Severe Para-Aminosalicylic Acid Hypersensitivity
Blood and Lymph Node Studies

By W. Cannemeyer, J. R. Thompson and M. R. Lichtenstein

Para-aminosalicylic acid (PAS) is a drug which has a bacteriostatic effect on the tubercle bacillus and is widely used in the treatment of patients with tuberculosis. In a previous report we have described the clinical picture of severe PAS hypersensitivity simulating infectious hepatitis or mononucleosis. The present study is intended to illustrate and describe in greater detail the blood and lymph node changes which occur in this condition. The significance of atypical lymphocytes and liver involvement in hypersensitivity to a simple chemical will be discussed.

Clinical Characteristics of the Reaction

Fourteen patients of approximately 5,000 taking PAS in this institution acquired a severe hypersensitivity to the drug. The reaction began 15 to 43 days after the beginning of therapy and all cases developed fever (100.2 to 105° F.), rash and pruritus (table 1). The rash involved the face, neck, and extremities in the milder cases and was generalized in the severer ones. Usually it was erythematous, macular, or morbilliform, but in one case it was urticarial. The pruritus was fairly severe in all but 3 patients. Chills frequently accompanied the fever and were severe in 4 cases. Nausea was experienced by most patients and burning of the eyes and lacrimation added to the discomfort of headache and generalized aching. Cervical lymphadenopathy was noted in eleven patients; axillary and inguinal nodes were palpable in a few. Tenderness and enlargement of the liver was found in 5 patients; three had a splenomegaly and two had obvious jaundice.

It will be noted from table 1 that there occurred considerable variation in the extent and intensity of the reaction. The case reports which follow will further illustrate these variations.

Case Reports

Case 1—M. L.

This white woman, age 26 years, was classified as moderately advanced pulmonary tuberculosis with infiltration involving the left apex. A few days before antimicrobial therapy, her blood count was essentially normal except for a slight hypochromia. Treatment with streptomycin (1 Gm. twice weekly) and PAS (12 Gm. daily in 3 divided doses) was successful until the thirty-fourth day when she suddenly developed fever (101.2 F.), chills, burning of the eyes and lacrimation, nausea and an extremely pruritic erythematous macular rash which involved the face, arms and legs. The blood count showed leukocyte count 6,800 per cu. mm; neutrophiles 37 per cent, eosinophiles 26 per cent, atypical lymphocytes 10 per cent (Downey's type I) and plasma cells 1 per cent. Pertinent blood chemistry findings were cephalin flocculation 3 plus and serum bilirubin 1.9 mg. per 100 ml. Blood cultures and agglutination tests including Paul-Bunnell reactions were negative. Patch tests revealed a
negative reaction to streptomycin and a doubtful positive to PAS. Roentgenogram of the chest revealed no change from the status prior to the reaction. PAS was immediately discontinued and benadryl was given for the rash with calamine lotion applied to affected areas.

Within 10 days from the onset she had completely recovered and the blood count was normal except for an occasional plasma cell and 5 per cent eosinophils. Two weeks after recovery she was given a trial dose of PAS (4 Gm. sodium PAS) along with pyribenzamine. Within one hour her temperature rose to 100 F., her face became flushed, her eyes burned and she developed a headache and a generalized pruritus. The second trial dose (1 Gm. calcium PAS) was given one week later and evoked a similar response. The blood picture after each trial dose changed abruptly from normal to one showing a marked toxic neutrophilic left shift (40 per cent bandforms), eosinophilia (9 per cent) and the reappearance of plasma cells and an occasional atypical lymphocyte. The patient recovered completely from the test dose reactions within a few days. Streptomycin was given and isoniazid was substituted for PAS.

Comment on Case 1

This case demonstrates a mild reaction to PAS showing some hepatic involvement. The patient responded so well to streptomycin and isoniazid that desensitization to PAS was not attempted.

Case 2—A. G.

A white female, age 34 years, was readmitted to the M. T. S., a case of far advanced pulmonary tuberculosis. Her admission blood count was essentially normal except for a slight neutrophilic left shift and a rise in monocytes (9 per cent). Streptomycin, 1 Gm. semiweekly, and PAS, 12 Gm. daily, were successfully tolerated for 20 days. On the twenty-first day she had a severe chill and fever (104 F.). The next day she was covered with an erythematous macular rash and cervical, axillary, and inguinal lymph nodes were palpable and tender. PAS and streptomycin were discontinued. The blood count showed total leukocyte count 6,400 per cu. mm., neutrophiles 61 per cent with 36 per cent bandforms, eosinophiles 8 per cent, atypical lymphocytes 8 per cent (Downey's type I forms) and a few plasma cells. Approximately one week later streptomycin therapy was resumed. However, within 5 hours after a 1 Gm. injection she had a severe chill, fever (102 F.), nausea and vomiting, headache, arthralgia, numbness of the hands and feet, and painful lymphadenopathy. She became acutely ill—confused and apprehensive, dyspneic and cyanotic. The liver was enlarged (2 fingers) and extremely tender. The blood count at this time showed leukocyte count 17,000 per cu. mm., neutrophiles 95 per cent (bandforms 42 per cent) and atypical lymphocytes 2 per cent. Blood chemistry findings were cephalin flocculation 3 plus, alkaline phosphatase 12.4 units, bilirubin 1.5 mg. per 100 ml., sulfobromophthalein (Bromsulphalein) 10 per cent retention, and prothrombin 66 per cent of normal. Blood cultures, spinal fluid, cold agglutination and Paul-Bunnell reactions were all negative. The total leukocyte count dropped to 6,300 per cu. mm., neutrophiles 33 per cent, eosinophiles 21 per cent and an occasional atypical lymphocyte and plasma cell. Patch tests for PAS were highly positive and for streptomycin entirely negative except for itching. Chest roentgenogram showed a slight enlargement of the right apical cavity but no other extension of the diseased areas. The patient was treated with intravenous fluids (dextrose-saline), pyribenzamine (50 mg. three times a day) and calamine lotion locally. She completely recovered within 4 weeks from the onset of the streptomycin reaction and her blood count returned to normal except for a lingering eosinophilia (7 per cent). A test dose of streptomycin (0.25 Gm.) was then given. This was promptly followed by an acute rise in temperature (104.6 F.), chills, generalized erythema and itching, and a severe headache. The blood count showed a leukocyte count of 6,540 per cu. mm. and neutrophiles 97 per cent with 45 per cent toxic bandforms. Three days later the eosinophiles were 10 per cent and a few atypical lymphocytes and plasma cells were found.

Ten days after the test dose of streptomycin, when the blood count was again normal, a 5 minum dose of PAS was attempted. This resulted in a rise of temperature to 99.8 F. and
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<th>Gastrointestinal symptoms</th>
<th>Burning of eyes and lacrimation</th>
<th>Type of rash</th>
<th>Distribution of rash</th>
<th>Pruritus</th>
<th>Adenopathy</th>
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<td>-</td>
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<td>Erythematous Macular</td>
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Table 1.—Clinical Characteristics of the Reaction
66 PARA-AMINOSALICYLIC ACID SENSITIVITY

a marked erythema and itching at the site of the PAS patch test. No significant change occurred in the blood picture at this time except a transient eosinophilia (7 per cent). Streptomycin therapy was abandoned and dropwise desensitization to PAS was started. This progressed successfully and within 8 months the patient was taking the full dose of PAS daily. Repeat patch tests to PAS and streptomycin revealed both to be completely negative. A trial dose of streptomycin (1 Gm.) was attempted again and this time caused no reaction. The patient is at present taking successfully PAS (12 Gm. daily), streptomycin (1 Gm. twice weekly) and isoniazid (100 mg. daily).

Comment on Case 2

In this case, there was extreme morbidity and the regular recurrence of symptoms with even small doses of the drugs; although not desensitized to streptomycin, the patient was able to tolerate this drug after desensitization to PAS had been achieved.

Case 3—D. S.

A white woman, age 27 years, was diagnosed as moderately advanced pulmonary tuberculosis with cavitation in the left apex. The pre-therapy blood count revealed a slight leu
trophilic left shift and hypochromia of the red cells (table 2). The patient was started on streptomycin, 1 Gm. semiweekly, and PAS, 12 Gm. daily in 3 divided doses. The drugs were well tolerated until the twenty-fourth day when the patient noticed some nausea and vague abdominal discomfort. On the twenty-eighth day she suddenly developed severe chills, perspiration and an elevated temperature (102.6 F.). An erythematous rash appeared over the trunk and extremities and on the third day after the sudden onset she complained of periods of extreme nausea, tenderness over the region of the liver, and general achiness. The following day the liver and spleen were palpable, the rash, now morbilliform, in full bloom, and the skin irritation and pruritus intense. The blood count showed leukocyte count 8,150...

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Table 3.—(Case D. S.)—Blood Chemistry Findings at the Height of Reaction and for Five Months thereforher in a Patient with Jaundice

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<th>Fibrin, gm/100 ml</th>
<th>Albumen, gm/100 ml</th>
<th>Glob., gm/100 ml</th>
<th>A/G ratio</th>
<th>Total proteins, gm/100 ml</th>
<th>Bilirubin, mg/100 ml</th>
<th>Thymol turb., units</th>
<th>Alkaline phosphates, units</th>
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per cu. mm., neutrophiles 33 per cent with bandforms 18 per cent, eosinophiles 8 per cent, and atypical lymphocytes 18 per cent (table 2). PAS and streptomycin were discontinued. Benadryl and pyribenzamine were given for the rash. The reaction continued to progress: temperature up to 101 F., definite cervical and inguinal lymphadenopathy and visible jaundice. On the fourteenth day of the reaction the blood count showed leukocyte count 15,050 per cu. mm., neutrophiles 30 per cent, eosinophiles 21 per cent and atypical lymphocytes 3 per cent. The blood chemistry: cephalin flocculation 4 plus, alkaline phosphatases 21.4 units, thymol turbidity 19 units, bilirubin 3.2 mg. per 100 ml., albumen 2.8 Gm. per 100 ml. and globulin 3.68 Gm. per 100 ml. (table 3). Complete blood cultures, cold agglutination and Paul-Bunnell reactions were consistently negative. A chest roentgenogram revealed no extension or change in the character of the tuberculous lesion. During the fourth week after the onset of the reaction the patient was definitely better: liver, spleen and nodes were no longer palpable, the rash had completely disappeared, the temperature was normal and the ieterus scarcely visible. The blood picture and blood chemistry values were approaching normal. Patch tests for the drugs were positive to PAS and negative to streptomycin. Two months after the beginning of the reaction a single test dose (1 Gm.) of PAS was given. Within 3 hours after ingestion, the patient developed weakness and faintness, a painful headache, arthralgia and an erythematous edematous reaction of the skin. Her temperature rose to 101.4 F. and she complained of tenderness over the region of the liver. The blood picture showed an abrupt change: a neutrophilic left shift with toxic granulation, eosinophilia (8 per cent) and the reappearance of a few atypical lymphocytes and plasma cells. Pyribenzamine (50 mg, three times daily) was given and within 48 hours she was normal again. Further testing and PAS desensitization were refused. Streptomycin was resumed and she tolerated this drug fairly well although at times under cover of pyribenzamine.

Comment on Case 3

This was one of the first cases we encountered and we feel now that if the drugs had been stopped sooner she might not have progressed to liver damage and jaundice. This case illustrates well the similarity of PAS hypersensitivity to infectious hepatitis and mononucleosis and points to the value of repeated trial doses, blood studies, and skin testing in the differential diagnosis.

Laboratory Characteristics of the Reaction

Hematology

Hematological findings in severe PAS hypersensitivity may vary considerably. Acute hemolytic anemia, neutrophilic leukocytosis, neutropenia, eosinophilia,
lymphocytosis⁴ and atypical lymphocytes⁵ have been reported. In the 14 cases observed at the Municipal Tuberculosis Sanitarium, the most remarkable blood changes at the height of the reaction were a relative or absolute lymphocytosis with atypical forms and an eosinophilia. The atypical lymphocytes (fig. 1) were similar to those found in infectious hepatitis, mononucleosis, “viral” respiratory disease, and allergic states⁶ and constituted from 1 per cent to 21 per cent of the total leukocytes. The majority of these cells could be classified as Downey’s type I forms.⁷ They were quite large (12–15 micra) with marked basophilic cytoplasm which was either mottled or vacuolated and frequently contained azurophilic granules. The nuclei were usually eccentrically placed, often indented and occasionally twisted. The chromatin was arranged in strands; nucleoli were usually absent. Lymphocytes similar to Downey’s type III were also found—up to 4 per cent in one case. These cells were large (15–18 micra) and not like the highly differentiated type I forms. The nuclei were immature, had a diffuse thready chromatin network and 1 to 3 nucleoli. The cytoplasm was moderately basophilic and did not contain granules. An occasional “plasma-cell” type—Downey’s type II, was found in all cases. These cells were smaller (10 to 12 micra) and had dense round or oval-shaped nuclei eccentrically placed in an extremely basophilic cytoplasm. Irregular lymphocytes could be found in the peripheral circulation in within 4 to 15 days during the original reaction. The eosinophiles varied from 7 per cent to 56 per cent; however, most of the counts showed from 12 per cent to 25 per cent. Some of these cells were considerably larger than normal (up to 2 X) and areas of pale basophilic cytoplasm were clearly visible between widely scattered granules. The eosinophiles tapered off to normal levels within 3 to 6 weeks after the onset.

The total leukocyte counts varied between 6,000 and 15,000 per cu.mm. However, 4 patients had occasional counts between 20,000 and 33,000 at the time of acute eosinophilia and lymphocytosis and 3 patients dropped to a leukopenia (3,500 to 4,500 per cu.mm.). Relative neutropenia was a common finding and 4 patients showed an absolute decrease as well (1,800–3,000 neutrophiles per cu.mm.). All cases showed a neutrophilic left shift during the acute phase of the reaction (12 per cent to 30 per cent bandforms). Marked left shifts with bandforms as high as 50 per cent and toxic granulation were observed to occur immediately after test doses of the drug. A definite increase in the number of basophiles (up to 5 per cent) was noted in 3 cases. In most of the cases the monocytes did not demonstrate any changes above the usual increase in active tuberculosis. In 2 patients, however, there occurred a temporary sharp rise in the absolute number (1,980 and 2,110 per cu.mm.) toward the end of the reaction period and in one case a few promonocytes were seen.
None of the patients developed an appreciable anemia; in fact, only five showed a significant decrease in the red count (300,000 to 500,000 per cu.mm.) and hemoglobin value (0.8 to 1.5 Gm.) below the pre-reaction level. All patients maintained normal thrombocytes, in number and morphology, throughout the reactions.

Within 3 to 4 weeks the entire blood picture showed a return to its pre-reaction status. However, after each trial dose of the drug, there occurred a sudden pronounced neutrophilic leukocytosis with a marked left shift and toxic granulation. This phase lasted from 5 to 8 hours and was followed by a rapid increase in eosinophiles, a drop in neutrophiles, a marked increase in lymphocytes with a preponderance of large forms and a few plasma cells. Within 24 hours atypical lymphocytes appeared, although fewer in number than in the original reaction. Test dose reactions usually lasted from 3 to 5 days and within a week all blood elements would again approach normal levels. Typical fluctuations in all series are illustrated in table 2.

Phagocytic Function

Studies in phagocytosis were carried out in 7 cases using Staphylococcus aureus as test particles. The cells of the buffy coat of 5 cc. heparinized blood were resuspended in 0.1 cc. of a 1:10 dilution of normal serum in salt solution. To this was added 0.2 cc. of heat killed Staph. aureus (2 billion per cc.) and the suspension was incubated in a 37 C. water bath for 30 minutes, mixing thoroughly every 2 or 3 minutes. One drop of normal serum was then added and smears, as done in blood, were made and stained with Wright's stain. The neutrophiles, eosinophiles and monocytes exhibited active phagocytosis whereas the lymphocytes, normal and atypical, failed to show this property in our preparations (fig. 2). Strumia and Boerner found lymphocytes to be incapable of phagocytosis in their series of experiments. Hertzog, on the other hand, was able to demonstrate this function in 1.17 per cent of small lymphocytes, in 7.45 per cent of large lymphocytes, and in as many as 12 per cent of the leukocytoid lymphs of infectious mononucleosis. He concluded from this that "lymphocytes in their..."
pre-phagocytic stage may occasionally show phagocytosis under experimental conditions.”

**Bone Marrow**

Examination of sternal bone marrow revealed the tendency to a left myeloid shift and a definite increase in the eosinophiles with as high as 8 per cent eosinophilic myelocytes in one case. Plasma cells were found in all specimens of marrow but only one patient showed a slight increase in these forms (2.5 per cent). An occasional atypical lymphocyte was seen in most of the preparations but never in the proportions found in blood. “L.E.” cells were carefully examined for but never found in our cases. The erythroid series did not show any deviations from the normal.

**Agglutination Tests**

Cold agglutination tests and Paul-Bunnell reactions (repeatedly performed in each patient) were consistently negative.

**Blood Chemistry**

Liver profile studies showed slight to marked deviations from normal, the most significant changes occurring in the patients with hepatomegaly, splenomegaly and jaundice. Alkaline phosphatase values of 13.7 units, 21.4 units, 28.0 units and 52.6 units were found in these patients. The thymol turbidity was above normal in 6 cases, varying from 8 units to 24 units. Elevated serum bilirubin was found to occur in 4 patients (1.9 mg. to 6.4 mg.). Cephalin flocculation was 3 to 4 plus in 8 patients). The sulfobromophthaleim (Bromsulphalein) test showed excessive retention in 3 cases—15 per cent, 20 per cent and 30 per cent.

Analysis of the blood proteins demonstrated definite alterations in the albumen-globulin ratio characterized by a drop in the albumen level and an increase in globulin. The most significant resulting A/G ratios were 0.5 and 0.7 which occurred in 2 severely ill patients concurrent with the most outstanding changes in their liver profiles (table 3, case D. S.). Non-protein nitrogen levels remained within the normal range in all cases. All segments of the liver profile and the plasma proteins tended to approach normal within 1 to 2 months of the onset.

**Lymph Node Biopsies**

Posterior auricular lymph nodes were studied in 7 patients. The capsule of each node was intact and not invaded or involved in any fashion. The striking change was the loss of the normal architectural pattern and the marked hyperplasia of the reticuloendothelial elements (fig. 4a and 4b). Seldom could any distinct lymph follicles or cortical nodules be demonstrated in the sections. The lymphoid elements consisted for the most part of mature lymphocytes but a number of immature cells were noted. In one instance the lymphoid cells were diffusely scattered and appeared to be separated by reticuloendothelial cells with no sharp line of demarcation (fig. 5). In all the sections studied, many eosinophiles were seen as well as neutrophiles. Some of these polymorphonuclear...
Fig. 3. - Lymph node imprints demonstrating the huge atypical lymphocytes. Note the diffuse thready chromatin network of the nuclei. Size comparison can be made with mature lymphocytes in the field (×100).

Fig. 4a. - Section of a lymph node showing a marked reticulo-endothelial proliferation. Note the intact capsule and the absence of follicles in the cortex (×100).

leukocytes appeared to be disintegrating. In one node a large amount of fibrinoid or hyaline type matrix was noted (fig. 6). This was seen to a lesser degree in some of the other sections. The blood vessels did not show any significant changes and in only one section was there any evidence of hemorrhage. This hemorrhage was thought to be due to trauma at the time of biopsy. The changes in the lymph nodes are similar to those described by Hayes and Weiss in one biopsied node which was reported as showing a reactive type of hyperplasia with congestion and acute adenitis, along with hyperplasia of the reticuloendothelial elements. They too noted an increase in the number of eosinophiles and, in addition, some fine arteriolar changes.
FIG. 4b.—Higher magnification showing some immature lymphoid cells and large reticulo-endothelial cells (X400).

FIG. 5.—Section of a lymph node showing the small dark staining lymphoid elements separated by large pale staining cells. As in figure 4a, there are no follicles and the capsule is uninvolved (X100).
Fig. 6.—High magnification of one node to show the large amount of fibrinoid or hyaline-type stroma (X400).

Lymph Node Imprints

Imprints of biopsied nodes were made by bisecting them immediately on removal and touching the cut surface gently to slides. The preparations were air-dried, stained with Wright's stain, and restained with Giemsa's stain in the same manner as were the blood and bone marrow smears. Examination of the imprints revealed many atypical lymphocytes (fig. 3) similar to those found in peripheral blood. The “plasma-cell” type was very prominent in some cases and a few neutrophiles, eosinophiles, and mast cells could be demonstrated on all slides.

Skin Tests

Scratch, intradermal, patch, and passive transfer tests were performed. The most useful of these was the patch test which was frequently positive when a 33 per cent ointment of the drug in lanolin was applied to the intact skin for 48 hours. A reaction was considered positive if it showed definite nodules and erythema.

Discussion

Sudden onset with fever, rash, lymphadenopathy and photophobia is commonly found in many drug allergies. The clinical picture of PAS hypersensitivity is similar and in a very small percentage of the cases a more severe form of hypersensitivity may occur, with additional findings simulating infectious hepatitis or mononucleosis (table 1). Since the condition may proceed to a fatal termination, it is important that it be recognized early so that the drug will be stopped in time. That the condition is caused by PAS hypersensitivity is clearly evident:
the reaction subsides rapidly upon discontinuance of the drug; it can be repeatedly induced by very small test doses; and a positive skin test (patch reaction to PAS) can usually be demonstrated. Moreover, as previously indicated, an abrupt change occurs in the blood picture with eosinophiles and atypical lymphocytes reappearing soon after a small test dose is given to a hypersensitive patient. That the reaction is not due to a toxic effect of the drug per se is substantiated by the fact that thousands of tuberculous patients take 12 Gm. of PAS daily for many months without any complaints or ill effects, whereas, those who develop the reaction do so within the first few weeks. It is obvious that this phenomenon is immunologic in nature but like many other forms of allergic response, it is difficult to perceive any beneficial effect of the reaction.

The presence of atypical lymphocytes has been described in several apparently unrelated conditions. Randolph6 described them in food allergies. Their presence has been noted in respiratory diseases and viral infections and they constitute the outstanding finding in mononucleosis. The fact that hypersensitivity to a simple chemical such as PAS can cause the production of atypical lymphocytes suggests the possibility that the common denominator in all these conditions may also be a hypersensitivity. Thus, in viral infections, although the condition may basically be an infection with viruses, it is possible to speculate that the atypical lymphocytosis may be induced by hypersensitivity to a chemical derived from the virus. In mononucleosis whose viral origin has not been conclusively proved, there is room to speculate that the entire picture may be caused by hypersensitivity to an unknown antigen.

Infectious hepatitis has been proved to be of viral nature. The similarity in the picture produced by PAS hypersensitivity suggests the possibility that the liver damage, enlargement, and jaundice which occur in hepatitis may be the result of hypersensitivity to a chemical derived from the virus, rather than the result of the infection per se. Concomitant infection and hypersensitivity to a chemical derived from the infecting agent is common in disease. It is well illustrated in tuberculosis in which hypersensitivity to the tuberculoprotein produces many of the symptoms.

The entire sequence of events in PAS hypersensitivity may be visualized as follows: the drug conjugates with blood proteins and forms an antigen which stimulates the reticuloendothelial system to form antibodies. The hyperactivity of the reticuloendothelium is manifested clinically by lymphadenopathy in mild cases and by enlargement of the liver and spleen in more severe ones. The antibodies may be formed in, or at least attached to, cells of the leukocytic series (lymphocytes or plasma cells?). These cells are released into the circulation, where, according to the concept of Frank and Dougherty,12 adrenocortical hormones produce karyorrhexis of the cells releasing the antibodies into the plasma and tissue fluids. The antibodies then attach themselves to various tissues including the skin and mucous membranes. Wherever they contact the antigen (PAS plus blood protein) or its haptene (PAS alone), an antigen-antibody reaction occurs with the release of material which causes local injury manifested clinically by the skin rash, etc.

In virus infections the same sequence of events may possibly be initiated by a chemical substance derived from the virus and the clinical disease, as in tuberculosis, may be partly a manifestation of infection, partly of hypersensitivity.
The above speculations are subject to criticism because drug allergy has not been proved to be an antigen-antibody reaction nor has the question of antibody carriers been completely settled. The hormonal release of antibodies from white blood cells is likewise controversial. However, these speculations may have some value as a working hypothesis for further studies in drug allergy. PAS hypersensitivity is an excellent condition for further studies of this type in the human because of the simplicity of the chemical involved, the characteristic clinical picture, and its reproducibility.

**SUMMARY**

A severe form of hypersensitivity to para-aminosalicylic acid in patients with tuberculosis was studied. The blood picture, lymph node biopsies, and imprints are described. The similarities between this hypersensitivity to a simple chemical and infectious mononucleosis and infectious hepatitis are discussed. The possibility is suggested that some of the findings in viral diseases are due to hypersensitivity to chemical substances derived from the virus rather than to infection per se.

**SUMMARIO IN INTERLINGUA**

Esseva studiate un forma sever de hypersensibilitate a acido para-aminosalicylic in patientes tuberculotic. Es describte le stato del sanguine e biopsias e impressiones del nodos lymphatic. Seque un discussion del similaritates inter iste hypersensibilitate de un parte e un simple mononucleosis chimic e infectiose e hepatitis infectiose del altere. Es proponite le possibilitate que alcunas del constatationes in morbos viral es debite a hypersensibilitate a substantias chimic derivate ab le virus plus tosto que a infectiones per se.

**REFERENCES**

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Severe Para-Aminosalicylic Acid Hypersensitivity: Blood and Lymph Node Studies

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