MEDICAL STAFF CONFERENCE

Eosinophilia and Eosinophilic Carditis

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California Medical Center, San Francisco. Taken from transcriptions, they are prepared by Drs. Martin J. Cline and Hibbard E. Williams, Associate Professors of Medicine, under the direction of Dr. Lloyd H. Smith, Jr., Professor of Medicine and Chairman of the Department of Medicine.

DR. SMITH:* The discussion today relates to eosinophilia. The case presentation will be given by Dr. Homer Boushey.

DR. BOUSHEY:† This 48-year-old Caucasian male was a disabled laborer who was admitted to the hospital for the fifth time on 1 July 1969 for severe chest pain and recurrent shortness of breath. In 1965 tenderness and swelling of the right calf developed and thrombophlebitis was diagnosed. At that time an eosinophil count of 10 percent was noted. The disease appeared to respond to symptomatic therapy; however, after leaving the hospital the patient continued to have painful swelling of both calves and noted weight loss and wasting of the muscles of the legs. Consequently, he reentered the hospital. A muscle biopsy was interpreted as showing acute eosinophilic myositis at a time when the peripheral eosinophil count was 21 percent. The patient first noted palpitations during that stay in hospital.

In 1968 the patient entered this hospital for the first time. Serum levels of "muscle enzymes" were elevated. The diagnosis of eosinophilic myositis was confirmed by a muscle biopsy in which nearly all the inflammatory cells seen were eosinophils.

Screening tests, including upper gastrointestinal series, barium enema, and sigmoidoscopy, were negative. A gastric ulcer was found which subsequently responded to medical management. Cardiomyopathy was also diagnosed on the basis of cardiomegaly, conduction defects, and arrhythmias, including wandering atrial pacemaker and intermittent two to one A-V dissociation.

In September 1968 the patient was admitted to the neurology service for evaluation. On the day of entry he had a syncopal episode and was found to have complete heart block. A pacemaker was inserted which produced good control of the ventricular rate. At that time peripheral eosinophils were only 1.0 percent with an absolute count of only 74 per cu mm. Corticosteroid therapy was started but discontinued because of exacerbation of abdominal pain associated with a recurrent gastric ulcer.

The patient entered this hospital for the third time in December 1968 because of incomplete small bowel obstruction, which responded to conservative management. During this period the patient's congestive heart failure increased in severity, probably as a result of fluid overload. The patient left the hospital and did relatively well with no specific medication for the myositis. He gained weight and generally felt better.

In April 1969 he entered this hospital for the fourth time, because of recurrent shortness of breath. Intermittent failure of the pacemaker to capture the ventricle was noted, and a pacemaker was reinserted with good control of the ventricular response. He continued, however, to have episodic shortness of breath, increasing cardiomegaly, and pleural effusions. A lung scan showed multiple perfusion defects consistent with pulmonary emboli, and anticoagulant therapy was given. Eosin-

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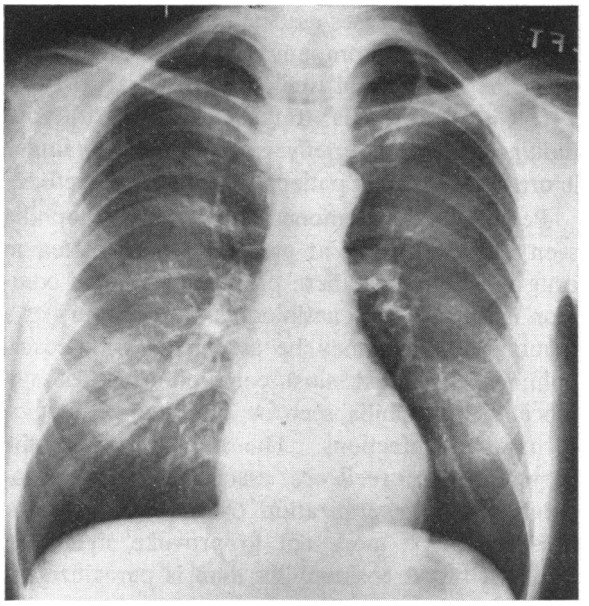

Figure 1.—Radiographic film taken in April 1968, showing normal heart size.

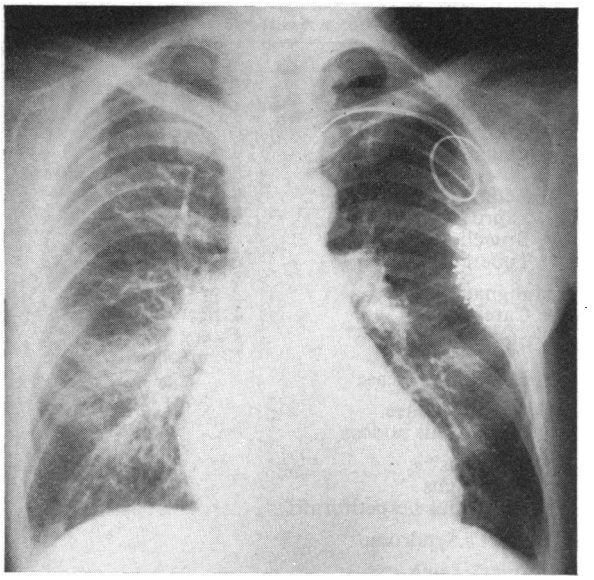

Figure 2.—Radiographic film taken in April 1969, showing increased heart size.

ophils during this admission were never higher than 0.5 percent and an absolute count was 143 per cu mm.

The patient last entered this hospital on 1 July 1969 for evaluation of severe pain of eight hours' duration occurring two days before admission. This pain radiated from the left side of the chest to the right. He had increasingly severe shortness of breath but no cough or hemoptysis.

On physical examination the patient appeared wasted and chronically ill with sunken cheeks and eyes. A livido reticularis pattern was present over the trunk and extremities; the ear lobes were cyanotic. The jugular venous pulse was elevated to 4.0 cm above the clavicles at 30° elevation. The point of maximal impulse was diffusely located over the fifth intercostal space, 1.0 to 2.0 cm lateral to the midclavicular line. A grade ii/vi systolic ejection murmur and a prominent S_3 gallop were heard but no S_4 was evident. The liver was not palpable and there was no pheripheral edema. Pronounced generalized muscle wasting was present with no differential between the proximal and distal muscle groups. Results of neurological examination were within normal limits.

An electrocardiogram showed no important change from previous tracings. Leukocytes numbered 7,000 per cu mm of blood, with no eosinophils. The serum glutamic oxalic transaminase and creatine phosphokinase were elevated as they had been on all previous admissions, presumably because of muscle disease. A lung scan showed considerable clearing since the last admission and no new perfusion defects.

On 3 July 1969 cyanosis and hypotension developed, and a harsh pericardial rub was heard over the entire precordium. Prednisone therapy was begun for the possibility of eosinophilic myositis and pericarditis, but shortly afterward the patient died.

DR AMBERG:* Here is a series of x-ray films beginning 11 April 1968 when the cardiomyopathy was first diagnosed. It is evident that the heart size was completely normal at that time (Figure 1). When he entered the hospital with complete heart block, the heart size was very slightly enlarged. A pacemaker was inserted, and the heart size returned to normal. In April 1969, one year later, the pacemaker failed and the heart size again increased considerably; the patient was in frank congestive failure with much pulmonary congestion (Figure 2). The decubitus film showed free pleural effusion.

DR. SMITH: I suppose now it is unnecessary to introduce Dr. Amberg. We are delighted to have him here representing the Department of Radiology. He is Professor of Radiology and was formerly Chief of the Radiology Department at Fort Miley Veterans Administration Hospital in San Francisco.

*John R. Amberg, M.D., Professor of Radiology.

TABLE 1.—*Conditions Associated with Eosinophilia*

Drug Reactions	
Examples:	Iodide
	Penicillin
Parasitosis	
Examples:	Trichinosis
	Visceral larva migrans
Infections	
Leprosy	Fungal
Brucellosis	infections
Tuberculosis	Scarlet fever
Malignancies	
Carcinoma:	Lung
	Ovary
	Stomach
Hodgkin's disease	
Collagen Disease	
Periarteritis nodosa	
"Cutaneous"	
Pemphigus	
Dermatitis herpetiformis	
Loeffler's Syndrome	
Farmer's Lung	
Asthma, Hay Fever	
Leukemia	
Chronic myelocytic	
Eosinophilic	
Eosinophilic Endocarditis	(Loeffler's Endocarditis)
?Radiation	
Unknown Cause	
Idiopathic	Cigarette smoking
Sarcoidosis	Tropical eosinophilia

This patient had a very complex illness extending over a four-year period and leading to death with cardiac complications. We have asked Dr. Martin Cline to discuss the patient and the disease entity which this patient represents. We have asked him to focus more specifically on the significance of the eosinophil, its normal function, and the disorders which call forth high levels of this peculiar cell.

DR. CLINE:* Dr. Smith, it is a privilege to be here; it is always flattering when a hematologist is asked to discuss that organ involved in the propulsion of blood rather than the fluid and cellular elements. I shall, however, resist the temptations to discuss the nuances of electrocardiographic abnormalities in eosinophilic carditis. Instead I would like to examine an approach to the diagnostic problem of eosinophilia and to consider where the clinical picture presented this morning may fit into such a classification. Finally I should like to consider the eosinophil itself and its possible pathogenetic significance.

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The list of diseases associated with eosinophilia can be gleaned from any standard textbook of medicine and several weeks in the library (Table 1). It is a list familiar to most of you. With your indulgence, I will briefly examine this catalogue in order to place our patient in proper perspective.

Perhaps the commonest form of eosinophilia seen in our hospital at present is that related to drug reactions. Of these probably the most common is sensitivity to antibiotics; although any of a number of drugs may be associated with eosinophilia.[1] The next most common cause of significant eosinophilia seen on our medical service is parasitic infections. The nematodes are the parasites *par excellence* associated with eosinophilia. As a generalization, tissue phases of parasites are much more apt to provoke significant levels of blood eosinophilia than is parasitization of the gut alone.

Visceral larva migrans, as part of the "cat sandbox syndrome," is one of the more interesting causes of parasitic eosinophilia and deserves some comment.[2] This condition is occasionally diagnosed as eosinophilic leukemia. I can clearly remember a small child entering the National Institutes of Health with pronounced hepatosplenomegaly, a blood eosinophil count in the range of 100,000 per cu mm, and a diagnosis of eosinophilic leukemia. Because of the extreme rarity of true eosinophilic leukemia, other diagnostic possibilities were pursued. A liver biopsy demonstrated the typical histologic features of *Toxocara canis*.

Eosinophilia may also be part of a number of infectious processes, including tuberculosis, brucellosis, fungal infections, leprosy, and scarlet fever. It is quite interesting to me to observe some of the names associated with the descriptions of eosinophilia and infection. Franz Ingelfinger,[3] the prominent gastroenterologist and now Editor of the *New England Journal of Medicine,* was one of the first to call attention to the presence of eosinophilia in brucellosis.

Because increase in the number of blood eosinophils is sometimes associated with malignant lesions, an intensive search for the presence of occult neoplasms was made in the patient whose history was presented today. By far the most common malignant change in which eosinophilia is a prominent feature is Hodgkin's disease. In this disorder eosinophil concentrations may reach the level of 50,000 to 70,000 per cu mm. Occasionally eosinophilia is reported in association with car-

cinoma of the stomach, lung and ovary. From my own experience, I can recall one patient with carcinoma of the lung and eosinophils in the range of 50,000 per cu mm.

Among the connective tissue diseases, periarteritis nodosa has been most frequently associated with eosinophilia. It is reported that eosinophilia is rare in periarteritis in the absence of pulmonary involvement; with pulmonary involvement, it is quite common. Rheumatoid arthritis may also occasionally be associated with significant blood eosinophilia.

The concurrency of certain cutaneous diseases and elevated levels of blood eosinophils is well known, although the mechanism involved is, of course, quite obscure.

Loeffler's syndrome consists of blood eosinophilia, transient pulmonary infiltrates, and eosinophils appearing in the sputum.[4] Usually the pulmonary infiltrate persists no longer than two weeks; Loeffler himself used the word *fluchtig,* meaning fleeting. The course is generally benign and the cause unclear, although it has been suggested that in some patients the clinical manifestations are the result of the migration of certain parasites through the lungs as part of their life cycle.

Farmer's lung as a cause of eosinophilia is thought to result from the inhalation of mold and a subsequent allergic reaction. The eosinophil may be one of the prominent cells in the acute inflammatory process in this condition.

Association of eosinophilia with asthma and hay fever is, of course, well known. There are some interesting sub-syndromes within these disease categories. At the University of California hospitals two patients were seen recently who had abrupt onset of asthma, fleeting pulmonary infiltrates in an unusual distribution, and a high blood concentration of eosinophils. Both the asthma and the eosinophilia responded dramatically to treatment with adrenocorticosteroids. These patients may have had a recently described disease syndrome, chronic eosinophilic pneumonia.[5] In one of the references which I have given you,[6] there is a notation that patients dying in acute asthmatic attacks may have eosinophilic infiltration of the myocardium as well as patchy myocardial fibrosis. This may have some bearing on what I am going to discuss shortly.

Eosinophilia may be a part of the disease picture of chronic myelocytic leukemia, just as increased blood basophilia is a frequent finding. Eosinophils are rarely the predominant cell in this disorder, but the absolute number of these cells is often increased. I am going to spend most of the next few minutes talking about two diseases: eosinophilic leukemia and eosinophilic endocarditis. The patient presented today may have had eosinophilic carditis. For the sake of completeness, however, I should like to finish my cataloging and then return to these entities.

Exposure to irradiation is said to be associated occasionally with elevated levels of blood eosinophils. One tends to dismiss this association because one cannot readily conceive of the mechanism; however, in my own limited experience I have seen two patients with history of significant exposure to irradiation who had prominent blood eosinophilia. One patient was a technician at the Livermore Laboratories and the clinical manifestations resembled those of eosinophilic leukemia over a course lasting several years.

In Table 1 I have included a category of eosinophilia of unknown cause (not suggesting, however, that we know the cause of the eosinophilia in those diseases already cited). Tropical eosinophilia is a disease characterized by blood eosinophilia and nocturnal cough; it was a significant problem among combat personnel in the Korean War. The cause may be microfilarial parasitization.[7]

Within the category of eosinophilia of unknown origin, there is at least one recorded case of eosinophilia occurring in a patient whenever he smoked cigarettes.[8] Eosinophilia may also occur in sarcoidosis. I found an interesting reference to eosinophilia and "chronic nervous exhaustion" in the *American Journal of Insanity.* Unfortunately that journal stopped publication in the early 1920s, and I was unable to get an adequate follow-up and documentation of this particular cause.

Finally, there is an entity called "idiopathic eosinophilia" which does not conveniently fit into any of the previously mentioned disease categories. The important point to remember is that idiopathic eosinophilia is generally a benign condition. In a good study[9] in which 38 patients with idiopathic eosinophilia were followed, six died during a five-year period—two of chronic myelocytic leukemia, one of carcinoma of the stomach, and the other three of apparently unrelated causes. In general, therefore, idiopathic eosinophilia appears to be without serious pathologic import.

I would like to consider briefly eosinophilic leukemia and whether or not it exists as a disease

entity. Until 1960 there were approximately 30 cases of so-called eosinophilic leukemia in the world's literature. This "leukemia" had certain rather peculiar features[10]: In the reported cases anemia as well as thrombocytopenia were somewhat rare. In addition, an extremely high incidence of myocardial involvement was reported, and most of the patients died either of myocardial failure or of peripheral embolization. I believe that most of these descriptions of "eosinophilic leukemia" are actually examples of the syndrome of *eosinophilic endocarditis.* It is likely, however, that eosinophilic leukemia does exist as a separate disease entity; it is, however, extremely rare and considerably less common than eosinophilic carditis. The statement that eosinophilic leukemia does exist is based on the occurrence of the Philadelphia chromosome in a patient with blood eosinophilia, organomegaly, and diffuse organ infiltration with eosinophils.[11] This patient subsequently died in a blast crisis. The entire clinical and pathological picture was quite compatible with that of chronic granulocytic leukemias.

The patient presented this morning was thought to have "fibroplastic parietal endocarditis with blood eosinophils," a disease process described by Loeffler in 1936 in the *Swiss Journal of Medicine.*[12] The major clinical features of the original case were significant: peripheral blood eosinophilia, cardiac failure, and peripheral emboli. At autopsy the patient was found to have fibrosis involving the walls of the heart rather than the valves. Both the ventricular walls and the septum were fibrous, and mural thrombi were present. Since the original report of this entity, there have been approximately 40 cases described. Eosinophilic endocarditis is the usual name applied to the syndrome.

The clinical characteristics of these 40 cases are briefly summarized in Table 2. Although a wide age range has been represented, most cases have been in adults, usually between 30 and 50 years of age and predominantly in males. Almost all the initial reports were from Europe and thus involved a Caucasian population. More recently there have been several cases reported from South Africa involving Negroes.[13] The onset of symptomatic disease has varied from acute to gradual. The duration of disease has also ranged widely from three months to six years; however, I would point out that almost half of the patients died within a year of the onset of significant symptoms. It is a highly lethal disease. Additional manifestations have included central nervous system signs, with seizures being the most prominent feature. Peripheral and pulmonary embolic phenomena have been common. Approximately half of the patients described had a murmur consistent with mitral insufficiency; in the other half the murmur was not clearly defined. There was often a disparity between heart size and the degree of congestive failure, a phenomenon characteristic of constrictive pericarditis. I visualize this disparity as resulting from extensive fibrosis of the endocardium. The course was in general afebrile. Most of the patients had persistent eosinophilia ranging from 30 to 70 percent, but a few were reported as having only very transient blood eosinophilia even though there was eosinophilic infiltrate in organs, including the heart. Electrocardiograms were generally not helpful because they lacked specificity. Only three patients had electrocardiographic evidence consistent with left ventricular hypertrophy. A characteristic feature of the disease entity was a poor response to therapy, including cardiac glycosides and other routine methods of treating congestive heart failure.

Eosinophilic endocarditis has a rather characteristic pathologic picture (Table 3): Early in the disease there is evidence of endocardial and myocardial necrosis distributed in a spotty fashion throughout the heart. These early lesions may be

TABLE 2.—*Eosinophilic Carditis: Clinical Features in Approximately 40 Patients*

Age Range
7 to 65 years
(Usually 30 to 50 years)
Male to Female Ratio
3:1
Population
Negro and Caucasian
Onset
Acute or gradual
Duration
3 months to 6 years
(19 out of 40 patients died within 12 months)
Manifestations
Afebrile
Eosinophilia
Electrocardiogram
Nonspecific ST and T changes
(16 out of 40 patients)
Left ventricular hypertrophy
(3 out of 40 patients)
Possible embolic phenomenon
Murmur of mitral insufficiency
(20 out of 40 patients)
Possible central nervous system signs
Therapy
Poor response

TABLE 3.—*Pathologic Features of Eosinophilic Carditis*

Early Features
Necrosis
Endocardial
Myocardial
Possible small vessel inflammation
Cellular infiltrate with eosinophils
Late Features
Fibroelastosis
Chronic inflammatory changes

TABLE 4.—*Characteristics of Eosinophils*

Motile
Granules
Poor in lysozyme
Rich in peroxidase
Contain protein inclusions
Phagocytic of Microorganisms
(Less phagocytic than neutrophils)
Phagocytic of Antigen-Antibody Aggregates
Attraction by Antigen-Antibody Aggregates

accompanied by inflammation of small vessels, and eosinophils are the predominant cellular infiltrate. Near the time of death there are generally extensive fibrotic changes in which both collagen and elastic tissue are involved. In these chronic inflammatory lesions eosinophils may persist, but in general the predominant cell types are macrophages and lymphocytes.

Taken together, the major clinical and pathologic features of the syndrome are

- Refractory congestive heart failure
- Blood eosinophilia
- Endocardial and myocardial fibrosis (usually involving the right ventricle more than the left)
- Frequent mural thrombi and peripheral emboli.

Did the patient presented this morning in fact have eosinophilic endocarditis? The clinical phenomena were consistent with this disease except that eosinophilia was only transient. Among the reported cases, fleeting eosinophilia is extremely rare. The following is a review of the pathologic findings at autopsy: The major pathologic change was limited to the heart which grossly showed endocardial fibrosis primarily involving the right ventricle. Microscopy revealed scattered myocardial fibrosis. In most areas the fibrosis was of long standing, and chronic inflammatory cells rather than eosinophils were present. There were a few areas that appeared to be of recent origin in which eosinophilic infiltrates were present.

I think the patient whose case we are considering today had an unusual variant of eosinophilic endocarditis in that he did not die during a phase of acute blood eosinophilia or of eosinophilic infiltration of the tissues.

I would now like to discuss the eosinophil itself; perhaps what we know of this cell will help to explain some of the pathologic changes or pathogenetic mechanisms of eosinophilic carditis. This is the basic question: Is the eosinophil pathogenic in this disease entity or is it merely an accompaniment of other primary pathologic processes—an epiphenomenon, as it were?

When discussing a similar case two years ago there was only one thing I was very secure about: Eosinophils are red. Since that time we have gained some additional knowledge (Table 4). Eosinophils have crystalline inclusions within their granules. The inclusions are protein, but the nature of the protein is unknown. The granules are poor in lysozymes (presumably they are not involved in the degradation of certain bacterial cell walls) but have a great deal of peroxidase.[14] This peroxidase is chemically and immunologically distinct from the myeloperoxidase of the neutrophil. Human eosinophils are probably rich in antibacterial, cationic proteins, although this fact has not been clearly substantiated. Like granulocytes, eosinophils are motile and phagocytic of microorganisms. They are not, however, either as motile or as phagocytic as the neutrophils.[15]

Two characteristics of the eosinophil which have generated the most attention and speculation are their attraction by antigen-antibody aggregates and their ability to phagocytize such aggregates.[16] Neutrophils are also attracted by antigen-antibody aggregates which have activated certain components of the complement sequence. However, these aggregates appear to be more strongly chemotactic for the eosinophil. The unanswered question is, what is the eosinophil doing to the aggregate or, conversely, what is the aggregate doing to the eosinophil?

In the last few years we have gained additional insight into what the eosinophil may be doing. First, consider the distribution of the eosinophil: It spends most of its life span in the tissues and resides only very briefly (a matter of hours) in the blood stream. Hence the tissue pools of eosinophils are enormously greater than those in the circulation. Eosinophils are found in interfaces; that is, they are found at the body surface in contact with our environment. Eosinophils are abundant on the

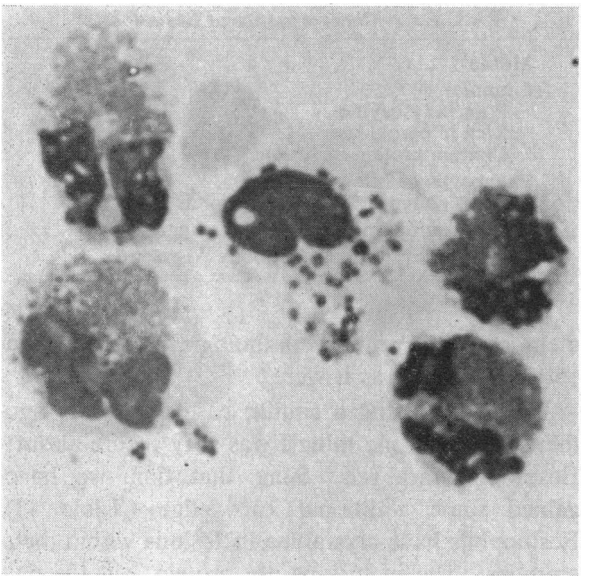

Figure 3.—Neutrophil with many ingested *Staphylococcus aureus* surrounded by comparatively non-phagocytic eosinophils.

gut mucosa, in association with alveolar macrophages at the lung surface, and in the skin. This distribution suggests that the eosinophil may be a first-line defense cell against certain noxious aspects of the environment. Of course, similar suggestions have been made for the lymphocyte in Waldeyer's tonsillar ring and Peyer's patches. It is likely that eosinophils have evolved for a specific purpose rather than being a "phylogenetic carry-over" from more primitive life forms. In all probability, the eosinophil has evolved in higher animals for a specific function which is presumably carried out at interfaces.

In addition, we have noted that eosinophils are attracted by antigen-antibody aggregates. They are not attracted by either antigen or antibody singly but only once the two have formed a complex. The attraction appears independent of the specific antigens involved in the complex and independent of the size of either antigen or antibody. What are the cells doing with these complexes? Clearly they can ingest them; in addition, Archer[17] has published the interesting observation that one can extract from eosinophils substances that antagonize the biological effects of serotonin, bradykinin, and histamine. One may suggest that the eosinophil may be functioning in this regard in order to protect us against the harmful effects of antigen-antibody interactions as well as the pharmacologically active substances generated by such interaction.

The eosinophil is a poor phagocyte in comparison with the neutrophil. I could spend a considerable amount of time documenting this statement,[15] but I would rather show this figure (Figure 3) demonstrating a group of eosinophils and a sole neutrophil exposed to *Staphylococcus aureus*. Obviously the neutrophil, not the eosinophil, has been most effective in ingesting the bacteria. This phenomenon occurs with a number of particles, both bacterial and fungal. The eosinophil simply cannot compete with the faster, more efficient neutrophil.

If the eosinophil is such a poor phagocyte, what then is its function? One observation becomes obvious as one studies eosinophils in tissue culture: With particle ingestion the cell often extrudes its granules intact. One may see intact eosinophil granules circulating in the medium. Is it possible that this granule extrusion plays a role? Is the eosinophil's major function actually not to internalize and digest substances, but rather to release its arsenal into the medium to create an environmental bacteriostatic system or pharmacologic blockade?

In summary, one can consider these possibilities:

- The eosinophil may function to induce bacteriostasis in the environment by extruding its granules, which are rich in cationic proteins and peroxidase.
- Eosinophils prevent tissue injury by antibody-antigen complexes and complement and the associated vasoactive amines and peptides.

What evidence suggests a primary role for these cells in the induction of myocardial fibrosis? To my mind there is no primary evidence that the eosinophils themselves produce tissue injury. All the evidence suggests that they are an epiphenomenon; that is, they are attracted to the sites of myocardial injury which results from another cause. For example, such injury may be induced by a myotropic virus. It is quite interesting that, in an early series of patients with the postmyocardial infarction syndrome,[18] occasionally one had eosinophilia and roughly 20 percent of those patients who came to autopsy had eosinophilic infiltration with spotty myocardial fibrosis. This observation may be one more bit of evidence that eosinophilia is a secondary manifestation of other injuries to the heart.

DR. SMITH: Thank you very much, Dr. Cline. There is time for questions concerning the patient presented this morning or concerning the eosinophil in general.

Martin, could you tell me if other patients have

shown evidence of peripheral muscle involvement by eosinophils such as this patient apparently had?

DR. CLINE: The patients described in the literature often had widespread eosinophilic infiltrations involving lymph nodes, spleen, pancreas and other organs. I have not found a specific documentation of myositis extrinsic to the heart.

QUESTION: Have you found any patients who had lesions similar to those in the heart in the capillaries or in the small arteries of the lung? If so, do these lesions resemble those of periarteritis?

DR. CLINE: No, they apparently are distinct from periarteritis. Patients with eosinophilic carditis may have small vessel involvement in the lung, but this involvement generally lacks the typical nodular features of periarteritis. I might say that only some 45 patients are described in the literature; yet we have had two patients with this diagnosis at this Medical Center in the last four years. Therefore, we must be considered an endemic area.

QUESTION: Are the eosinophils in this disease morphologically different from eosinophils in other kinds of eosinophilia?

DR. CLINE: No, it is extremely rare in any situation to see an eosinophil younger than the myelocyte stage of differentiation. Even in most cases of eosinophilic leukemia, the predominant cell is relatively mature.

QUESTION: The patient presented today had an enlarged heart. Is that typical of this syndrome? What was the cause of the endocarditis?

DR. CLINE: Cardiac enlargement has varied. Often a disparity has occurred between the size of the heart and the degree of congestive heart failure, presumed to result from the constrictive nature of the disease. At least one-third of the patients had cardiomegaly, as in Loeffler's original cases. As to your second question, about the cause of endocarditis, I don't know the answer. I might say parenthetically that the coronary vessels of our patient today were totally patent.

DR. SMITH: I gather that with the exception of the presence of the eosinophil, the terminal pathologic features do not differ very much from those of other types of idiopathic fibroelastosis or cardiofibroelastosis.

DR. CLINE: Generally that statement is correct except when one reviews the whole series. The frequent right ventricular predominance of fibrosis in eosinophilic endocarditis is rather unusual. In most types of acquired endocardial elastosis, such as that associated with hypertension, beri-beri, and others, I believe that usually the left ventricle is more involved. The cardiologists may be able to clarify that statement. Pathologically, the only difference between eosinophilic and other forms of carditis is the eosinophilic infiltration.

QUESTION: Is steroid therapy useful in this disease?

DR. CLINE: There is no convincing evidence that it is useful. Steroids have been used in only a minority of cases — those recognized since approximately 1950. Generally the reaction to steroids is a transient or sustained decrease in the blood eosinophil level with no clear-cut, beneficial effect to the patient or to his cardiac function. Apparently steroids inhibit the release of eosinophils or increase their turnover in the peripheral blood rather than interfere with their production.*

*_Addendum:_ Since this discussion an additional review of eosinophilic carditis has appeared.[19]

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