Chest Disease in Patients with Agammaglobulinemia*†

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Introduction

As a new disease entity is studied it becomes apparent that certain clinical and laboratory features are particularly helpful to the clinician in the recognition of the disorder. A consideration of the recent literature indicates that recurrent pulmonary disease has assumed this role in the disease syndrome associated with agammaglobulinemia. Recurrent pulmonary infections including bronchitis, pneumonitis, and pneumonia at times leading to pulmonary fibrosis, bronchiectasis, and empyema, appear to be extremely frequent manifestations of agammaglobulinemia and as reporting becomes more complete it seems likely that pulmonary disease may become the clinical sin qua non of this syndrome. Consequently, it seems especially pertinent that a complete review of reported cases of agammaglobulinemia be submitted to chest physicians who are among those most likely to encounter patients suffering from this metabolic disturbance. It is the purpose of this report to present a thorough review of the reported experience with agammaglobulinemia and to emphasize the pulmonary manifestations observed in our cases and those studied by others.

Agammaglobulinemia is a metabolic disorder featured by an enhanced susceptibility to bacterial infection, absence of gamma globulin from the serum, absence of antibodies from the blood and tissues, and failure of immunologic response to antigenic stimulation.1-3 Evidence has been submitted indicating that this disorder reflects a disturbance in function of the hematopoietic reticulum (mesenchyme) which is expressed in each patient as a failure of plasma cell formation and consequent failure of antibody production in response to antigenic stimulation.4-8

On the basis of clinical and laboratory data this disorder can be subdivided into a congenital and an acquired type.3,8 In both diseases the chief clinical manifestation is the occurrence of recurrent severe bacterial infections. The congenital disease is, in general, expressed early in life, and, like hemophilia, appears to be an inborn error of protein synthesis transmitted as a sex-linked recessive trait.2,9 Thus, this form of agammaglobulinemia occurs only in male children, frequently in more than one member of a

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sibship, and suggestive evidence links its transmission to the female. In
contradistinction, the acquired diseased is much less selective in nature
appearing in either sex at any age. Significantly patients with this form
of agammaglobulinemia give a history of having been healthy up to a
certain time in their lives. Following what is interpreted to be the develop-
ment of agammaglobulinemia, changes of a dramatic nature occur, and
existence for these people becomes almost a continuous round of bacterial
infections. Thus, by history at least, the agammaglobulinemia in these pa-
tients has a well defined onset. So far direct biochemical proof of
the acquisition of agammaglobulinemia is lacking.

Although the term agammaglobulinemia is used to describe both the
congenital and acquired disease, in the strict sense it is probably always a
mismomer based on lack of sensitivity of most methods currently used to
detect and measure the gamma globulin concentration in the serum or
plasma. Critical immunological methods suggest that minute amounts of
gamma globulin are present in the serum of almost all of the so called
agammaglobulinemic patients. Although there appears to be some
overlapping somewhat larger amounts of gamma globulin are generally
present in the sera of the patients with acquired agammaglobulinemia than
in the sera of those with the congenital disorder. In spite of the obvious
differences in the basis of the two forms of agammaglobulinemia a common
 denominator exists. In both disorders there appears to be a dysfunction
of the reticular tissues (mesenchyme) associated with failure of plasma
cell and antibody production. Administration of sufficient gamma globulin
to bring the serum level to normal does not render either group of patients
capable of antibody production.

That Bruton’s first description of agammaglobulinemia in 1952 alerted
the medical profession to the existence of this disease is attested to by the
almost logarithmic increase in case reports appearing in medical journals
and at medical and scientific meetings, during the last years. In both its forms agammaglobulinemia has now been discovered in numerous
clinics in both America and Europe and it seems to conclude that agamma-
globulinemia is a widely distributed disease which may be much more
common than was anticipated when it was first described. Observations
also seem to establish that this disease, as a clinical entity, has been created
by antibiotic treatment in our era. Prior to the availability of antibiotics
to cure many severe bacterial infections which these patients have, all of
them doubtless died early and the clinical syndrome featured by recurrent
severe bacterial infection was not expressed. Thus to Bruton goes credit
for discovering a new disease which seems to be the product of medical
progress. Following Bruton’s initial description of the entity, Bruton et
al reported two additional patients having agammaglobulinemia, thus
launching a nation-wide search for patients with this disorder. These
initial cases of congenital agammaglobulinemia lacked immune bodies in
their blood and tissues and failed to form antibody in response to stimula-
tion with several bacterial antigens. In 1953 Janeway et al presented
clinical and laboratory observations on nine such cases entirely similar to
those of Bruton. All nine cases were males, each suffering from recurrent bacterial infections and falling in their immune response. In spite of the frequency and severity of bacterial infections in these patients it was noted that certain virus diseases gained the usual expression, and lasted the usual lengths of time with recovery occurring in the same way it does in normal persons.

Furthermore, it was noticed that in spite of heavy exposure, recurrence of certain virus infections did not take place. The authors submitted the concept that the agammaglobulinemia occurring in children is an inborn error of metabolism transmitted as a sex-linked recessive trait. Chief among the recurrent infections in these children were pneumonia and meningitis. Subsequently Good\textsuperscript{15,19} and Hayes et al\textsuperscript{17} have described an additional nine cases of the congenital disease. Like those cases previously reported, the clinical manifestations in these patients included numerous episodes of bacterial disease ranging from severe diarrhea, recurrent urinary tract and skin infections, to numerous episodes of respiratory infection. Most notable among the infections, however, was the recurrent involvement of the pulmonary parenchyma. In the three cases reported by Hayles et al,\textsuperscript{17} each had one severe respiratory infection after another, two of them ultimately dying with respiratory complications. Our six cases of congenital agammaglobulinemia likewise were featured clinically by recurrent pneumonia, one of the patients developing bronchiectasis following several such episodes. Jean\textsuperscript{21} reported a case of agammaglobulinemia in a seven year old boy. This child's disease too was featured by recurrent severe pulmonary infections leading to the development of bronchiectasis. That all 24 of the cases of congenital agammaglobulinemia thus far described have occurred in boys supports the concept originally expressed by Janeway et al\textsuperscript{9} that congenital agammaglobulinemia is an inborn error of metabolism transmitted as a sex-linked recessive trait.

Hypogammaglobulinemia and even agammaglobulinemia diagnosed according to electrophoretic criteria may occur in other diseases during childhood. For example, in the nephrotic syndrome loss of serum proteins in the urine results in both hypoalbuminemia and hypogammaglobulinemia.\textsuperscript{31} Loss of protein and poor nutrition may also result in serum deficiency of globulin as well as albumin in certain cases.\textsuperscript{32} As early as 1932 prior to the availability of electrophoretic methods, McQuarrie and colleagues\textsuperscript{33,34} described a patient having generalized edema, low serum proteins and enhanced susceptibility to infection. This patient ultimately died with bronchopneumonia. Fractionation of the serum proteins revealed both a hypoalbuminemia and extreme hypoglobulinemia, the globulin being only 0.4 gram on one occasion. From this protein partition there can be little doubt that the gamma globulin content as well as the content of other serum proteins was low. Cases similar to that described by McQuarrie have been reported by Meyers et al,\textsuperscript{35,36} Schick and Greenbaum\textsuperscript{37} and Fried and Henly.\textsuperscript{38} Although infection is not a regular concomitant of the latter syndrome, McQuarrie's case indicates that in this disorder, as in isolated agammaglobulinemia, the gamma globulin levels can become so low as to
be associated with failure of the immunological mechanism and increased susceptibility to bacterial disease. It should be emphasized that the syndrome originally described by McQuarrie et al.\textsuperscript{33, 34} appears to be distinct from the disease described by Bruton. In McQuarrie's syndrome a generalized deficiency in protein fabrication is characterized while in congenital agammaglobulinemia, the failure of gamma globulin formation is an isolated defect.\textsuperscript{2, 3, 9} Furthermore, McQuarrie's syndrome may occur in either sex\textsuperscript{83, 36, 37, 38} while congenital agammaglobulinemia occurs only in boys.

Hypogammaglobulinemia sometimes of extreme degree may also be noticed when a delayed assumption of gamma globulin synthesis occurs in the newborn period.\textsuperscript{40, 41} Although not yet proved it has been suggested that this form of hypogammaglobulinemia too may result in enhanced susceptibility to infection.\textsuperscript{42} Indeed preliminary data link the occurrence of certain crib deaths associated with pulmonary disease to this defect in protein synthesis.\textsuperscript{42}

As a probable example of transient hypogammaglobulinemia of infancy is the case reported by Keiden et al.\textsuperscript{13} The eight week old female infant which they described developed a progressive necrotizing reaction following smallpox vaccination and died with staphylococcus sepsis and bronchopneumonia. Although electrophoretic analysis revealed gamma globulin to be absent from the serum it seems likely that in this child the authors were dealing with a pathological extension of the physiological hypogammaglobulinemia of infancy and that this patient is not an example of isolated congenital agammaglobulinemia occurring in a female. A notable difference between Keiden's case and those studied by Janeway et al\textsuperscript{2} and Good et al\textsuperscript{2} was the presence of many plasma cells in the inflammatory exudates in Keiden's patient. These cells were virtually absent from the hematopoietic tissues and inflammatory exudates of the cases reported by Janeway and Good. Similar cases of transient hypogammaglobulinemia of infancy have been studied by Kelley et al\textsuperscript{44} and Ulstrom et al.\textsuperscript{45} In each of the latter two instances electrophoretically determined agammaglobulinemia was associated with increased susceptibility to infection and in each patient the extreme hypogammaglobulinemia was transient. The latter syndrome may occur in either sex and exists in patients two to six months of age following decay of the passively transferred maternal gamma globulin. Agammaglobulinemia in childhood may be based on still another mechanism, namely an increased rate of destruction of normally formed serum protein.\textsuperscript{46}

In addition to and apparently distinct from congenital agammaglobulinemia is the acquired disease which occurs primarily in adults and appears to show no preference for age or sex. This disorder like the childhood disease has been expressed clinically by the occurrence of repeated episodes of bacterial infection especially involving the upper and lower respiratory passages. Almost all of these patients have been troubled by recurrent pneumonia and many have developed empyema, pulmonary fibrosis, bronchiectasis or atelectasis. The complete case reports of acquired agamma-
globulinemia present in the literature show that the disease has a wide range with respect to age. The youngest patient was a 17 year old female and the oldest was our 58 year old man. Unlike the congenital disease, there seems to be no sex preference among patients with acquired agammaglobulinemia. In cases reported to date, seven have been females and 12 have been males. Both the younger patients and the older ones suffered from recurrent bacterial pneumonia, and bronchiectasis occurred as a complication in four of the reported cases. Although bronchiectasis has been noted to occur frequently in acquired agammaglobulinemia, the bronchiectasis-agammaglobulinemia syndrome is not distinctive of this form of the disease since four instances of bronchiectasis have also been noted in children having the congenital disease.

As is illustrated by the cases described by Collins and Dudley, bronchiectasis may be an early expression of the adult disease. In their patients the most prominent and earliest clinical manifestations of agammaglobulinemia were related to the bronchiectasis. Both of their patients had generalized bronchiectasis and empyema. One case was a 25 year old housewife who expired despite bilateral surgical resection of the involved pulmonary tissue while the other case was a 53 year old woman who expired from pulmonary failure even though surgery was not performed. These two cases emphasize the difficulty of diagnosing agammaglobulinemia unless the responsible physician is aware of its clinical nature. In general, repeated episodes of pneumonia serve to alert the physician to the possibility that agammaglobulinemia exists. In many such patients a fantastic experience with recurrent pneumonia is reported as in the patient reported by Prasad and Kosa who was also studied by Good. This woman suffered at least 34 attacks of pneumonia over an eight year period. In other cases only a few episodes of pneumonia result in irreversible destruction of the pulmonary parenchyma. Bronchiectasis, atelectasis, pulmonary fibrosis or empyema represent the major expression of the pulmonary disease in some of these cases. Following the many attacks of pneumonia, residual fibrosis of the lungs developed in some of these patients. Examples are the 37 year old man studied by Zinneman et al and the 30 year old female studied by Prasad and Kosa and Good.

Although it is clear that agammaglobulinemia occurring in adults is regularly an acquired disease, the literature and studies thus far available do not indicate whether it is a homogeneous entity or whether the failure of gamma globulin and antibody production has had multiple bases expressing themselves in this common metabolic disorder. Pertinent to this consideration is a patient reported by Rundles, Arends and Coonrad in whom a malignant lymphoma apparently resulted in failure of gamma globulin formation and the development of acquired agammaglobulinemia. This patient with a well defined malignant disease of the reticular tissues showed the same symptoms and signs as were noted in the other patients whose agammaglobulinemia was associated with poorly defined disturbance of mesenchymal tissue or in whom no hematological abnormalities were described. In some patients with multiple myeloma who are producing
### TABLE I
Pulmonary Manifestations in Patients with Congenital Agammaglobulinemia

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. Patients</th>
<th>Sex</th>
<th>Age</th>
<th>Pneumonia No. Episodes-Type</th>
<th>Pulmonary Complications</th>
<th>Bacteriology</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruton</td>
<td>1952</td>
<td>1</td>
<td>M</td>
<td>8</td>
<td>12 episodes Lobar pneumonia Bronchopneumonia</td>
<td>None</td>
<td>Pneumococcus</td>
<td>Many other kinds of severe bacterial infections</td>
</tr>
<tr>
<td>Bruton, et al</td>
<td>1952</td>
<td>2</td>
<td>M</td>
<td>9</td>
<td>Numerous attacks Pneumonia</td>
<td>None</td>
<td>Staphylococcus Pneumococcus</td>
<td>Many other kinds of severe bacterial infections</td>
</tr>
<tr>
<td>Janeway, et al</td>
<td>1953</td>
<td>all 9 males all children</td>
<td>M</td>
<td>7</td>
<td>All cases have had repeated episodes of bronchitis and pneumonia</td>
<td>2 cases bronchiectasis emphysema atelectasis</td>
<td>&quot;Common bacterial pathogens&quot;</td>
<td>Many other kinds of severe bacterial infections</td>
</tr>
<tr>
<td>Jean, R.</td>
<td>1953</td>
<td>1</td>
<td>M</td>
<td>7</td>
<td>&quot;Repeated severe pulmonary infections&quot; Pneumonia</td>
<td>Bronchiectasis</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>7 yr.</td>
<td></td>
<td></td>
<td>8 episodes Lobar pneumonia Bronchopneumonia</td>
<td>None</td>
<td>Pneumococci</td>
<td>Repeated attacks meningitis otitis, diarrhea, pharyngitis</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>6 yr.</td>
<td></td>
<td></td>
<td>12 episodes Lobar pneumonia Bronchopneumonia</td>
<td>Bronchiectasis Atelectasis</td>
<td>Group A streptococci Pneumococci Staphylococci</td>
<td>Repeated attacks meningitis otitis, diarrhea, pharyngitis</td>
</tr>
<tr>
<td>Good, R.</td>
<td>1954</td>
<td>6</td>
<td>M</td>
<td>20 mo.</td>
<td>10 episodes bronchial pneumonia, interstitial pneumonitis</td>
<td>Interstitial Organized</td>
<td>Hemophilus Group A streptococci</td>
<td>Repeated attacks otitis, sinusitis, urinary tract infection</td>
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<tr>
<td>M</td>
<td>15 mo.</td>
<td></td>
<td></td>
<td>About 10 episodes Bronchial pneumonia, Interstitial pneumonitis</td>
<td>None</td>
<td>Streptococci</td>
<td>Staphylococci</td>
<td>Repeated attacks otitis, sinusitis, urinary tract infection</td>
</tr>
<tr>
<td>M</td>
<td>10 yr.</td>
<td></td>
<td></td>
<td>3 attacks Bronchial pneumonia</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>1 yr.</td>
<td></td>
<td></td>
<td>1 episode Bronchial pneumonia</td>
<td>None</td>
<td>Hemophilus Type B</td>
<td>No other infections</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>5 mo.</td>
<td></td>
<td></td>
<td>Recurrent attacks bronchopneumonia</td>
<td>Chronic suppurative pneumonitis</td>
<td>Micrococcus pyogenes (staphylococci)</td>
<td>Granulomatous lesions in the liver</td>
<td></td>
</tr>
<tr>
<td>Hayles, et al</td>
<td>1954</td>
<td>3</td>
<td>M</td>
<td>9 yr.</td>
<td>Bronchitis Pleuritis</td>
<td>None</td>
<td>Not reported</td>
<td>Recurrent infections meningitis, died with myocarditis</td>
</tr>
<tr>
<td>M</td>
<td>9 yr.</td>
<td></td>
<td></td>
<td>Recurrent pneumonia</td>
<td>None</td>
<td>Not reported</td>
<td></td>
<td>Meningitis, osteomyelitis, virus infections without trouble, pyoderma</td>
</tr>
<tr>
<td>Tanis</td>
<td>1955</td>
<td>1</td>
<td>M</td>
<td>2 yr.</td>
<td>Recurrent pneumonia Suppurative bronchitis</td>
<td>None</td>
<td>Protexus</td>
<td></td>
</tr>
<tr>
<td>Fischer</td>
<td>1955</td>
<td>1</td>
<td>M</td>
<td>5 yr.</td>
<td>Recurrent pneumonia and recurrent bacterial respiratory bronchitis infections</td>
<td>None</td>
<td>Not reported</td>
<td>Skin infections, septic arthritis</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>No. Patients</td>
<td>Sex</td>
<td>Age</td>
<td>Pneumonia No. Episodes-Type</td>
<td>Pulmonary Complications</td>
<td>Bacteriology</td>
<td>Remarks</td>
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<tr>
<td>Young, et al</td>
<td>1954</td>
<td>4</td>
<td>M</td>
<td></td>
<td>Not completely reported</td>
<td></td>
<td></td>
<td>Cases as yet incompletely reported</td>
</tr>
<tr>
<td>Prasad &amp; Kosa*</td>
<td>1954</td>
<td>1</td>
<td>F</td>
<td>30</td>
<td>34 attacks</td>
<td>Bronchopneumonia</td>
<td>Pneumococcus repeatedly</td>
<td>Disease clearly acquired at about 22 years of age. Hypertension</td>
</tr>
<tr>
<td>Good, R. A.</td>
<td>1954</td>
<td>1</td>
<td>M</td>
<td>58</td>
<td>17 attacks</td>
<td>Lobar pneumonia</td>
<td>None</td>
<td>Disease acquired 4 years prior to study. Had huge thymoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M</td>
<td></td>
<td>29</td>
<td></td>
<td>RLL, RML, LLL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>M</td>
<td></td>
<td>37</td>
<td>1 episode definite</td>
<td>Fibrosis basilar lungs</td>
<td>Pneumococcus</td>
<td>Began in adult life.</td>
</tr>
<tr>
<td>Grant &amp; Wallace</td>
<td>1954</td>
<td>1</td>
<td>F</td>
<td>17</td>
<td>7 attacks pneumonia</td>
<td>None</td>
<td>Not described</td>
<td>Apparent onset at 15 years, associated Leukopenia</td>
</tr>
<tr>
<td>Arends, et al</td>
<td>1954</td>
<td>1</td>
<td>F</td>
<td>53</td>
<td>Repeated, severe</td>
<td>None</td>
<td>Not described</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>respiratory infections</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>lobar pneumonia</td>
<td>both lower lobes</td>
<td>hemolytic hemophilus</td>
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<td></td>
<td></td>
<td></td>
<td>bronchopneumonia</td>
<td></td>
<td>influenza</td>
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<tr>
<td>First Name, et al</td>
<td>Year</td>
<td>Gender</td>
<td>Age</td>
<td>Details</td>
<td>Other Information</td>
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<tr>
<td>Rohn, et al</td>
<td>1954</td>
<td>1</td>
<td>M</td>
<td>29</td>
<td>Not completely reported</td>
<td>Hypersplenism corrected by splenectomy</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>M</td>
<td>26</td>
<td>Repeated attacks of pneumonia</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>None</td>
<td>None</td>
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<td></td>
<td></td>
<td>Saslaw, et al</td>
<td>1954</td>
<td>2</td>
<td>M</td>
<td>40</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Lange, et al</td>
<td>1954</td>
<td>1</td>
<td>F</td>
<td>29</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Moenke</td>
<td>1954</td>
<td>1</td>
<td>M</td>
<td>18</td>
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<td></td>
<td></td>
<td>Collins &amp; Dudley</td>
<td>1955</td>
<td>2</td>
<td>F</td>
<td>31</td>
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<td></td>
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<td></td>
<td></td>
<td>Seltzer, Baron &amp; Taporek</td>
<td>1955</td>
<td>1</td>
<td>M</td>
<td>27</td>
</tr>
</tbody>
</table>

*Same case, L. L., studied by Good & Zinneman and Hall not duplicated in this table.*
large quantities of aberrant globulin, immunological capacity may be deficient and virtually no normal gamma globulin is produced.47-50

Observations

Summarized in Table I are the pulmonary disturbances thus far reported in children with agammaglobulinemia. Data are included from all the cases presented in the literature as well as our own patients. As may be seen from the Table, wherever reporting has been complete, all of the children suffering from agammaglobulinemia have been troubled with recurrent pulmonary disease including recurrent attacks of pneumonia. In several instances bronchiectasis has been the result of the recurrent pulmonary infection. In many instances the case reports clearly indicated that it was the pulmonary disease which brought the patients to the attention of the medical clinics where the diagnosis of agammaglobulinemia could be made. Wherever bacteriological data was available it was found that the ordinary pyogenic pathogens were the organisms responsible for the recurrent infections. As may be seen in the Table, the organisms most commonly infecting these patients have been the pneumococcus streptococcus, staphylococcus and hemophilus. Summarized in Table II are the cases of acquired agammaglobulinemia reported to date. It may readily be seen from the Table that in this syndrome, among the most prominent manifestations are pulmonary disorders. Severe life-threatening pulmonary complications include bronchiectasis observed on four occasions, and empyema observed in three cases. In addition late pulmonary fibrosis was described in two instances and generalized calcification due to histoplasmosis in one. In these patients as in the children the organisms producing infections have been primarily the usual pyogenic pathogens. The pneumococcus has been particularly troublesome, for example, producing in one of our cases many attacks of pneumonia and at least four attacks of meningitis.

In Table III the observations detailed in Tables I and II are digested and summarized. Although the opinion has been expressed that patients with acquired agammaglobulinemia have bronchiectasis more frequently than do patients with the congenital disease, the reported experience does not give full support to this view. Four of the 24 patients with congenital agammaglobulinemia have been shown to have bronchiectasis whereas four of 13 completely reported patients with the acquired disorder have developed this complication. Thus, to date it appears that of the pulmonary complications, noted in cases with recurrent pneumonitis, bronchiectasis was the most common. However, this complication occurred the same number of times in the group with congenital and the group with acquired agammaglobulinemia.

These data suggest, however, that bronchiectasis may be more frequent in the acquired form of agammaglobulinemia than in the congenital type but they do not yet support the concept that a bronchiectasis-agammaglobulinemia syndrome is an entity. Janeway, however, has stated that in his experience bronchiectasis is the most common clinical manifestation of
acquired agammaglobulinemia. This has not been our experience since neither of our cases of acquired agammaglobulinemia had bronchiectasis while one of our children with congenital agammaglobulinemia suffered from bronchiectasis. Until reporting is both more extensive and more complete it seems worthwhile merely to recognize the relative frequent occurrence of bronchiectasis in patients with both the congenital and acquired forms of agammaglobulinemia.

Of the eight cases of agammaglobulinemia studied at the University of Minnesota and Ancker Hospitals, six were of the congenital variety and two were acquired. All the patients with congenital agammaglobulinemia were males. Five of these patients presented histories of severe recurrent pulmonary infections with many attacks of pneumonia being diagnosed in each patient. In the sixth case, a sibling of a proved case of agammaglobulinemia, the protein disturbance was discovered when the baby was three months old. Except for one episode of diffuse respiratory disease, this child has been kept free of disease by treatment with prophylactic antibiotics and gamma globulin for approximately one year. In the two cases

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**TABLE III**

<table>
<thead>
<tr>
<th>Type of Agammaglobulinemia</th>
<th>No. Cases</th>
<th>No. Reported Pulmonary Infections</th>
<th>No. Pulmonary Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Agammaglobulinemia</td>
<td>24</td>
<td>24 reported*</td>
<td>4 bronchiectasis</td>
</tr>
<tr>
<td>Acquired Disease</td>
<td>19</td>
<td>13 reported*</td>
<td>7 severe pulmonary complications, empyema, calcification, bronchiectasis</td>
</tr>
</tbody>
</table>

*All cases without pulmonary disease incompletely reported.

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**Figure 1A**

*Figure 1: Episode of pneumonia in a patient with congenital agammaglobulinemia. Note the pericardial infiltration of the pulmonary parenchyma. This episode of pneumonia was associated with the presence of Type VII pneumococci in the sputum and nasopharynx. Note the clearing of the process in Figure 1B. It may be further seen that the many attacks of pneumonia which this patient has had have not produced roentgenologically apparent damage to the pulmonary parenchyma.*
of adult or acquired type of agammaglobulinemia, the disease presented as
a syndrome featured by recurrent attacks of pneumonia and pneumonitis. Meningitis, otitis media, and sinusitis were also recurrent problems in
these patients. Two of our total group of eight agammaglobulinemic patients
developed pulmonary complications secondary to pneumonia. One of the
children having bronchiectasis was unsuccessfully treated by right lower
lobectomy and the process has extended to involve virtually the entire re-
main- ing portions of the right lung at the present time. One of the adults
shows persistent diffuse pulmonary radio-densities at the lung bases bi-
laterally. These have been interpreted as indicating the presence of re-
idual pulmonary fibrosis resulting from 34 attacks of pneumonia over
an eight year period. Two children in whom agammaglobulinemia was
associated with a blood dyscrasia featured by agranulocytosis died of pul-
monary disease, post mortem examination revealing in each instance inter-
stitial pneumonitis and bronchopneumonia. In neither of these cases was
the diagnosis of agammaglobulinemia made antemortem but rather the
diagnosis became apparent later when stored serum was analyzed electropo-
hetically.

The following case summaries emphasize the importance of recognizing
numerous bouts of pneumonia, episodes of septicemia and meningitis as
manifestations of the immunologic deficiency associated with failure of
gamma globulin formation.

Case 1: E. S., a seven year old boy was well until seven months of age, when he
developed diarrhea and pneumonia. This infection responded rather promptly to treat-
ment with sulfanamides. Subsequently he has had at least eight episodes of pneumonia,
sometimes bronchial, sometimes lobar, in character. He was almost constantly ill, suffer-
ing at different times from numerous attacks of middle ear infection, sinus infection,
three attacks of meningitis, repeated urinary tract infections, and septicemia. The
microorganisms responsible for the infections have included pneumococci, hemophilus,
meningococci and proteus. A severe episode of laryngotracheobronchitis, one year prior
to the beginning of our study, necessitated tracheotomy. On Figure 1A is shown a
PA film of the chest taken during a typical episode of pneumococcal pneumonia in this
patient. Complete clearing of the density is illustrated in Figure 1B as is the absence
of residual parenchymal damage in spite of the many attacks of pneumonia.

Case 2: W. A., a six year old white male was well until seven months of age when he
developed meningitis. Treatment with penicillin and sulfadiazine resulted in re-
cov- ery. During the first four years of life he had seven episodes of pneumonia. Several
attacks of pneumonia occurred during 1955 following which bronchiectasis was dis-
covered in the right lower lobe. Figure 2A illustrates the PA view of the chest taken
at that time. Right lower lobectomy was performed which resulted in slight clinical
improvement. However, during the subsequent year he had several additional attacks
of pneumonia, numerous episodes of middle ear and sinus disease. Atelectasis and in-
filtration developed in the remaining portions of the right lung (Figure 2B) and bron-
chograms, (Figure 2C) showed that the bronchiectasis had extended to involve both
the remaining upper and middle lobes on the right. Bronchograms of the left lung
were normal. In Figure 3A is shown a medium power microscopic view of a typical
area from the excised right upper lobe of the lung. On this photomicrograph the
chronic inflammatory reaction and bronchiectatic process involving medium sized bron-
chi is illustrated. Under lower power view the inflammatory reaction at this site seems
no different from that observed in bronchiectasis occurring in other patients. In Figure
3A high power views of the bronchiectatic process in the agammaglobulinemic patient
is compared to high power view of the inflammatory process of an immunologically
normal patient with bronchiectasis (Figures 3C and 3D). The absence of plasma cells
in the chronic inflammatory exudate of the agammaglobulinemic patients represents a
striking contrast to the marked plasmacytosis in those non-agammaglobulinemic sub-
jects.

Case 3: T. A., a 12 month old child sibling of W. A. was discovered to be agamma-
globulinemic at three months of age as a consequence of performance of electrophoretic
FIGURE 2A. Bronchectasis in patient with congenital agammaglobulinemia. Infiltrative process—Figure 2B. One year following surgical resection of right upper lobe, there is no evidence of bronchectasis on the left.

FIGURE 2C. Bronchogram showing almost the entire right lung. Note evidence of extensive infiltration process as well as the infiltrative process of atelectasis. There is no evidence of bronchectasis on the right middle and right upper lobes.
FIGURE 3A: A X200 illustration of the bronchiectatic process in the right lower lobe removed surgically from patient with agammaglobulinemia. Note the extensive inflammatory exudate and the involvement of the bronchial wall. Figure 3B: X800 high power view of the inflammatory exudate in the patient with plasma cells are lacking.
Figure 3C: Bronchiectasis in an immunologically normal person. Note the abundant plasma cells in bronchiectatic lung of another immunologically normal patient. The death of plasma cells in the inflammatory exudate of the patients with agammaglobulinemia represents a striking reflection of the immunological handicap.
analysis on serum specimens from all the members of his family. He was treated with prophylactic broad spectrum antibiotics during a period of intensive study and recently has been maintained on gamma globulin administration every few weeks. During a period prior to gamma globulin therapy, after antibiotics had been discontinued, he developed otitis media and a bacterial respiratory infection shown to be due to pneumococci. The latter disease responded promptly to treatment with penicillin.

Case 4: F. T., a 20 month old child, was well until seven months of age, when onset of pneumonia occurred, and during the ensuing months he experienced 10 recurrent attacks of pneumonia. He expired during an episode of recurrent pulmonary infection and autopsy findings showed extensive interstitial pneumonia. In addition to agammaglobulinemia evidence was obtained indicating that the child had cyclic or intermittent neutropenia.

Case 5: T. T., a 15 month white male sibling of F. T., Case 4, had many severe episodes of pneumonia beginning when he was six months old. Persistent neutropenic was present in addition to the agammaglobulinemia. He died during one episode of pneumonia due to a resistant staphylococcus prior to the recognition of the true nature of his disease. In both of the latter two cases agammaglobulinemia was demonstrated on both paper and free electrophoresis of the serum.

Case 6: J. S., 10 month old white male had pneumonia at three months of age, which responded to therapy. Pneumonia recurred at five months of age and again when the child was six months old. Study of the child's serum when he was seven months old revealed the presence of agammaglobulinemia.

In the acquired type described below, the incidence of recurrent pulmonary disease is even more striking than that noted in the congenital type. Although cases of bronchiectasis have been reported by others, the only pulmonary complication noted in our patients was residual interstitial fibrosis of the right middle lobe in one case.

Case 7: F. H., was a 58 year old white male who was well until four years prior to study when he began to have recurrent attacks of pneumonia. A mediastinal mass was discovered and in 1951 a 540 gram thymoma was removed. A serum protein determination done just prior to surgery was 5.1 grams per cent. The tumor showed generalized proliferation of all the thymic elements, particularly benign proliferation of the thymic reticulum. In Figure 4A is illustrated the chest film of F. H. taken prior to surgery in 1951. The huge mediastinal mass is to be noted. Figure 4B shows chest film after surgery. During the three years following excision of the thymoma this patient suffered from recurrent episodes of pneumonia usually beginning with chills, high fever, and cough. The development of rusty sputum was commonly noted. The patient himself stated that because of his recurrent pulmonary disease he became virtually addicted to terramycin, carrying a bottle of capsules with him wherever he went. That the agam-

![FIGURE 4A](image-url)  
**Figure 4A:** Tumor of thymus in patient with acquired agammaglobulinemia.  

![FIGURE 4B](image-url)  
**Figure 4B:** Following surgical removal of the thymus tumor. Note complete absence of the mediastinal mass.
AGAMMAGLOBULINEMIA

FIGURE 5A
Pulmonary infiltrations in 58 year old male with acquired agammaglobuline mia. Note lobular consolidation in left lower lobe.

FIGURE 5B
FIGURE 5C
Clues to acute pneumonia several times associated with pneumococcal infection.
agammaglobulinemia was present at the time the thymoma was discovered is suggested by the observation that a total serum protein determination done at the time of his first hospital admission was 5.1 gram per cent, a value identical to that observed when the agammaglobulinemia was known to exist. Additional support for this conclusion was the fact that he had three episodes of pneumonia during the three month period following discovery of the tumor and its ultimate removal. Figures 5A, 5B and 5C illustrate the pulmonary infiltrations which featured the recurrent respiratory infections this patient suffered following the development of his clinical disease. In all, he had at least 17 separate attacks of bacterial pneumonia during the four years of his illness.

Case 8: L. L., 30 year old white female was well until eight years prior to study. With no apparent precipitating cause she began to have many severe bacterial infections. During the eight years of her disease she has had 34 episodes of pneumonia, sometimes lobar and other times bronchial in character. In addition to pneumonia, repeated episodes of otitis media, sinusitis, four attacks of pneumococcal meningitis and other severe bacterial infections kept this patient in almost constant need of medical and hospital care. Figure 6A shows the chest x-ray revealing pneumonia described by the roentgenologist as being limited primarily to the right perihilar region. This infection was associated with high fever, leukocytosis and the presence of pneumococci in her nose culture and sputum. Figure 6B shows her lungs during a separate episode of bilateral basilar pneumonia. A more characteristic lobar distribution is seen.

In Figure 7A the chest film reveals interstitial fibrosis following a six month period when she was kept free of demonstrable respiratory infection by continuous prophylactic antibiotic therapy. During this entire period she was free from recurrent pneumonia that had been a virtually constant problem since her illness began approximately eight years before. Bronchograms illustrated in Figure 7B indicate clearly that bronchiectasis has not yet occurred and does not account for the apparent fibrosis on the roentgenograms. This observation indicates further that adults with acquired agammaglobulinemia may have innumerable episodes of pneumonia without developing bronchiectasis. Similarly our other case of acquired agammaglobulinemia, F. H., had 17 attacks of bacterial pneumonia over a four year period without developing bronchiectatic changes.

Interestingly enough, both L. L. and F. H. had a hematological disorder associated with the agammaglobulinemia syndrome. As already mentioned with F. H., a benign thymoma featured by hyperplasia of the thymic reticulum was present. In the case of L. L. a diffuse hyperplasia of the fixed and free reticulum (mesenchyme) of the

**FIGURE 6A**

*Figure 6A:* Bilateral pneumonia in 30 year old female with acquired agammaglobulinemia. Note infiltration at lung bases bilaterally.

**FIGURE 6B**

*Figure 6B:* Recurrence of pneumonia this time with more of a lobar configuration at left base. Over an eight year period this patient suffered at least 34 attacks of pneumonia, four attacks of meningitis and numerous other episodes of bacterial infection.
Figure 7A: Residual "fibrosis" at the lung bases in patient whose earlier bronchopneumonic episodes are illustrated in Figure 6. Figure 7B: Bronchogram reveals the absence of bronchiectasis in the involved areas.
spleen, lymph nodes and bone marrow was present. In this instance hepatosplenomegaly was associated with the development of a Coombs-negative acquired hemolytic anemia and leukopenia. Splenectomy resulted in prompt disappearance of the hemolytic anemia. This observation of acquired hemolytic anemia in a patient incapable of antibody formation coupled with its dramatic cure by splenectomy is strong evidence in support of the concept of hypersplenism independent of immunological mechanism. An entirely similar case has been reported by Rhon et al. Microscopic study of the spleen revealed the same abnormality of the reticulum observed from study of the bone marrow and lymph nodes—namely a diffuse proliferation of the reticular stroma and the occurrence of a granulomatous process not further defined by the pathologist. These findings will be presented in greater detail in another report.

At the present time this patient is being maintained on continuous prophylactic treatment with penicillin and terramycin and during the past one and one-half years has been completely free of the recurrent bacterial infections which had been such a serious problem during the previous eight years.

**Discussion**

The relatively new disease agammaglobulinemia has been described from the point of view of the chest physician. Virtually all of the patients suffering from this disease present themselves to the doctor because of recurrent pulmonary infections. Many of them, both children and adults, suffer severe complications of their pulmonary infections namely bronchiectasis, empyema, lung abscess, atelectasis and pulmonary fibrosis. These observations make it particularly important for those concerned with the management of pulmonary disease to be aware of agammaglobulinemia, to make the diagnosis early and to institute treatment which will minimize the symptomatology and perhaps prevent the destructive consequences of recurrent severe bacterial disease of the pulmonary parenchyma.

It is now recognized that at least three forms of agammaglobulinemia exist. The disease first described by Bruton is a childhood form of agammaglobulinemia which occurs only in males and is transmitted as a sex-linked recessive trait. To date 24 cases of this form of agammaglobulinemia have been reported. In addition, and apparently distinct, is the form of agammaglobulinemia occurring in adults. This disease appears to occur at any age in either sex. Nineteen such cases have now been reported bringing the total number of agammaglobulinemic patients already described in the clinical literature to 43. The third type of agammaglobulinemia is a transient form which occurs in infants during the first six months of life. This form represents a delay in assumption by the infant of gamma globulin formation. Although several cases of the latter disease have been recognized, little critical information has so far been presented concerning this disturbance. It has, however, been suggested that this transient hypogammaglobulinemia of infancy may be associated with the pulmonary disease responsible for many unexpected or "crib" deaths occurring in infants.

In both the congenital and adult forms, the isolated deficiency of gamma globulin in the blood is associated with failure of the immune response which probably accounts for the extreme susceptibility of the patients with this metabolic disorder to bacterial disease, and accounts for the characteristic expression of the clinical syndrome.

Recent studies have indicated that underlying the deficiency of gamma
globulin and antibody formation in these patients is a disturbance of the hematopoietic tissues expressed in a variety of ways but in each instance featured by the absence of plasma cells and failure of plasma cell development in response to antigenic stimulation. This concept receives support from observations presented in this paper. In immunologically normal persons bronchiectasis is associated pathologically with the infiltration of the pulmonary parenchyma by leukocytes of both polymorphonuclear and mononuclear type. In the pathological material of every case of bronchiectasis which we have examined, numerous plasma cells were to be found among the mononuclear cells in the inflammatory exudate. To the pathologist these cells are recognized as signs of the chronicity of the inflammatory process. In the bronchiectatic pulmonary tissue removed from a patient with agammaglobulinemia herein described, the inflammatory exudate differed from that of the immunologically normal bronchiectatic patients in one particular—plasma cells were not to be found in the exudate. This observation lends strong support to the concept that in some way gamma globulin production and antibody formation are intimately associated with plasma cell formation and strengthens the concept that occurring in inflamed tissues these cells are the sign of local antibody production. With the recognition of the disease, completion of its primary classification and delineation of its distinctive features, it seemed worthwhile to stress the prominent part played by pulmonary infection in the course of both congenital and acquired types. It seems doubtful from the data presented here that significant differences in the incidence of lower respiratory tract infections exist between the two groups. All patients with agammaglobulinemia regardless of the sub-classification are inordinately susceptible to pulmonary infections with pneumococci, streptococci, hemophilus and staphylococci and without prophylactic treatment their lives are one round of severe pulmonary disease after another. Whether the complicating pulmonary disorders, e.g. bronchiectasis, occur more commonly in the adult form of agammaglobulinemia than in the childhood disease awaits further reporting. From the data currently available and presented in our Tables it would appear that approximately 17 per cent of the congenital cases thus far reported have developed bronchiectasis whereas 30 per cent of the adult cases which have been completely reported to date have had this complication. Personal communications concerning unreported and incompletely reported cases indicate that bronchiectasis may occur even more frequently in the adult disease than our summary would indicate. Contrariwise there is also a suggestion that our figures may be somewhat high for patients with the congenital disorder. Only future complete reporting will clarify this relationship. The fact that bronchiectasis does occur with considerable frequency in both the adult and childhood forms of agammaglobulinemia suggests, however, that it might be prudent to carry out electrophoretic analysis on serums of all patients with bronchiectasis particularly if the latter disease develops during adult life in an effort to ferret out the cases of agammaglobulinemia being expressed in this way.
Both of our cases of the acquired type of agammaglobulinemia had overt disease of the reticuloendothelial system. In one instance a huge benign tumor of the thymus was observed while the other case was featured by diffuse proliferation of the reticulum resulting in lymphadenopathy, hepatosplenomegaly and reticular hyperplasia of the bone marrow associated with hypersplenism. Just as was the case with the agammaglobulinemic children, neither of these patients was capable of plasma cell proliferation in response to antigenic stimulation. On the basis of the uniform occurrence of diverse hematological disturbances in patients with agammaglobulinemia including profound lymphopenia, neutropenia, eosinopenia, reticular hyperplasia, and thymic tumor, it has been postulated that the basic disease in both congenital and acquired agammaglobulinemia resides in a disordered reticular function which is expressed in all of the patients as a failure of antibody and gamma globulin production associated with failure of development of plasma cells from reticular cells—their natural precursor.

In sharp contrast to the extreme susceptibility of these patients to bacterial disease as documented in this and previous reports, virus diseases have not presented a serious problem. This paradox features both the congenital and the acquired forms of agammaglobulinemia.

For example, even with thorough re-exposure on numerous occasions, recurrences of measles, chickenpox and mumps have not been a problem and these patients do not appear to have any special difficulty with the common respiratory diseases or atypical pneumonia. The explanation for this relative resistance to virus infection has not been elucidated, nor is it certain that the resistance extends to all viruses. Suggesting that some virus infections may be poorly handled by these patients just as are bacterial infections is the fact that each of two patients with agammaglobulinemia known to have developed virus hepatitis died. In one of the patients fatal acute yellow atrophy of the liver resulted whereas the other succumbed after a prolonged illness diagnosed as chronic hepatitis.

Although much has been accomplished through treatment of patients with agammaglobulinemia the therapeutic approaches available are not yet entirely satisfactory. Replacement therapy in the form of injections of gamma globulin appears to be particularly beneficial in children. As usually carried out 0.6 cc. of concentrated gamma globulin solution containing 0.1 gram of gamma globulin per kg. of body weight is given intramuscularly. This dosage serves to bring the circulating gamma globulin concentration to levels approximating 100 mg. per cent which appear to be protective against many of the common bacterial infections. Since the half life of gamma globulin in these patients is approximately 30 days injections must be given every three or four weeks in order to provide continuous protection in this way.

The reported failure of gamma globulin to provide clinical improvement in adults or children with agammaglobulinemia is probably due in part at least to the use of insufficient quantities of gamma globulin. Prophylaxis with antibiotics has been advocated for these patients, an
approach which would be supported by our experience with L. L. This patient having an average of 4-6 attacks of pneumonia and many other severe infections each year has been kept free of bacterial infections for a period of one and one-half years through the use of prophylactic therapy with terramycin in a dosage of 15 mg./kg./day. Similarly, one of the children in whom the agammaglobulinemia is complicated by bronchiectasis, continuous administration of three antibiotics provided in rotation has resulted in striking clinical improvement which was not achieved by gamma globulin alone.

On theoretical grounds we hesitate to recommend reliance on antibiotics to protect these patients from recurrent bacterial disease. We fear the establishment of a potentially threatening flora of microorganisms resistant to available antibiotics in these patients who are characterized by a deficiency in one of the major defense mechanisms. However, with the ever increasing number of broad spectrum antibiotics available, ultimately a combination of prophylactic antibiotic and gamma globulin therapy may prove to be the most efficacious approach to this problem.

To those concerned with the mechanism underlying this disease agammaglobulinemia represents a challenging experiment of nature. The ultimately successful management of these patients must await more basic information on the nature of both the inherited and acquired forms of this molecular disease.

SUMMARY

1. Agammaglobulinemia—a relatively new disease is discussed from the standpoint of the chest physician.

2. Eight cases studied at the University of Minnesota during the past two years are briefly presented.

3. The available literature on agammaglobulinemia is reviewed to emphasize the importance of pulmonary manifestations in the clinical expression of this metabolic disorder.

4. Among the 43 cases reported to date, 24 have been of the congenital type which is transmitted as a sex-linked recessive trait and 19 have been of the acquired type.

5. The most consistent clinical finding in both groups of agammaglobulinemic patients is recurrent bacterial respiratory infection often expressed as lobar or bronchiopneumonia.

6. Bronchiectasis occurred in four of 24 cases of congenital agammaglobulinemia and four of 13 completely reported cases of acquired agammaglobulinemia.

7. Other pulmonary complications reported to date in agammaglobulinemic patients include empyema, lung abscess, atelectasis, pulmonary fibrosis and diffuse pulmonary calcifications.

8. The inflammatory exudate of the bronchiectatic processes of an agammaglobulinemic patient and of immunologically normal persons are compared. The characteristic absence of plasma cells from the exudate in the agammaglobulinemic patient is recorded.
9. The development of “acquired” agammaglobulinemia associated with the occurrence of a large thymoma in a 54 year old male is described.
10. The hematological basis of agammaglobulinemia is mentioned.
11. The therapeutic approach to agammaglobulinemia is discussed.

RESUMEN
1. La agamaglobulinemia es una enfermedad relativamente nueva que se discute aquí desde el punto de vista del especialista de tórax.
2. Se presentan de manera breve ocho casos que han sido estudiados en la Universidad de Minnesota durante los dos años pasados.
3. Se hace una revisión de la literatura sobre la agamaglobulinemia para hacer resaltar la importancia de las manifestaciones clínicas que expresan este trastorno metabólico.
4. Entre los 43 casos que se han relatados hasta ahora, 24 han sido de tipo congénito que es transmido como un carácter recesivo ligado al sexo y en 19 se ha encontrado que son adquiridos.
5. El hallazgo más constante clínicamente en ambos grupos de agammaglobulinemia es la infección respiratoria recurrente a menudo expresada como neumonía lobar o bronconeumonia.
6. Ocurrió la bronquiectasia en 4 de 24 casos de agammaglobulinemia congénita y 4 de 13 de los relatados completamente entre los de agammoglobinemia adquirida.
7. Otras complicaciones pulmonares que se han relatado hasta ahora son: empiema, absceso pulmonar, atelectasia, fibrosis pulmonar y calcificaciones pulmonares difusas.
8. Se ha comparado el exudado inflamatorio de los procesos bronquiec-tásicos de un enfermo de agamaglobulinemia y los de un enfermo que es normal en el aspecto inmunobiológico. Se refiere la ausencia característica de células plasmáticas en el exudado del enfermo con agamaglobulinemia.
9. Se describe el desarrollo de una agamaglobulinemia “adquirida” concurriendo con un timoma grande en un hombre de 54 años.
10. Se menciona la base hematológica de la agamaglobulinemia.
11. Se discute la conducta terapéutica en la agamaglobulinemia.

RESUME
1. Les auteurs discutent du point de vue du spécialiste des poumons “l'agammaglobulinémie,” maladie de découverte relativement récente.
2. Ils présentent brièvement huit cas étudiés à l'Université de Minnesota pendant les deux années qui viennent de s’écouler.
3. Ils font la revue de la littérature actuelle portant sur l’agammaglobulinémie, en insistant sur l’importance des manifestations pulmonaires dans l’expression clinique de ce trouble métabolique.
4. Parmi les 43 cas rapportés récemment, 24 ont été du type congénital, transmis comme un caractère récessif, et 19 ont été du type acquis.
5. La constatation clinique la plus caractéristique dans les deux groupes de malades atteints d’agammaglobulinémie est l’infection respiratoire bacterienne récidivante, souvent de type lobaire ou prenant la forme bronchopneumonique.
6. Une bronchiectasie survint dans 4 des 24 cas d'agammaglobulinémie congénitale, et dans quatre des 13 cas d'agammaglobulinémie acquise, rapportés en détail.

7. Les autres complications pulmonaires rapportées chez des malades atteints d'agammaglobulinémie, sont : l'épanchement pleural, l'abces pulmonaire, l'atélectasie, la fibrose pulmonaire et des calcifications pulmonaires diffuses.

8. Les auteurs ont comparé l'exsudat inflammatoire des processus bronchiectasiques d'un malade atteint d'agammaglobulinémie, et de personnes immunologiquement normales. Ils rapportent l'absence caractéistique de plasmocytes dans l'exsudat du malade atteint d'agammaglobulinémie.

9. Les auteurs décrient le développement d'une agammaglobulinémie acquise associée à l'apparition d'un thymome important, survenus chez un malade âgé de 54 ans.

10. Les auteurs mentionnent la base hématologique de l'agammaglobulinémie.

11. Ils discutent la conduite thérapeutique.

ZUSAMMENFASSUNG

1. Die Agammaglobulinämie, eine verhältnismässig neue Krankheit, wird vom Standpunkt des Thoraxspezialisten erörtert.

2. Acht während der letzten zwei Jahre an der Universität von Minnesota untersuchte Fälle werden kurz dargestellt.

3. Es wird ein Überblick über die verfügbare Literatur über Agammaglobulinämie gegeben, um die Bedeutung der Lungenerscheinungen im klinischen Bilde dieser Stoffwechselstörung hervorzuheben.

4. Von den bisher veröffentlichten 43 Fällen waren 24 kongenitaler Art, die als eine sechsgliedrige rezessive Anlage fortgepflanzt wurden, und bei den übrigen 19 handelte es sich um die erworbene Form.

5. In beiden Gruppen der Kranken mit Agammaglobulinämie ist der wichtigste Befund eine zu Rückfällen neigende respiratorische bakterielle Infektion, die häufig in Form einer lobären oder einer Bronchiopenonium zum Ausdruck kommt.


9. Es wird der Fall eines 54 jährigen Mannes beschrieben, bei dem gleichzeitig eine "erworbene" Agammaglobulinämie und ein grosses Thymom beobachtet wurden.
10. Die hämatologische Grundlage der Agammaglobulinämie wird erwähnt.
11. Wege zur Behandlung der Agammaglobulinämie werden erörtert.

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52 Janeway, C. A.: Personal communication.
54 Janeway, C. A.: Personal communication.