate men and women as Pharmacists. In a few places students have been trained in twos and threes and these have gone out and done good work in various hospitals.

But generally speaking, most of the dispensers have been men who have received a little training from the doctor in charge during his very limited spare time. All praise to these doctors for some of the men they have trained.

But with his multitudinous duties, the doctor cannot be expected to have time to give men anything like an adequate training in all the branches of Pharmacy. At the most, all he can do is to teach a man how to mix routine mixtures, to make some pills and other similar preparations.

But, after all, a little knowledge is a dangerous thing, and after being in China for several years, the writer began to see that what was badly needed in our Mission hospitals were good Pharmacists who could not only do the dispensing of drugs, but who could be given full responsibility for the running of that department of the hospital and thus relieve the doctor in charge of an extra burden. This could be done only if he had a man in charge who had a good knowledge of all branches of Pharmacy and who thus knew the why and wherefore of the theory as well as the practice of dispensing.
During the past seventeen years it has always been the writer's ideal to have a school of Pharmacy where such men could be trained. Till two years ago, it was only possible to take men in twos and threes and thus train them. Between the years 1923 and 1929 some 16 or 17 men had thus been trained, some only partly finishing their course or being rejected as not up to standard. Eleven were graduated and received Diplomas. These men were distributed as follows:

- Our own Cheeloo hospital ..... 4
- Other Shantung hospitals ..... 3
- Honan ..... 1
- Shansi ..... 1
- To foreign firms or Government hospitals 2

As these few went out and became known, applications began coming in from other hospitals, and in the autumn of 1929 the writer attained his ideal of many years in being able to open a proper Pharmacy school. A course in Pharmacy was limitedly advertised, and in a few months no less than 83 applications were received. We felt that a small beginning as an experiment was best, and owing to our limited dispensary space we decided to take in only 12 men.

These were carefully selected from the applicants, preference being given to suitable men of good character from Mission hospitals. Eight such students sent by hospitals and four unattached men were accepted.

Our teaching staff was limited to three: the writer and two of his own graduates, Mr. Chu Ching Shen to help with the theory teaching and Mr. Liu Chen Fa to supervise the practical dispensing in the hospital dispensary.

Two very happy years have been spent with these 12 men, and this coming June it is hoped that they will all graduate and go out to their life-work.

The following is a brief outline of the course we have taken.

1. **Botany.** About 180 hours. Lectures with some practical work. In this course a general outline of Plant Morphology, Physiology and Histology has been given. About 30 Natural Orders have been dissected in class, some 100 odd microscopic slides illustrating plant structure have been examined.
This course has been given on the lines of the Minor pharmacist examination of Great Britain, the aim being to help the student in the recognition of crude drugs.

2. **Chemistry.**

   (a) *Inorganic Chemistry.* 120 hours. Lectures and experiments in class. The chief elements and their compounds have been dealt with.

   (b) *Organic Chemistry.* 150 hours. Lectures and experiments in class. In this course the chief classes of Organic compounds are being dealt with, the student being taught to see how the synthesis of the many new and useful organic drugs has been brought about.

   (c) *Qualitative analysis.* 40 hours lectures and about 160 hours of practical laboratory work. The tests for the chief metals and acids have been done by each student and then unknown salts are analysed and reported on by each man.

   (d) *Volumetric analysis.* 20 lectures and about 40 hours laboratory work. The student is taught to perform the chief titrations of the B.P. and U.S.P.

3. **Business methods.** A short course of about 20 hours in which the students are taught how to keep card indexes of all the stock, stocktaking, account-keeping, recording consumption of drugs by the wards, operating room, O.P.D. departments, foreign exchange, working out gross and nett cost of drugs, overhead charges etc.

4. **Dispensing.** First a practical course of 100 hours was given in the class room where most of our common stock preparations, ointments, pills, suppositories, etc. were explained and then made by the students. After this course the students were divided into four groups which in succession go to the hospital dispensary for practical work in actual dispensing, being supervised by our Nos. 1, 2 and 3 staff dispensers there. At least 500 hours must be put in the dispensary during the two years.
5. *Materia Medica.* 150 hours. Lectures and recognition of the crude drugs and all preparations of the Pharmacopeias, their doses, preparations, incompatibles etc.

6. *Pharmacy.* 150 hours. Lectures and experiments in class. In this course the chief pharmaceutical processes are dealt with and then the students are taken through the B.P. and U.S.P., details of assay processes and their theory, etc. being given.

7. *Latin and Prescription reading and criticism.* 50 hours. This course consists first in giving all the abbreviated names of drugs, chemicals and their preparations, abbreviations used in prescription writing. Then some elementary Latin is given, the five declensions being treated, adjectives, the few prepositions and verbs used in common pharmacy, this in order to let the student clearly see the reason for the changes in the Latin names of some drugs e.g. why sometimes it is Opii and sometimes Opio.

    Then difficult prescriptions are dealt with, translated and criticised, others with overdoses or incompatibles are given for criticism, etc., the idea of this course being to make the student alert and critical to every prescription with which he deals.

8. *English.* A short course of about 50 hours is given in conversational English as used in a dispensary between a doctor and the dispenser.

From the above outline (based very much on the British Minor examination) it will be seen that at the end of his training, the student should be well versed in both theory and practice of Pharmacy.

All the teaching is given in Mandarin, but in order to help the students' English, some of the notes are written on the blackboard in English.

The whole class has proved very keen, and we all feel that the course has been well worth the large amount of time we have put into it.

With regard to fees and cost of the course to the student, they are as follows:
Tuition fee:—$30 per term (two terms per year)
Dormitory fee:—$30 per year (approx)
Light fee:—$4 per year
Food:—$100 per year (approx)
Books:—$30 per year
Breakage fee:—$10 per year (returnable in part)
Athletic fee:—$2 per term.
Cheeloo Year book $2 per first year, $4 in graduating year.

Thus, exclusive of travel, a careful student should be able to get through the course on just over $250 per year.

Owing to our limited class-room laboratory, and dispensary space, we can at present only take in students in alternate years. Further, our teaching staff will not permit us at present running two classes (a first and second year) at the same time. Another graduate is joining the teaching staff this year.

Another class is being taken in this September, and we are hoping to take in 16 students (or possibly 20). The regulations for the new course are:

1. The course is one of TWO YEARS, open to men and women alike.

2. All students must be graduates of a 6-year Middle school.

3. All students must take the Cheeloo University Entrance examination in the following subjects:— (1) Tang I (2) Mathematics (3) Chinese (4) History (5) English and (6) Chemistry.

4. The entrance examination will be competitive, and, the class being limited to 16 (or 20) students, we shall choose the best 16 from the examination results, special emphasis being placed on Chemistry.

5. The admission examination may be taken not only in Tsinan, but also at the same centres at which other intending students take it.

Already we have over 40 applications for the new class, many of our Mission hospitals being desirous of sending students or one of their graduate nurses to us for training. The new course without our advertising it much is bringing in many applicants.
Of the eleven men trained previous to 1929, out of a possible 53 years of service since their graduation, no less than 48 have been spent in the service of our Mission hospitals.

The present graduating class represents the following provinces:

Shantung 5, Honan 1, Kiangsi 2, Fukien 1, Anhui 1, Shansi 1, and Hupeh 1.

For the 4 men who are seeking posts we have had many applications and unfortunately the supply is totally inadequate to meet the demand.

For Mission hospitals who wish to have such a man trained, we would suggest that the surest way to get such a man is to find a reliable, honest and keen Christian Middle school graduate, help him with part of his course expenses on the basis that he returns to the hospital after graduation.

The commencing salaries of graduates are about $30 per month with room, and often with board too, but of course, salaries vary with the locality. In places like Shanghai we have our graduates getting anything from $70 to $120 per month, and to any but those who have the real spirit of Christian service to their own hospital, the temptation to go to such lucrative posts is great.

Finally, but by no means least in importance (rather the greatest of all), we are trying our best to develop the moral and spiritual lives of the students we train. In any dispensary, to any but men of real Christian honesty of spirit, the temptations to dishonesty are many. During their course with us, we have voluntary Bible classes and group meetings with our students in which we discuss together the many religious difficulties and problems that confront young China today, and above all we try to emphasise that only as the life is built on the sure foundation of Jesus Christ and His principles can any man become a real patriot and help to Society. The development of life-long friendships between us and our graduates during their course, and afterwards by periodical letters has made this work well worth while, for not only are we seeking to meet a long felt need by our Mission hospitals in supplying them with well-trained Pharmacists, but at the same time we are endeavouring to give to them men who are also full of the true Christian spirit of service to their fellow-men.
AN UNUSUAL CYST

Under this caption we published in the Journal of May, 1930 (C.M.J. xlv, 172) an account of a cyst of the frontal region by Dr. Snell of Soochow accompanied by photographs of the tumour. We have now received from Dr. Snell a copy of his correspondence on the subject giving a detailed pathological report. We print this below. As the letter contains a brief resume of the history we need only refer readers to the original paper for a fuller account of this extraordinary case. We are reproducing however the original pictures of the tumour.—Editor.

Dear Dr. Snell,

Dr. Bloodgood has referred your interesting reprint to me for study. It is quite unusual. We have nothing in the laboratory approaching it. The patient is a Chinese male farmer, age 59, who carries a huge tumor attached to his right frontal region. Eight years ago he had a severe attack of pain in the right eye for twelve days. A year later another attack came on and after incision dark fluid came out. Some months after, a small growth appeared on the upper eyelid which slowly and progressively enlarged up to about a year ago when it was a less than half its present size. The growth during the past year has been very rapid. There has never been any pain associated with the tumor.

At operation, December 17th, 1929, under novocaine anaesthesia, the wall of cyst was found to be intimately attached to the cranial bone. The cyst contained a large quantity of dark fluid and a great many fine shining particles. The emptying of the cyst revealed a large cavity in the frontal region of the cranium. This cavity was 6 cm. deep, the dura forming the
posterior and lateral walls. Below was the thin remains of the orbital ring, the roof of the orbital cavity serving as a base to the cyst cavity. The right, left and superior borders were formed by the frontal bones to which the cyst wall was firmly and strongly grown. The epithelial surface was rubbed with gauze and with a curette and touched with strong iodine. The atrophied eye was enucleated together with all the mucosa and lidmargins.

The cavity left by the cyst was soon filled by the dura coming forward and on discharge of the patient there was only a slight indentation at the lower margin.

In the comment on the above history and operative note you dismiss the eyelid as the origin for the tumor since it would have then hung by a pedicle from the lid. The right frontal sinus is assumed as the most probable origin of the cyst.

Two diagnoses are suggested to me by the above data; Dentigerous cyst and mucocele. The age of the patient and the location of the tumor was against dentigerous cyst. The largest age incidence of the dentigerous cyst is about the time of second dentition from twelve to twenty-five years. Kleider (Über Keiferzysten, Inaug. Diss. Jena, 1902) however, mentions two cases of seventy and seventy-three years in which the wisdom tooth was affected. The location, the frontal sinus, points to mucocele, rather than to dentigerous cyst. Henke—Lubarsch reports the occurrence of dentigerous cyst arising from misplac-ed toothbuds in the fossa canina, in the hard palate, vomer, nasal cavity and floor of the orbit (Handbuch der pathol. Anatomie IV, II, page 414.) But G. W. Howorth, in his Hunterian Lecture on Mucocoeles, (Lancet-1921 II, pp. 744-746) contends that many cases recorded as bone cysts in the region of the orbit and accessory sinuses would appear to be true mucocoeles.

I am of the opinion, then, that this case is an amazing example of that rare group of cysts called Mucocoeles. Up to 1923, only about one hundred cases were reported in the literature. Mucocoeles are produced by an accumulation and blockage of mucus in any of the parasinuses, although rarely the ethmoids. The bony walls of the sinus are thinned out and distended causing the roof of the orbit to give way usually just behind the trochlear fossa, displacing the eyeball downward and outward. At first, the swelling is hard and bony but as
the bony shell is thinned parchment crepitation may be elicited and later definite fluctuation. There is no tenderness or pain on manipulation. The skin is not adherent, the contents of the cyst vary. Usually there is a thick glairy opalescent and almost gelatinous fluid of varying color. The shining particles which you found at operation are probably cholesterin crystals. Cultures of the contents are usually sterile, when infected, the cyst is called a pyelocoele.

The growth is slow and painless except in the beginning. The duration is lengthy, in certain cases as long as 20 years. The growth may however, remain stationary for many years. Garretson (Laryngoscope 37:350'27) reports cases occurring between the ages of 35 and 85. This age incidence differentiates the mucocoeles from dermoids and meningocoeles which occur much earlier and are congenital in origin.

Under etiological factors are mentioned chronic sinusitis and traumatism.

Pathological Report. December 15, 1930

Gross Specimen. An oblong empty sac thirty by twenty centimeters in diameter covered by thick grayish corrugated skin about one half centimeter thick. The lining is a thin wrinkled membrane, in places covering distended blood vessels and brownish molelike excrescences varying in size from three millimeters to one centimeter in diameter. Other raised areas show a brownish orange discoloration. The remainder of the inside of the cyst wall is smooth. On the outside one small area of the skin is ulcerated.

The following blocks were taken for microscopic section.

Block 1: Area 4 cm. from edge of specimen containing skin and normal appearing lining membrane.

Block 2: Area of ulceration of the skin about 7 cm. distal to No. 1. On the inner surface an area of dilated veins is present.

Block 3: Taken through an area of brownish coloration of the inner wall of the cyst.

Block 4: An area containing a molelike growth of the inner wall.

The fluid contents of the cyst, a sample of which is included in the small vial, contain a heavy sediment filled with shining crystals. The fluid is a brownish orange liquid of watery con-
sistency. Microscopically cholesterin crystals and cellular detritus are found.

Microscopic Description:

1. This section through the wall of the cyst shows the skin of a pigmental person well supplied with sebaceous glands lying in a dense fibrous stroma diffusely infiltrated with round cells, predominantly plasma cells. There are a few mast cells and lymphocytes. The cellular infiltration is marked about each hair follicle. In the periphery of the section is seen a small sebaceous cyst. Adjacent to the inner wall, running in streaks parallel to the surface are lines of round cell infiltration. Upon the surface, in a few places, remains of epithelium can be detected, the inner lining of the cyst.

2. This section shows an area of ulceration in the skin densely infiltrated with round cells. The entire tissue is quite vascular, all vessels showing a perivascular round cell infiltration. Bordering the inner surface is a zone of hemorrhage. Above this are numerous dilated vessels and small areas of hemorrhage. No epithelial lining is found.

3. This section through a brownish area of the lining membrane reveals a fibrous wall quite vascular and containing many areas of round cell infiltrations. Immediately adjacent to the inner wall are numerous small areas of hemorrhage in which lie macrophages loaded with blood pigment. This explains the discoloration. A small strip of stratified squamous epithelium is found, the remains of the epithelial lining of the cyst.

4. The point of interest in this section is found on the inner surface of the cyst wall in a baylike indentation of which is seen desquamating squamous epithelial cells. This is clear evidence that the diagnosis of Dr. Snell: A cyst arising from the frontal sinus, is correct. The bone cyst of Osteitis fibrosa cystica is not lined by epithelium. Adjacent to this area of epithelium in the cyst wall is that surface which in the gross appeared to be a mole. On microscopic scrutiny it is seen to be a superficial chronic ulcer heavily infiltrated with macrophages fat with blood pigment.

Microscopic Diagnosis:

Fibrous hemorrhagic wall of an epithelial lined cyst covered by a pigmented epidermis. Mucocele of frontal sinus.

Richard F. C. Kegel.
"An Unusual Cyst"
Case 24065—Mucocele of Ethmoidal Sinus
(Left)
Huchow General Hospital, Huchow, Chekiang
(Photo by S.P.T.)
Judging from the scanty records in medical literature bony cysts of accessory sinuses are rare. So far as I know none have been reported from China.* The following is the first case of mucocele of ethmoidal sinus that we have seen and because it has presented many points of interest, we are reporting it.

Case 24065—Male, farmer, 23 years old, complained of protrusion of left eye of four years duration.

P.I. Four years ago, while chopping, a piece of bamboo struck the bridge of nose, causing severe pain which lasted for four days. There was no apparent wound at site of blow. One year later, he complained of pain in left eye especially after exertion, and associated with occasional redness and lachrymation. Six months later, the eye began to protrude and although this protrusion was gradual it was not associated with pain. One year ago, he, again, felt pain in left eye after two days of hard work. Following this the sight became cloudy. The right nostril became partially blocked and the left completely obstructed. Appetite good, bowels regular.

P.H. Could not recall having had diseases of childhood. Had malaria four years ago. Denied venereal diseases.

F.H. Unimportant.

P.C. Well nourished and well developed young adult of clear mentality was admitted on October 23rd, 1930. The left eye was pushed forward, outward and downward by a firm immovable mass extending from the upper lateral aspect of nose outward to the middle third of orbit. At the time of admission two-thirds of the eyeball was out of its orbit. Left nostril was completely obstructed—the right, partially. Vision of left eye—only light perception remained. The bulbar conjunctiva was moderately congested but more so in the lower inner quadrant. The pupil was larger than that of the right eye but reacted to

*But see foregoing notes on “An Unusual Cyst.”—Editor.
light and accommodation sluggishly. Nothing abnormal found on cornea. The anterior chamber of each eye was within normal depth. Tension normal. Fundus of left eye showed a swollen, projecting, whitish disc with constriction of vessels. The retinal color was paler than usual. Rhinoscopy revealed a marked deflection of septum to the right caused by a large smooth, pinkish mass blocking the left nostril completely both in front and behind. The right nostril was also partially blocked. Oropharynx was red and dry. Tonsils were not enlarged but chronically inflamed. Larynx normal. Ear drums retracted. Chest—symmetrical and fairly well developed. Lungs, heart and abdomen normal. Neither spleen nor liver palpable. Epitrochlear and inguinal glands were slightly enlarged. Extremities normal.

Laboratory Findings: Blood—R.B.C. 4,800,000; W.B.C. 9,100; Hgb. 85%; Polymorph. 80%, S.L. 16%, L.M. 1%, Eosin. 3%; Thick and thin smears negative. Wassermann and Kahn tests 4 plus.

X-Ray Report: “Rt. Side—Frontal sinus, poorly defined. In the midline shadow extends one inch above the orbit. Below and to the outer side the shadow is much darker—probably ethmoid. To the median side of this shadow the nasal bone shows erosion. Maxillary sinus—foggy, but outline distinct.

Lt. Side—Frontal sinus extends to the same height as its fellow but on account of the absence of the inner third of the orbit its shadow below merges with the shadow of the orbit. The orbit is irregular in outline and along the inner side there is no limiting wall. A dark indistinct shadow, pushing to the right of the median line and extending well below the floor of the orbit, appears as a continuation of the orbital shadow. Maxillary sinus—the outline can scarcely be made out.”

Operation was performed on patient under ether anesthesia and a postnasal tampon was inserted into the nasopharynx. The operating field was prepared with iodine and alcohol as per general surgical routine. An incision was made from the middle third of left supra orbital margin curving around the inner canthus to the side of the bridge of nose. The periosteum was incised and elevated. A deep bluish soft tumor in the ethmoidal region was seen. The ethmoidal bone was very thin and brittle and in attempting to remove it the tumor, which
proved to be a cyst, was ruptured. A straw colored gelatinous fluid came out in high tension and in large quantity. After drying the cystic cavity with gauze it measured 7 cm. vertically and 4½ cm. horizontally and 6 cm. antero-posteriorly. The cystic wall was very thin, so it was removed partially by dissection and partially by curettage. The turbinate bodies of left nostril were found to be atrophic in appearance. The cavity was packed with iodoform gauze and drained through an opening made at the middle meatal region. The external wound was closed with silk stitches. On the second day after operation, the left eye sunk into its orbit and patient could count fingers at three feet. Much edema of eyelids and area around the wound were noted. The iodoform gauze was removed and replaced by a rubber tube. On the eighth day after operation all stitches were removed. Looking into the cavity from the nose, it was found to be dry. Fundus of left eye revealed a small round disc of clearly defined margin with slight degree of hyperemia. Vessels of retina were 2 to 2. The retinal color seemed to be normal. Vision was 10/200. A month later, the eye was found to have a vision of 20/50. The hyperemia of the disc was gone. No change of retinal color was found. The wound had healed. The patient was then discharged. A month after discharge, he was reexamined, and his condition was found to be the same as that of the previous month.

**Diagnosis.**—The history of slow growth, limited to an area immediately above the inner canthus, in a young adult, suggested a benign tumor of ethmoidal sinus, although the huge, firm swelling pushing the eyeball out of its orbit was not unlike malignancy. The latter growth, however, progresses more rapidly, causes more pain and involves the optic nerve much earlier. The X-Ray report of absent inner orbital wall points to osteoma, but the operative finding of soft tumor containing straw gelatinous fluid, which showed no growth on culture, disproved it. Moreover, X-Ray of osteoma usually gives a very opaque picture of the region involved.

**Etiology.**—Mucocele, while rare in the accessory sinuses, is quite common in the middle turbinate. Frequently, while operating on hypertrophied middle turbinate cases, big air cells of that body were found. Sometimes mucopus is noted in the big air cells, and again, none at all is seen.
The next order of frequency is the ethmoidal sinus, but more rarely observed in sphenoidal, frontal and maxillary sinuses. Logan Turner doubts the existence of true mucocele in the antrum, since many cases of cystic growth reported were of dental origin. Watson Williams claims that the relative frequent occurrence of mucocele in ethmoidal sinuses might probably be due to the greater secreting activity and richer glandular supply of the lining mucosa, as compared with that of frontal and maxillary sinuses, their much smaller apertures of exit and their more direct exposure and liability to catarrhal inflammation. Skillern reports that the cystic formation is more common in anterior ethmoidal cells than in the posterior group of cells. The above case is evidently a cystic distension of both anterior and posterior ethmoidal cells, as the enlargement pushed the eyeball forward anteriorly and obstructed the nasopharynx posteriorly.

The exact cause for such a cystic formation in an accessory sinus is still obscure but it usually arises as a result of retained secretion caused by complete obstruction of its outlet. This obstruction may be due to injury but is more commonly due to nasal catarrh. Whether or not the blow inflicted on the bridge of the nose had anything to do with the origin of this growth can not be certain. It is not only possible but fairly probable that the blow did interfere with the drainage of the ethmoid cells and thus predisposed to mucocele formation. Moreover, the atrophic appearance of the middle turbinate and the absence of polypoid or chronic inflammatory conditions of nasal mucosa prove this assumption. The value of positive blood Wassermann has no bearing, we think, on etiology. A gradual growth, hidden in a sinus like the ethmoid, producing remote symptoms, makes it impossible to more than theorize as to the cause and exact time of origin.

REFERENCES


Watson Williams—"Rhinology," 1910, p 249.

Skillern—"Accessory Sinus of Nose" 1916, p 343.
Editorials

GLANDULAR FEVER

We have to thank Dr. Hasselmann for the comprehensive paper on Glandular Fever which takes up a large part of this issue. The article is longer than we ordinarily allow space for in this Journal but the subject is of so much importance that no objection can be taken to this.

On one point Dr. Hasselmann is not quite correct and inadvertently he does an injustice to his predecessors. This is not the first time that glandular fever has been reported from the tropics and we believe it is correct to state that some reference to it will be found in nearly all textbooks of tropical medicine, certainly in those printed in the English language.

Referring to China only, an account of an epidemic in Swatow has been described in the pages of the Journal by the late Dr. P. B. Cousland (C.M.J. xxiv, 24). Dr. Cousland's interesting paper on this subject though not printed till 1910 referred to an epidemic dating back to 1901. Yet another epidemic was described by Dr. Chalmers Dale of Shanghang, Fukien, on the Kwangtung border, not more than a degree north of the tropics, (C.M.J. xxviii, 385), the outbreak taking place in the year 1914. These as far as we know are the only recorded epidemics of glandular fever in China but there is some reason to believe that sporadic cases are not very uncommon. In view of the few centres from which reports of diseases reach us, epidemic conditions where life is not threatened very easily escape notice, and it may be that these are not as rare as the published accounts may suggest. Apart from reported cases the late Dr. John Anderson gave us personal information of sporadic outbreaks of glandular fever in Hongkong.

With the exception of Dr. Anderson's unreported cases where the examination showed typical findings, we have no accompanying statements of blood conditions. The lack of these does not however in any way invalidate the value of the reports as contributions to the epidemiological history of the
disease. To suggest this would be on a par with discounting the early stories of plague epidemics before *B. pestis* was discovered. The disallowance of Dr. Hasselmann's claim that his cases constitute the first report of glandular fever from the tropics does not however minimize the value of this interesting paper which is we believe the first full report of such cases from a pathological point of view out here. It deals mainly with the disease from the sporadic rather than the epidemic standpoint.

The diagnosis of glandular fever occurring in epidemic form is easy and it is hard to believe that any error can arise in the recognition of such an epidemic. When sporadic cases occur the story is entirely different and considerable acumen may be required to arrive at a true diagnosis. That this is correct we know from the fact that cases are sometimes treated by skilled physicians for considerable periods without a true realisation of the nature of the illness being reached. We have long suspected that such cases are to be met with in China and it may be that they are more common than we realise, and go but to swell the unfortunately large group of undiagnosed fevers or that they are classed under the more common forms of anginal disease. We welcome Dr. Hasselmann's paper as giving us an exhaustive description of glandular fever as a standard for reference in the Far East and we trust that the physicians through China will keep the possibility, if not the probability, of meeting this disease in view, and will thereby be able to arrive at a correct diagnosis.

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**MUCOCELES**

These tumours are of rare occurrence and escape anything but a passing and very brief notice in even the largest surgical textbooks. It is therefore especially interesting that we are able to record in detail two examples in the current issue of the *Journal*.

Mucocelle of the frontal sinus is particularly rare and we believe that we are correct in stating that no such example as
that described under the caption "An Unique Tumour" in the *China Medical Journal* of May, 1930, by Dr. Snell and here reproduced with complete pathological report has ever been described.

The ethmoidal mucocele described and pictured by Dr. Ts’en is a less rare variety than that of the frontal sinus, but is uncommon enough and few of us in China have seen examples of these tumours. It is not our business to be always looking out for rarities, but from time to time puzzles of this nature reach most surgeons in this country and it is well to have the possibility of such tumours in mind.

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**CHINESE MEDICAL STUDENTS IN THE U.S.A.**

We wish to call special attention to the letter and statement which we print under *Announcements* in this issue, and which calls attention to health and financial difficulties of medical students in the States. The Committee, whose names are given, are many of them well-known here and their desire is to make the residence of Chinese medical students in their country as smooth as possible.

The same applies to students going abroad to Great Britain or Europe and especially at this time when the phenomenal fall in exchange has made the position more than usually difficult.

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**CORRIGENDA**

Dr. M. L. Hu asks us to insert the following alterations to the paper on Lateral Sinus Thrombosis of Otitic Origin appearing in the *China Medical Journal* of April, 1931.

Page 302, line 24. For 40.6°C read 41.6°C.
Page 307, line 7. For March 17th read March 18th.
Page 307, second line from bottom. For pulse 178 read pulse 158.

We have been asked to correct a statement in the March issue that Dr. H. W. Wade was formerly Director of the leprosy work at Culion his *official* position there was that of Chief Pathologist to the Colony.
The South China Branch of the China Medical Association has held two regular meetings this year. The first meeting was held in Leung Kwong Hospital on Jan. 30th. The following officers were elected for the year:

- President: Dr. A. C. Siddall
- Vice president: Dr. Y. P. Chan
- Secy-Treas.: Dr. C. M. Bau
- Chairman of Program Committee: Dr. W. W. Cadbury

The program for the meeting was as follows:

**Cases demonstrated.**
1. Mastoid operation
2. Splenomegaly
3. Lupus erythematosisis.

**Papers read.**
1. Nephritis. Dr. J. F. Karcher
2. Report of Bangkok meeting.
   a. Tropical typhus and Beriberi. Dr. W. W. Cadbury.
   b. Malarial control. Dr. Hartman.

The second meeting was held in Chung San Hospital on Mar. 27 at 4:30 p.m. The program for the day was:

**Clinical cases:** A case of Darier's disease
A case of foreign body in the bronchus.

**Papers read:**
- Dr. Basler: The centre of gravity in human body.
- Dr. Leavell: The treatment of lobar pneumonia due to pneumococcus infection.
- Dr. McClure: Fevers of obscure origin.
- Dr. Kudicke: Lantern slide demonstration on sleeping sickness.

We had quite large attendances for the meetings both by members and visitors.

C. M. Bau
Secy-Treas. of the Branch.
Announcements

THE WELLCOME FOUNDATION MEDICAL AND CHEMICAL RESEARCH BUILDING

The Wellcome Foundation Ltd. is about to erect a new medical and chemical research building at the corner of Gordon Street and Euston Road on the site, 225 feet by 135 feet, now partly occupied by their Bureau of Scientific Research. During many years the Foundation has maintained medical and chemical research laboratories, but recent developments have made it necessary to co-ordinate and extend these activities. The new building will furnish the additional accommodation required, and be provided with the most modern research equipment.

CHINESE STUDENTS

419 Fourth Avenue New York
March 28, 1931.

My dear Dr. Maxwell:

The Medical Committee of the Committee of Reference and Counsel have been reminded by sad experiences of the fact that medical students coming to this country from China frequently have most disastrous and difficult experiences, both through lack of preparation and because of inadequate financial resources. The recognition of this difficulty and the desire to be of genuine help to those who come to us from other countries has led to the preparation of the enclosed statement. The Committee has asked us to forward this to you in the hope that you might give it publicity through the columns of your Medical Journal.

Experiences of the sort which some students have had in this country react most unfavorably both on the future usefulness of the individual, and upon his attitude toward the medical profession and toward the citizens of the United States.
We give herewith a list of the members of our Medical Committee:

Dr. P. H. J. Lerrigo    Dr. J. C. King
Mrs. E. B. Cotton       Dr. W. W. Peter
Dr. R. L. Dickinson     Dr. T. D. Sloan
Dr. E. M. Dodd          Dr. J. G. Vaughan
Canon S. Gould          Dr. Mark H. Ward
Dr. E. H. Hume          Mrs. J. H. Warnshuis

You will see that many of them have been engaged in missionary work in China and are all of them most enthusiastic for raising the grade of the medical profession. We are sure you will recognize their desire to be of utmost help.

Faithfully yours, For the Medical Committee:

J. G. VAUGHAN, Acting Chairman.
LESLIE B. MOSS, Secretary.

To Our Chinese Confreres

Medical men in the United States, and particularly those having deep interest in the missionary enterprise, are always eager to welcome those from abroad who may be able to come to the United States for graduate study and clinical work. We trust that the attractive facilities for medical study to be found in some of our American centers will continue in the future as in the past to enrich the professional lives of our friends in the Orient. We stand ready to help by our counsel, and will also do what we can to open positions for clinical experience.

We feel, however, that a note of warning should be sent to those contemplating the expensive and arduous task of sojourn for medical study in the United States. Living costs are high, and tuition costs for courses running the school year amount to a considerable figure. It has been our sad experience to find, also, that not infrequently our Chinese and Korean friends in their attempt to economize in living expense, bring about conditions of ill health that are most distressing.
In view of these facts we would like to urge anyone of limited means who is contemplating a trip to the United States for medical study to consider most carefully whether he can not get just as good, if not better, clinical contacts and help in post-graduate study at Peking Union Medical College, or some other high-grade medical school in the Orient.

If after counselling with American friends in China and corresponding with responsible agents in America is seems best to come here for graduate study, we would urge that the following requirements be faithfully met.

1. One's professional ability and earlier training must be firstclass. One need not be a genius, but he should have a type of training and professional ability that will be well rated by the medical men with whom he must be associated in America.

2. It is essential that one be quite competent to understand and speak English fluently. This fact should be certified by some American or English friend.

3. One's financial ability to meet not only travel expense to and from the destination in America, but also to meet tuition fees and living expense while in America should be guaranteed. This is the minimum. Of course one should have additional funds to meet such emergencies as sickness.

4. One's health must be certified by a searching physical examination including careful stereoscopic X-rays of the chest. There must be no question of tuberculosis present.

In putting these rather difficult barriers before our friends whom we would delight to see in the United States, we wish it to be understood that our only desire is to see their best interests furthered and to save them from unnecessary hardships and distress.
The Second International Congress for Light
will be held in Copenhagen from August 15th to August 18th 1932

The subjects selected for discussion are:

1. The role of pigment in light biology and the therapeutic effect of general light baths.
   Principal Speakers: Dr. Brody (France).
   Prof. Miescher (Switzerland).

2. How is the action of the general light bath in Tuberculosis to be explained?
   Principal Speakers: Sir Henry Gauvain (England).
   Prof. Jesionek (Germany).

3. Helio-climatological research in relation to Public Health—its organisation and physiological basis.
   Principal Speakers: Prof. W. Hausmann (Austria).
   Prof. A. Rollier (Switzerland).

   Read by Dr. Saidman (France).

The names of the other leading speakers will be published in a further communication.

Further any member of the Congress may also read papers on a suitable subject selected by himself provided he complies with the rules of the Congress.

The Committee venture to hope that a large number of doctors and physicists from different countries will take part in the deliberations of the Congress and in this way encourage and organise international research work dealing with the therapeutic applications of light.
WILLIAMS-PORTER HOSPITALS
Tehchow, Shantung, China

This is to us an entirely new suggestion of how to bring the needs of a hospital home to its supporter. It has certain very evident advantages over a formal report and we think the superintendents of other hospitals will appreciate having this brought to their notice. It has also the advantage which we trust will not be neglected of leaving the hospital free to publish a separate Medical report without going to the expense of getting out two pamphlets.

Editor.

Jan. 1, 1930 to Jan. 1, 1931.

HALF MINUTE SUMMARY
(We realize minutes are valuable)

Outstanding Events:
Hospital used as base hospital for every advancing and retreating army.
For three months emergency war hospital in Confucian temple maintained.
Cessation civil warfare.
Good beginnings of a democratic central government.

Material Items:
Towne-Goodnow Kitchen and Dining Room Pavilion for Nurses completed.
Supplementary Electric Light Plant added. X-Ray Plant started.
Third attempt for deep well. (Good water essential).
Hostel and other buildings renovated and painted.
Three additional rainwater cisterns built.
Building for Electric Light Plant and Incinerator added.
Automobile found to be invaluable in extension work.
(Funds needed for upkeep).

Community Touch:
Hospital now controlled by Board of Managers.
(A number of leading men of city serving on Board).
Branch Dispensary resumed (for communities with no other medical aid).
Health campaigns and Vaccinations included.
Only Hospital in densely populated community of over two and a half million. (Inpatient cost, inclusive of nursing, food, &c. averages 30 cts. a day).
Facts and Figures:

Four graduate nurses and 26 pupil nurses.
Major operations 301; Minor operations 719.
Inpatients; 796 men and 296 women and children.
Dispensary Calls; 7,517 men and 3,805 women and children.
Laboratory tests, &c., 2,827.

Hospital Religious Work and Branch Church

(Connected with Hospital activities)

Workers: Chaplain, matron, one evangelist on follow up work.
Twenty three taken first or second steps to enter Church (a gain of 46%).
Depts. of Church School: Kindergarten, Intermediate, Adult.
Women's Society.
Daily Chapel Exercises (Voluntary and well-attended).
Classes for reading and instruction of workmen.
Stereopticon in wards; phonographs.

Nothing better than a New York Draft. It proves this ½ Minute well spent.

Staff of

WILLIAMS-PORTER HOSPITAL.

F. F. Tucker, M.D., Tehchow, Shantung, China.

AMERICAN PRESBYTERIAN HOSPITAL, HOIHOW, HAINAN 1930

Staff: Drs. N. Bercovitz, H. Y. Cheong, S. Y. Tang

Nurses. One Foreign, 5 Chinese graduates, 12 pupil nurses.

Inpatients 2,345 Outpatient attendances 17,884

The report opens with a brief review of the history of the hospital emphasizing the remarkable work done by Dr. H. M. McCandliss in the 41 years that he spent in medical missionary work in Hainan and in whose memory a new building containing operating suite and x-ray plant has recently been erected.

There follows a section on the improvements made in the course of the year to the hospital buildings and outlining the present more urgent needs.
The report includes some very interesting medical notes from which we gather that the prevailing medical ailments apart from tuberculosis are malaria, amoebic dysentery, hookworm, and stomach and duodenal ulcers. So severe is the malaria that at least 15 children were brought to the hospital in a moribund condition from subtertian fever. There were no serious epidemics in the course of the year.

The maternity department reported 712 cases admitted during the year. The surgical department reports a busy year but to an old hand it seems a little queer that x-ray should be considered of importance in the diagnosis of vesical calculus, we can hardly believe we ever missed a case before x-ray came on the scene.

It is very encouraging to note that systematic work for lepers under proper conditions in a new colony is likely to be arranged, this, like leper work in most parts of China is long overdue.

The report is well illustrated but falls off badly in statistical tables. There are no tables of diseases and that of operations leaves much to be desired both as to spelling and description. For example, where "Tumours" end is far from clear and Excision of the Parotid is simply not done as an ordinary surgical procedure. An important hospital such as this deserves something better in the way of statistical tables and might contribute considerably to our knowledge of diseases in China.

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**PAGODA HOSPITAL, FOOCHOW. A.B.C.F.M. 1930**

**Staff:** Dr. C. L. Gillette.

**Nurses:** Three graduate Chinese, two student nurses.

Inpatients 582. Outpatient attendances 5,176.

A brief but interesting report a large part of which is taken up with a table of inpatient diseases. There is one very striking feature in this viz. the number of cases of beri-beri admitted to the hospital. These total 56 and with the exception
of syphilis (57) form the largest group of inpatients. They constitute nearly 10 per cent of cases admitted.

Among diagnoses that seldom figure in hospital lists in China was one of "Tiger bites."

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**DIONG-LOH HOSPITAL, FU. **A.B.C.F.M. 1930

**Staff:** Dr. E. M. Ngu.

Nurses. Two graduate Chinese, two student nurses.

Inpatients 148 Out-patient attendances 7,668.

This hospital is run in connection with Pagoda Hospital details of which are given above.

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**AMERICAN CHRISTIAN HOSPITAL, MESHED, PERSIA** 1929-1930 A.P.N.

**Medical Superintendent:** Dr. R. E. Hoffman

**Beds 50**  **Inpatients 855**  **Outpatient attendance 36,782**  **Leper Treatments 9,100**

This is quite one of the best hospital reports that has come through our hands, interestingly written, printed on excellent paper, well illustrated and altogether the sort of report which it is a pleasure to handle and read. It should commend itself and the work to the home constituency and is a valuable record from a medical point of view.

The report contains an interesting account of the progress of scientific medicine in Persia and deals with the difficulties so ever present in this country also of accommodation and finance. A very complete list of diseases of inpatients is given and a further table of operations performed.

An excellent survey of the work among the lepers appears in the report. It is carried on in an old established leper colony
where for the past four years regular treatment has been established by the Mission. While much in the way of actual cure is not claimed, the unasked for statements of the lepers themselves are the best testimony for the value of the treatment and the improvement of their condition. Many have come on foot the thousand miles from Tabriz begging their way as they came, when they learnt of the new hope of relief from their sufferings.

The report closes with an interesting account of a medico-evangelistic tour and the work that this entailed.

ANNUAL REPORT OF THE WEST CHINA COUNCIL ON HEALTH EDUCATION, 1930

This report which presumably is by the energetic Dr. Crawford is full of interest and encouragement, so much so that we see no reason why the writer should have concealed his identity. The only signature is to the Foreword by the Chairman, Dr. A. E. Best.

An outline of the aims and objects of the Council is given in the opening pages of the report and classifies its activities under eight heads: Translation, Publicity, Campaigns, Publications, Welfare Work, Research, Small-pox Eradication, Health Demonstration Area. Something has been attempted and quite a little has been accomplished along all these lines except that of Research during the past year, and the greater part of this report is taken up in the detailed account of the work.

The activities of the Council have been carried on at a time of considerable difficulty and not a little political disturbance and it is to be congratulated on the amount it has accomplished despite these adverse circumstances.

The work of tract publication and sales has been specially notable, no fewer than 260,000 tracts having been sold during the year.

The report closes with a brief financial statement.
REPORT ON A CASE OF CARBOLIC ACID POISONING

JULIAN TAYLOR, M.S.

The case is reported in order to show the extreme rapidity with which carbolic acid may be absorbed through the skin, and that prompt treatment may be effective in reducing the intensity of the consequent poisoning.

On September 18th, 1930, a nurse had the misfortune to slip on a wet floor, upsetting in her fall a vessel containing a moderate quantity of "pure carbolic," i.e., acidum carbolicum liquefactum, B.P. The drug was spilt over a considerable area of her clothing, but as the accident occurred near an operating theatre where an operation was about to begin, the surgeon, Mr. R. M. Walker, was able immediately to remove the clothing and to apply large quantities of methylated spirit, the traditional antidote for carbolic acid burns. There was no question of associated head injury and at first the subject was able to assist in the removal of her clothing and to ask that spirit should be used, also oil for her eyes. In a very short time she was unable to sit up and her consciousness rapidly became clouded, and before three minutes from the time of the accident she was completely unconscious. Transferred to a ward, she was seen by me, in consultation with Dr. A. S. Wesson, less than ten minutes after the accident. She was then in deep coma, her four limbs and her face were continuously twitching, her pupils were semi-dilated and fixed, her colour was a greyish-blue and was visibly deepening, her respirations were laboured and bubbling, her mouth and nasal cavities were full of frothy mucus and no pulse could be felt at the cardiac apex or wrist. She had every appearance of being moribund. Her clothing had now been completely removed, she had been washed all over with large quantities of water and her conjunctivæ had been irrigated with normal saline. Her extremities rapidly cooled and her condition was clearly deteriorating. Thirty ounces of normal saline containing one drachm and a half of sodium bicarbonate
were infused into a vein. During the infusion a definite effect was seen, inasmuch as from having been completely inert she began to toss about and to be difficult to restrain and at the same time to make inarticulate cries. The twitching ceased, the pulse began to be occasionally palpable at the wrist and by the time the venesection wound was being closed had definitely returned, though still small and very frequent. The insertion of stitches made her cry loudly, though she was still unconscious.

In about two hours' time she was completely conscious and reasonable. During the following twenty-four hours she vomited incessantly and continued to do so occasionally during the three days succeeding the accident. Her urine was at first dark green and contained albumin; it remained green for two days and albuminous for three. It was never diminished in quantity and microscopic examination failed to show the presence of any casts.

The burns, which were all superficial, were treated by the tannic acid method and, except for a small area on the right arm, remained almost everywhere dry. Nowhere was the whole thickness of the skin destroyed and only in the patch referred to were red papillae visible.

The actual sites affected were the whole face and neck, the whole length of both upper limbs, the chest and upper abdomen, and small areas on the back and both lower limbs. The total area subsequently measured proved to be 3,340 square centimetres.

It is noteworthy that although for the immediate treatment of such an accident she could hardly have been more favourably placed (a surgeon with assistants and nurses being present at the time of the accident) and although the carbolic acid was washed off so promptly that nowhere the whole thickness of the skin was destroyed, yet absorption was so rapid that she was in deep coma before three minutes had elapsed.

The changes in the skin were also of interest, the dead grey white of ischaemia in the earlier minutes changing to a dusky purple with the onset of general cyanosis. With the disappearance of the cyanosis the purple gave place to a dull red, suggesting vasomotor paralysis, and this in turn was followed by the brown discoloration of the dead cuticle. The shedding of
the cuticle proceeded from the seventh to the fourteenth day, the underlying skin being then seen to have made a perfect recovery except in those patches where the deeper layers were affected.

The effect of intravenous saline was also striking, and is to be attributed either to dilution of the phenol content of the blood or to encouraging excretion by promoting a flow of urine, or just possibly to the presence of sodium bicarbonate. The change in the patient's condition while the infusion was taking place, from that of obvious decline to one of equally obvious improvement, was such that none of the observers had the slightest doubt that the improvement was the consequence of the treatment. It is partly for this reason that the accident is now brought to the notice of the Section. It is noteworthy also that she never had any suppression of urine such as may be a fatal consequence of carboolic poisoning. The traditional remedy of sodium sulphate was not used. It is stated by Sollmann that the combination of sulphates with phenol to form the innocuous sulpho-carbolate is so slow a reaction as to be useless where a rapid effect is wanted, as must usually be the case.

*Proceedings of the Royal Society of Medicine, November, 1930.*

*Note by Editor C.M.J.:—The danger of a rapidly fatal carbolic acid poisoning is perhaps not sufficiently recognised. We know personally of a case where a Chinese midwife died in a few hours from upsetting in a fall a bottle of liquified carbolic acid on herself.*

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**ACIDOSIS FROM THE CLINICIAN'S POINT OF VIEW**

Leonard Findlay, M.D., D.Sc., M.R.C.P.

Broadly speaking, acidosis may be looked upon as a disorder of metabolism accompanying many diseased processes. I would compare it in this respect with fever. In both, the disturbing factor, acid in the one case and heat in the other, is produced under normal conditions, and the abnormal state results from
a disturbance of the balance between production and loss. It cannot be too strongly stated that in neither case have we got to the root of matters by merely recognizing an increased accumulation of acid or of heat in the body. We are only detecting the general results of disordered action of the tissues, which is in no way pathognomonic of any particular diseased process, though there may be variations in degree and in type in different diseases. Hence to raise acidosis to the position of a clinical entity, far from being an advance in the classification of disease, as some writers would appear to think, is as retrograde a step as it would be to classify disease according to the presence or absence of fever. Testing for acidosis is, like taking the temperature, of help in deciding if there is any evidence of abnormal action of the tissues, and probably therefore of active disease. Good comparable examples of the value of the thermometer and of the test for acetonuria are tuberculosis and diabetes.

I admit that we may be forced occasionally to a diagnosis of febricula, but it is a confession of our ignorance, and a diagnosis of which, I think, we are always ashamed. In the same way a diagnosis of acidosis should be equally guarded against. It may sometimes be the only abnormality detectable, but that does not mean that we understand what is wrong with the patient. Our predecessors frequently spoke of death from hyperpyrexia when the temperature of the body was above a certain level, but hyperpyrexia as a cause of death is seldom heard of to-day, because it is known that it is not a means of differentiating one type of a particular disease from another, far less different diseases from each other. Nevertheless, it is found advisable in treatment to try to prevent the heat of the body from rising above a certain level, and it is without doubt equally advisable to control the accumulation of the acid elements in the blood and tissue juices, because the tissues have their optimum activity at a certain definite temperature and a certain definite reaction of the blood and of the fluids which bathe them.

*B. M. J., March 14, 1931.*
RESEARCH FOR A NON-HABIT-FORMING SUBSTITUTE FOR MORPHINE

The popularity of endocrine, vitamin and diverse synthetic medicinal products in recent years has tended to obscure the significance of active constituents derived from the plant kingdom. The greater number of dependable and useful substances of natural origin in the therapeutic armamentarium may be forgotten because of the emphasis placed on synthetic products offered by the chemical industry.

The subordination of interest in natural products is the outcome of recognized commercial possibilities of synthetic products rather than a limitation of opportunities for achievement along fundamental and practical lines. The sterility that has possessed this field is to be deplored. To-day, exceedingly few chemists and pharmacists concern themselves with the isolation and analysis of medicinal plant constituents. Some manufacturers prepare and market the few constituents that appear indispensable, but generally industry is indifferent to the investigation of new possibilities. Examples of rewarded efforts are nevertheless at hand. For instance, hardly any one would deny that the additional, though belated, efforts were not well spent on two of the oldest alkaloids, ephedrine and quinidine, which have achieved prominence and value.

Although the active constituents of many important medicinal plants are known, there is still plenty of room and opportunity for effective and creative work. The chemistry of most of the most important constituents remains unsettled, notable among these being morphine. The chemical structure and synthesis of this indispensable alkaloid still remain in doubt. Therefore it is news of more than usual interest that the Committee on Drug Addiction of the National Research Council announces a large collaborative research in alkaloidal chemistry by chemists and pharmacologists of this country. Apparently the present object of the committee is to prepare a non-habit-forming substitute for morphine that would yet possess the desirable actions of morphine. The ideal molecule, apparently some hybrid molecule, is to be built up out of the most desirable features of the morphine and codeine molecules. The experiment will be watched with much interest from many sides. If
it merely stimulates interest and work in the chemistry of alkaloids and other natural medicinal constituents, the effort will have been well repaid. Thorough investigation of the natural products is likely to prove more instructive and important for a selected materia medica than the multiplication of synthetics, which in many instances represent minor modifications of a single product.

J. A. M. A., March 14, 1931.

PALLIATIVE INTRAVENOUS INJECTIONS OF MORPHINE IN CANCER

H. Iacobaeus devoted a recent address at a meeting of the Danish Medical Society to the palliative treatment of inoperable cancer by intravenous injections of morphine. The histories of 8 cases treated in hospital show how varied and uncertain is the response of patients suffering from inoperable cancer to analgesics. Thus morphine, given hypodermically in a case of metastatic cancer of the spine associated with severe pain, gave comparatively little relief, whereas intravenously it acted like a charm. It was not equally successful in all the 8 cases. The procedure in one of his cases was as follows: Every morning at 10 o'clock, 1.5 cgm. of morphine was given intravenously. There was complete freedom from pain till 6 or 7 in the evening, when 3 cgm. were given hypodermically. Another hypodermic injection of 3 cgm. was given next morning. The action of the intravenous injection was more rapid, complete and lasting in this case than that of the hypodermic injections. In several cases he noticed that hypodermic injections which had failed to relieve pain when given alone did so when supplemented by an intravenous injection. In some cases the pain became less after the intravenous injections had been given for some time. This suggests that morphine so administered sooner or later reduces the capacity of the brain to register pain. The address was summed up as follows: When morphine is introduced direct into the blood, a more rapid, effective, and, in many cases also
The China Medical Journal

a more prolonged, response is obtained than from hypodermic injections. Much smaller doses can therefore be given by the intravenous route than are needed hypodermically.

Clinical Journal, February 18, 1931.

DENGUE
Experimental Researches on Dengue
Georges Blanc and J. Caminopetros

This long article gives an account of the experimental work carried on at the Pasteur Institute in Athens during the epidemic of dengue in that city during 1927-1928.

The new facts arising out of this work are given as follows:—

1. The serum of a dengue patient kept in the dark in sealed tubes at room temperature will retain its virulence for at least fifty-four days.

2. Man may suffer from an attack of inapparent dengue. During such an attack the blood is virulent and immunity follows.

3. The guineapig if inoculated with virulent dengue blood is not affected, but five days later its blood can be shown to be virulent.

American workers, in 1924, showed that Culex fatigans is not capable of conveying the disease which is readily transmitted by Aedes aegypti (Stegomyia). The authors worked with this species in Greece, and a very elaborate account of the methods they adopted in keeping and breeding the insect is given; this chapter is fully illustrated.

Mosquitoes captured in Athens and kept in captivity in the laboratory remained alive from October 9th to May 25th, or 228 days. (Some mosquitoes bred in the laboratory lived for 186 days.) The mosquitoes were fed regularly on human blood and laid numerous eggs.
Transmission experiments are described and full protocols given. In one interesting experiment two batches of mosquitoes were employed, one of Stegomyia and one of Culex pipiens. These mosquitoes had been fed on the same dengue patient and kept at a temperature of 22°C., for ten days. The batches were then fed on healthy volunteers; none of the eight volunteers on whom the pipiens fed suffered in any way, whereas the cage of Stegomyia infected eight out of eleven volunteers.

An interesting fact noted was that if the mosquitoes are kept at a temperature below 16°C., they do not become infective or if they are infective and are kept for a few days at, or below, the temperature, they loose their infectivity, but regain it again if the temperature is raised above this point.

The authors, as a result of their experiences, consider that mosquitoes do not become infective until eight days after the infecting feed. Mosquitoes once infective remain so for life provided the temperature does not fall below 22°C. for any prolonged period. The most favourable time to infect mosquitoes is in the first three days of the fever, but experiment showed that the blood may be infective as long as fever lasts. It was proved that the virus of dengue in the mosquito is readily filterable.

The authors are convinced that an attack of dengue confers a strong and lasting immunity although the serum of a convalescent has no inhibitory action when inoculated along with virus.


**PSITTACOSIS, OR PARROT FEVER**

Psittacosis, or parrot fever, is primarily a disease of birds which can be conveyed to persons through more or less intimate contact with recently imported infected parrots, and sometimes by parrakeets, love birds, canaries, and possibly other tropical species. It is, therefore, of especial interest to all bird fanciers.
The symptoms of the disease in birds are not sufficiently characteristic to be diagnostic; hence, the disease in them is usually detected only after one or more human cases of parrot fever have resulted. The birds which usually are responsible for the human cases are those which have been imported recently and usually they also show signs of illness, such as loss of appetite, roughing of feathers, and sometimes cough and diarrhea, although occasionally birds apparently well have served to infect persons as long as eight months after importation. The facility with which the disease is spread from infected birds to man makes it one of the most highly contagious diseases known.

Infected persons usually become sick in from 6 to 15 days following exposure and have symptoms suggesting influenza. The onset is sudden, with chilly feeling, intense headache, and fever. A peculiar type of localized pneumonia soon develops. It is largely upon the extent of this pneumonia and the age of the patient that the outcome of the disease depends; it is especially dangerous in persons over 60 years old. In mild cases the initial pneumonia ceases to spread and the fever and other symptoms tend to disappear after eight to ten days. In severe cases, however, the lung becomes progressively more and more involved, and unless the process can be checked death will result, usually in the third week of the disease. When recovery sets in, the physician must guard his patient from getting about too soon, as relapses during the weeks immediately following the return of the temperature to normal occur not infrequently, though they tend to be milder than the original attack.

Psittacosis of man has been reported for the United States in 1904, 1906, 1925 and 1927. The 1929-1930 outbreak is, however, by far the most extensive yet reported for the United States. Nevertheless, it seems certain that this outbreak would largely have escaped detection as to its real nature had not the press brought the condition and its striking association with parrots before the public and the medical profession.
The records of the Public Health Service indicate that there were 74 places of infection, which gave rise to 169 cases with 33 deaths from November 23, 1929, to May 7, 1930. These cases occurred in 15 States and the District of Columbia, and do not include 16 laboratory infections with 2 deaths, or 12 probable cases which were moved from two merchant ships entering ports of the United States following exposure aboard ship to parrots purchased abroad.

Among the 167 cases of known sex which occurred in the United States, 105 were females, or 63.37 per cent of the total. This preponderance of cases among females is probably a reflection of the fact that in this country exposure usually occurred in the home where women spend a relatively larger amount of their time than do the men. The care of the birds also commonly falls to the women. In an outbreak which occurred in Argentine where exposure was largely from an exhibit of fancy birds, the infection was reported as being three times as prevalent among males as among females.


SCREENING AND MOSQUITO PROOFING AS ELEMENTS IN MALARIA CONTROL

Screening alone must not be confused with mosquito proofing. In a large percentage of tenants' homes [in Tennessee] screening of the doors and windows is only part of the job of preventing the ingress of anopheles. Carpenter work is often necessary, floor cracks have to be stopped up or covered, walls papered to cover cracks or holes, naphthalene put into the chimneys and other work done. In addition intensive educational programs are carried on emphasizing the proper use and care of the screens as well as general malaria prevention.

Howard R. Fullerton, C. E.
THE AFRICAN REPUBLIC OF LIBERIA AND THE BELGIAN CONGO. Based on the observations made and material collected during the Harvard African Expedition, 1926-1927. Edited by Richard P. Strong, Ph.B., M.D., S.D., Professor of Tropical Medicine, Harvard University Medical School. Published by Harvard University Press, Cambridge, Massachusetts. 2 Volumes. Price G.$15.00.

The writer has received the gift of a copy of these volumes from their editor and would like to take this opportunity of briefly calling attention to a work of very considerable interest both sociological and scientific. The two volumes run to over a thousand pages, are beautifully got up and profusely illustrated with excellent pictures.

The work is divided into three parts:

Part I. deals very largely with the social and political conditions and includes: Geography and climate, Inhabitants and conditions under which they live, Tribal customs, Slavery, etc. and has chapters on Zoology and Sanitary conditions. The general picture is far from an attractive one and the amount and results of slavery, direct and indirect, form a very dark commentary on the name “Liberia.” It is encouraging, however, to know that the problem has now been taken up by the League of Nations with prospects of a marked improvement of native conditions.

Part II. on Medical and Pathological Investigations is the division of the work that is of the greatest interest to us in China. This includes chapters on such subjects as: Infectious diseases, Filariasis, Keloid formation, Juxta-articular nodules, Yaws and Syphilis, Leprosy and skin diseases.

The first of these chapters contains an interesting and very well balanced discussion on mycotic splenomegaly, a subject as yet practically untouched in this country but one of very considerable importance.

The section on leprosy is of special value as dealing with the relation of leprosy to blastomycosis, the confusion that sometimes arises in the differentiation between leprosy and infections with certain vegetable organisms and the special difficulties that a double infection may introduce. These are very practical difficulties which have largely escaped consideration in the ordinary discussions of leprosy.

It is impossible, in the short space at our disposal, to touch on many of the interesting features of this section.
Part III. of the book deals with Medical and Biological Investigations. The report of this expedition is in series with the report on the Hamilton Rice Expedition to the Amazon and continues the very valuable investigations then carried out. It is almost impossible to exaggerate the importance of such systematic work.

J. L. M.


In our review of the International Health Year-Book of 1928 we called attention to the phenomenal growth in size of these reports. The present volume is increased by a further three hundred odd pages to a total of over 1,500. It does not however contain any report from China which is undoubtedly a very serious if unavoidable defect.

The object of the Year-Book is to give a survey of the progress made by the various countries in the domain of public health. It indicates new developments in the working of the various health services, gives the most recent data as regards vital and health statistics and reviews the work of the principal international organisations dealing with public health. The Year-Book also contains a survey of industrial hygiene in Germany, Belgium, Great Britain, Italy and the Netherlands.

While China does not figure in this report there is a good deal of information about health conditions in Japan and some interesting comparisons between diseases in the East and the West can thus be drawn.

Taking England and Wales as a standard for comparison we note: Cancer adds only half to the mortality lists of Japan as compared to what it does in England. Japan 7.1 per 10,000: England, 14.25. It is notable, however, that about two thirds of the deaths from cancer in Japan are due to disease of the stomach and liver while only about 1½ per cent are from cancer of the breast. In England and Wales, on the other hand, the proportion of stomach and liver cancers is probably not much more than 40 per cent of the whole whereas breast cancers are proportionally more than five times as numerous as they are in Japan.

When we turn however from cancer to infectious diseases the position is very much reversed. Typhoid fever has an incidence of 6.81 and paratyphoid of 0.79 per 10,000 for Japan against 0.9 for the combined diseases in England and Wales, and Tuberculosis 19.48 against 9.72.

It is quite impossible to do justice to a volume of this nature in a brief review, it is indispensable to any student of public health statistics.

J. L. M.

The clinical part has been thoroughly revised by such excellent authorities as Ruge and Muhlens with a simplicity and clearness which make it quite easy for the non-German reader to follow. Great importance is attached to the question of malaria, which is Ruge's and Muhlen's work. Amongst the new remedies Plasmochin and Neostibosan are widely discussed. A most remarkable part of the book is the chapter of Spirochae-tosis written by Muhlens. The part of tropical hygiene has been rewritten in a very able manner by von zur Verth and Heinrich Ruge, the son of R. Ruge. Both of these authors added an important chapter by giving a little more space to the tropical skin-diseases, which, however, are still not treated extensively enough, especially compared with other subjects. This applies especially to the chapter on cosmopolitan skin—and venereal—diseases.

The book is illustrated with excellent pictures, a few of which are new to this edition.

F. R.


Young's Handbook of Anatomy written specially for medical students is so well known that a further revision by Dr. George W. Miller attracts attention. The most striking modification which has been made is the whole-hearted adoption of the Basle nomenclature, which as Dr. Miller says in his preface adds a further 5,000 words to the 50,000 anatomical terms already in use. While the adoption of a standard nomenclature is desirable it would have been better in the reviewer's opinion to have retained in the text some of the names in common use, e.g. while we all know that the correct name for the heart is "cor" it is adding to the perplexities of the student to read "the cor is a hollow, muscular organ etc., etc." or instead of the kidneys to read "the renes are two glandular organs situated deeply on the lumbar region, etc." and yet a tooth is not called a "dens." Moreover, the "thyroid gland" retains the name while the "thyroid gland" is called the "glandula thyroidea."

Some of the illustrations, such as those of the arteries in Fig. 81, 82, 84, 85 are of little use, as they do not depict any of the surrounding
THE ORIGIN OF THE HUMAN SKELETON, by R. Broom, D.Sc., F.R.S.

We have here a fascinating book on evolution, Dr. Broom has devoted 33 years to the study of the mammal-like reptiles of South Africa and feels that he has been successful in solving the question of the mammalian origin. It will be interesting to follow his argument when his fuller monograph is published. Meanwhile the present book deals with the evolution of the skeleton.

The first chapter sketches the main lines of vertebrate evolution and the following three the evolution of the mammalian skull, on which there has been such diversity of opinion. Chapter Five is devoted to the vertebrae and sternum but it is to be regretted that while the segmental character of the vertebrate animals is accepted, there is little discussion as to why the lower orders have not a segmented sternum while in the higher orders segmentation of the sternum appears. The fact is admitted that "in the monotremes we meet for the first time with a segmented sternum" but no mention is made of the fact that the ossification centres in "homo sapiens" are all against a segmental origin.

Chapters Six and Seven are devoted to the evolution of the Anterior and Posterior limbs while Chapter Eight is an interesting one on homologies.

The Last Chapter on "Evolution factors" is perhaps the most interesting and demonstrates the broad-mindedness of the author. He discusses Darwinism and Lamarckism and points out the weakness of each theory. He quotes Watson in his address as President of the Zoological Section of the British Association in 1929 as saying, "The only two theories of evolution which have gained any general currency—those of Lamarck and Darwin—rest on a most insecure basis, and the validity of the assumptions on which they rest has seldom been seriously examined." He closes his book with the following words:

"When the Scientists have failed to give us a satisfactory explanation of evolution we feel driven to consult the Philosophers. It may be that no explanation hitherto given is sound. It may be that we shall never be able to realise what is behind evolution. But it does seem that there is a "something" that cannot be weighed by physics or analysed by chemistry."

H. G. T.

This is a very convenient sized book on a subject that is all too often not understood by the nurse. The average School of Nursing curriculum does not give much time to the study of the care, and problems of the tuberculosis patient.

This book is written in a very clear and interesting manner. All a nurse should know about how tuberculosis is spread, and measures for the prevention of the spread of this disease, both in the hospital and the home, is well covered. It is presented in a way that should not only be of interest, and value to nurses, but to high school students, and for public health programmes. All types of tuberculosis are treated, and the chapter on surgical tuberculosis, gives a very clear idea of the nursing care, and procedures necessary in caring for this class of patients in the hospital.

All the latest treatments are clearly explained and there are many good illustrations which make for clearer understanding, of the apparatuses used. Such treatments as Pneumothorax, light treatments, the use of tuberculin for diagnosis and many others are well explained, and is interesting as well as instructive reading.

The summary at the end of each chapter is of great help to the teacher as it can be used for a review period after the chapter has been finished.

E. M. P.


The fact that four editions of a book this size have had to be published in seven years is sufficient proof of the claim the volume may make to meet the needs of the man in general practice. It well deserves the reputation it has secured and is indeed one of the few medical books that we should be inclined to put on the indispensable list.

The work is divided into two parts the first dealing with: General Therapeutics—The Methods used in Treatment, and the second with: Special Therapeutics—The Application of Therapeutics to Particular Diseases. This is a logically sound division and is worked out excellently in the text.

The first part includes chapters on Rest, Drugs, Biologicitherapy and Prophylaxis, Extracts of Ductless glands, Dietetics, Heat and Cold, and
Mechanotherapy in its various forms. It has also a short chapter on Psychotherapy.

The second part applies the rules already given to the different systems and has also chapters on diseases due to Allergy, Intoxications and some common Nervous Disorders.

At the end of each chapter is placed a short list of references especially to articles in the English language. This is excellent, the references are well chosen and the long lists of articles in foreign languages which are not likely to be available to the ordinary reader are avoided.

As regards most of the chapters in this volume the information is wonderfully up to date but it falls down where it approaches the realms of tropical medicine. The treatment of malaria is not, we trust, that usually followed despite the high authority on which it is based and in any case all absence of reference to an important new drug such as plasmochin hardly corresponds with the title of the book. Still more serious and less excusable is the omission of carbon tetrachloride from the drugs used in the treatment of hookworm; as is also the statement that santonin is an effective drug in the treatment of Oxyuris.

There are also a few extraordinary mistakes such as referring to Ascaris Lumbricoides as the "Threadworm." The index to the book is rather disappointing from a lack of fulness and the number of mistakes in the figures of the pages referred to.

These little mistakes stand out as mere blemishes on an exceptionally valuable book and perhaps from that very fact become unreasonably noticeable.

J. L. M.

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Registrar.
University of Hong Kong,
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