

**CONSTITUTIONAL FACTORS IN ARTHRITIS WITH
SPECIAL REFERENCE TO INCIDENCE AND
RÔLE OF ALLERGIC DISEASES**

By **ROBERT T. POTTENGER, M.D.**

Reprinted from **ANNALS OF INTERNAL MEDICINE**, Vol. 12, No. 3, September, 1938

CONSTITUTIONAL FACTORS IN ARTHRITIS WITH SPECIAL REFERENCE TO INCIDENCE AND RÔLE OF ALLERGIC DISEASES *

By ROBERT T. POTTENGER, M.D., *Pasadena, California*

CHRONIC arthritis of the atrophic and hypertrophic types is the most common chronic illness and ranks first among the causes of disability. The high incidence of this disease is indicated by a survey in Massachusetts where 3.2 per cent of the total population and 30 per cent of the disabled were found to be suffering from rheumatoid disease.¹ In spite of its prevalence the medical profession as a whole is discouraged or at least apathetic in its treatment.

There is no agreement among students of chronic arthritis as to the basic factors or diathesis predisposing the patient to the disease nor is there agreement as to the nature of the causative agent. The American Committee for the Control of Rheumatism stated that it "conceives of the disease as a generalized disease with joint manifestations." Yet the joint manifestations must be present to diagnose the disease.

This confusion led me to analyze my first 50 cases in which arthritis was the chief or a prominent complaint, not only from the standpoint of the signs and symptoms of arthritis but also from the standpoint of complications disclosed both in the history and physical examination. Certain relationships appeared quite striking. In the next 50 cases special attention was paid to them. An analysis of this series again suggested further studies. As a result the statistics which follow will be in part based on 150 consecutive cases, while some of the statistics will be based on separate series of 50 patients. At times this may be confusing but it is difficult to get the same data in a series of patients unless special thought is given to it.

In this paper both clinical types of arthritis, the atrophic and hypertrophic have been grouped together as it appears that fundamentally they are the same disease. However as this is not proved and time does not permit a defense of this position the series was classified as to predominant type.

Type	Number of Cases	Per Cent
Hypertrophic.....	95	62½
Atrophic.....	47	31½
Mixed.....	8	5½

There were 22 males or 14 per cent and 128 females or 86 per cent. This series is rather overloaded with females as it is generally considered that the incidence is only about twice as great among females. The average age of the 150 patients was 53.3 years.

* Received for publication September 21, 1937.

CLINICAL MANIFESTATIONS OF ARTHRITIS

My studies lend support to the conception that arthritis is a generalized disease with joint manifestations. In the first place the symptoms as given by the patient are not confined to the joints; secondly, the general symptoms tend to precede joint symptoms or to persist during periods of freedom from joint symptoms; and finally there are definite constitutional trends shown by the group.

The first 50 cases were tabulated with regard to the major symptoms shown.

Class of Symptoms	Symptoms	Per Cent
Constitutional	Mild malaise or feeling of being less well	84%
	Of inability to sleep well not necessarily from pain	74%
	Nervousness and depression	74%
Gastrointestinal	All varieties as will be taken up later	88%
	Of various grades of constipation With two or more stools a day	8%
Circulatory	Facial pallor and delayed capillary circulation in the finger tips in all active cases	
	Numbness of extremities	54%
	Cramping of muscles	32%
Skeletal	Pain	100%
	Stiffness	74%
	Swelling of joints	50%
	Weakness or atrophy of muscles	34%

It will be noted that only 50 per cent were recorded as having joint swelling. Arthritis in the spine, sacroiliac and hips will not give joint swelling perceptible on ordinary examination nor will an early joint involvement without effusion and before marked thickening of the capsule.

A study of the clinical course of arthritis as shown in the histories again illustrates the generalized character of the disease. Usually there is a history of 'never being sick but never being really well,' of constipation and of poor circulation for years before the onset of joint symptoms. We have all seen cases with well marked hypertrophic spurs who have never or have only recently had joint symptoms; an experience which forces us to the conclusion that arthritis has been present without joint symptoms. Consequently the disappearance of joint symptoms cannot be regarded as proof of the cure of the disease. The last 50 patients in the series were studied with this in mind. In 48 patients the age of onset of the first joint symptoms was noted and in 49 the age of onset of continuous joint symptoms. In 12 of 23 cases of the atrophic type and in 9 of 27 cases of the hypertrophic type the onset of the first joint symptoms and that of continuous joint symptoms were the same. Consequently 58 per cent of the cases had definite attacks of joint symptoms with periods of freedom before the onset

of continuous joint symptoms. The fact that 20 per cent of the cases were under 45 and 10 per cent had symptoms less than one year makes it probable that even a greater per cent would have remissions if followed long enough.

CONSTITUTIONAL BACKGROUND

Certain hereditary and constitutional factors seem to furnish the soil on which arthritis develops. In 73 per cent of 150 cases there was a family history of allergic diseases and in 52 per cent a history of arthritis. In 80 per cent one or the other or both were noted. Due to the lack of specific knowledge about blood relatives these figures from the histories are more suggestive than absolute.

In the first 50 cases a definite trend to longevity was noted, so that in the subsequent 100 cases the ages of 196 of the 200 parents were obtained. One hundred five of these had died at ages over 70 or were still living at an age greater than 70. Fifteen parents under 70 were still alive. Taking their ages and using the American Men's Ultimate Mortality Table it was computed that 9 of the 15 living should reach 70. Thus 114 or 57 per cent of the parents of these arthritics live to 70. Assuming that the average age of the parents at the time of birth of the patient was 30 and using the American Experience Mortality Table for comparison we find that 45.1 per cent of people aged 30 would reach 70 and 57 per cent would reach a fraction over 65. Since longevity has been proved to be inherited arthritis may be said to have a constitutional background of longevity.

The group showed a definite tendency to low blood pressure at the initial examination, but as the group as a whole was not studied carefully and repeatedly from this point of view statistics would be misleading. However, only 4 or 2.7 per cent of the 150 patients had diastolic pressures of 100 or over. Only 2 per cent of the last 100 showed persistent albuminuria and casts and low specific gravity indicative of any considerable grade of nephritis. An analysis of the blood pressures and urinary findings indicates that arthritics develop primarily arteriosclerosis rather than hypertension and nephritis.

FOCAL INFECTION

Having found that there is a constitutional background and generalized physiological disturbances associated with the joint symptoms of arthritis we turn to the subject of focal infection. Pemberton² noted in one series of 545 cases of arthritis demonstrable foci in 70 per cent while in another series of 100 non-arthritics 87 per cent had demonstrable foci of infection. In this second series in a general medical ward, nephritis and cardiac conditions were the chief disease states. Thus focal infection is not a condition peculiar to arthritis. In reviewing 100 cases in which special attention was given to the history of removal of foci I found I was entering upon a well tilled field as most of the patients had had previous medical care and

87 per cent had had active disease more than one year. The figures illustrate the persistence of arthritis in spite of the absence of foci in the usual location, teeth, tonsils, sinuses, gall-bladder and appendix.

In regard to teeth 25 per cent of the patients were edentulous, 13 per cent having been so before the onset of their arthritis, 12 per cent having had all the remaining teeth extracted because of it. In another 28 per cent some teeth had been extracted because of rheumatism. A further 8 per cent were found to require dental care. The tonsils were well attended to; in 28 per cent they had been removed before the onset of the arthritis and in 27 per cent tonsillectomies had been performed for the joint symptoms. Thus in 55 per cent rheumatism persisted in the absence of tonsils. The appendix had been removed in 23 per cent and probably in 2 others who had had pelvic operations. Only 8 per cent had had nasal operations, which is noteworthy as a large number had nasal symptoms as will be shown later. Six had had gall-bladder operations. In two others there was a history of jaundice in adult life but none of colic. Many of the patients had had gall-bladder roentgen-ray studies at some time during their illness. As to genito-urinary foci one had pus in the prostatic secretion and five gave a history of urinary tract infections in the past.

These figures are given not with the intent of proving that removal of foci is of no value in arthritis but to emphasize that arthritis will persist after the usual foci have been removed. Many physicians have observed that marked benefit from the removal of foci in arthritis is rarely seen except early in the course of the disease, and these patients in my series represent the ones who were not permanently benefited by such removals.

It would be poor medicine, however, to tell a person who had an abscessed tooth that he should neglect it because careful examination brought out no evidence of any systemic pathological disturbance from it. Whether a focus of infection is the direct cause of joint symptoms or not, it may when added to other factors already operating be sufficient to upset the physiological balance of the patient and precipitate symptoms just as other infections, fatigue, meteorological disturbances and menstruation will. Many of my patients gave a history of being benefited by removal of foci, many were made worse and most noticed no effect. Focal infection in arthritis presents no more urgent problem than in other diseases and should be attacked with due regard to the patient's vitality.

FREQUENCY OF ALLERGIC MANIFESTATIONS

When the first 50 cases were reviewed, the incidence of a history of asthma, hay fever, hives, eczema, bilious headaches and canker sores was very high. The incidence of asthma was 4 per cent, that of nasal allergy 20 per cent, hives 12 per cent, eczema 16 per cent, migraine 14 per cent and other sick headaches another 26 per cent, canker sores 36 per cent. It was found that 78 per cent had at least one of these allergic manifestations.

Eczema, hives, canker sores and sick headaches are generally regarded as being due to protein sensitization in which food is the offending factor, while asthma and nasal allergy may or may not be. Curiously enough I had found four of the eleven patients in whom no note was made of other evidence of allergy, sensitive to foods in the diet I was using. As was mentioned earlier 96 per cent of this first group of 50 had abnormal bowel function. The next 100 cases were studied carefully from the standpoint of food allergy.

The following table shows the frequency and distribution of the various types of allergic manifestations in the next 100 cases as noted either in the past history or the progress notes.

Nasal allergy.....	50
Asthma.....	11
Eczema.....	13
Bilious headache including migraine.....	38
Canker sores.....	42
Gastrointestinal.....	94
Bladder.....	17
Urticaria.....	13

DISTRIBUTION AMONG PATIENTS

DISTRIBUTION AMONG PATIENTS

	6 Types	5 Types	4 Types	3 Types	2 Types	1 Type	None
No. Pts.....	1	6	23	29	28	10	3

In two of the three cases where no allergic manifestations were noted the history was inadequate and treatment too short to determine the presence of allergic manifestations and in one case the symptoms might have been caused by an active tuberculosis, observation again being too short to be certain.

It is noteworthy that 94 of the 100 patients had gastrointestinal symptoms that were considered due to food allergy. In 6 of 8 cases where the period of observation was less than one month, a history of food disagreement was considered adequate evidence. In 88 of the remaining 92 cases of the series the presence of food allergy was proved by the precipitation of their gastrointestinal symptoms by the addition of offending foods, and the relief of the symptoms by the subsequent removal of the foods. This statement that 94 per cent of this series of arthritics had symptoms of gastrointestinal food allergy does not mean that food allergy is the only disturbance present in the gastrointestinal tract and in fact it appears at times to be conditioned by other abdominal pathologic processes.

GASTROINTESTINAL TRACT IN ARTHRITIS

At this point it would be well to review briefly the gastrointestinal symptoms present in this series. A study of the last 50 patients from the standpoint of their gastrointestinal symptoms failed to reveal any characteristic syndrome, such as is found in peptic ulcer. Perhaps the most characteristic notation was the patient's observation of gastrointestinal disturbances following ingestion of certain foods or overeating. The table below shows the incidence of the more common gastrointestinal symptoms, the first column shows the percentage in which the symptom was mild or inconstant, the second in which it was severe or of concern to the patient and the third the total per cent in which the symptom was found. Twenty per cent of the

Symptom	% Mild	% Severe	% Total
Anorexia.....	40	10	50
Coated tongue.....	42	20	62
Nausea and vomiting.....	32	12	44
Distress after eating.....	26	20	46
Belching.....	22	18	40
Heart burn.....	28	4	32
Bloating.....	36	18	54
Soreness and cramping.....	32	8	40
Flatulence.....	16	14	30
Constipation.....			86
Occasional laxative.....	22		
1-5 a week.....		20	
Daily.....		44	
Excessive number stools.....	16	8	24
Mucus in stool.....	32	14	46
Periodic bloody mucus.....	6		6

group did not complain of any severe gastrointestinal symptoms. Of the 14 per cent without constipation 10 per cent gave a history of mucus in the stools including in 8 per cent an excessive number of stools. The remaining 4 per cent complained of no symptoms referable to the gastrointestinal tract except a coated tongue. Both of these later showed disturbances due to food sensitization.

These figures indicate that arthritics as a group have gastrointestinal symptoms but of no definite pattern; their severity correlates more with the nervous instability of the patient than with the severity of the disease. Three of these patients had definite pathologic lesions; one gall stones, one an abdominal fistula with three openings into the bowel and one had had repeated attacks of diverticulitis.

My experience with gastrointestinal roentgen-ray studies has been very limited. Consequently I will quote directly from Pemberton's³ book, "Arthritis and Rheumatoid Conditions, Their Nature and Treatment."

The type of colon which is met with in many arthritics is characterized chiefly by a tendency to greater caliber, greater length, a more convoluted appearance and sometimes reduplication. . . . It is to be borne in mind that many apparently healthy

people harbor diseased tonsils, for example, and by the same token the bowel may be potentially the cause of disease, by virtue of faulty anatomy or dysfunction, without having as yet brought this about. The colon will, therefore, be found in a certain limited proportion of apparently normal subjects also to approximate the type here described. . . . Other departures from theoretical normality show themselves in the gastrointestinal tract as the result of roentgen-ray studies among arthritics. These are chiefly in the direction of a somewhat delayed transit of the barium meal together with more or less ptosis of the stomach and colon. It is of the highest importance to note that marked stasis may exist in the presence of apparently adequate daily bowel movements. Another outstanding feature which is encountered in a given proportion of cases is the regurgitation of the barium through the ileocecal valve.

The "marked stasis" of which Pemberton speaks can frequently be shown by giving carmine dye by mouth. This method is used in metabolic work to mark the beginning and end of the portion of the stool belonging to a certain period of the experiment. In a strictly normal bowel action definite segments of stool show the dye. In some arthritics the dye may appear in from 24 to 72 hours and continue up to 120 hours. It is uncommon to find one segment of the stool colored and the other not colored.

DISCUSSION

An attempt has been made to show the constitutional trends and the physiological disturbances that those who suffer from chronic joint disease of the so-called hypertrophic and atrophic varieties have in common. This was done to emphasize what has been observed already that an individual arthritic suffers from ill health as well as joint pain and that his ill health is not peculiar to him as an individual but that both the ill health and joint changes are part of the same physiological disturbance. Considerable space was given to allergic manifestations. Unfortunately attaching a name to a clinically common and unimportant phenomenon tends to exaggerate its importance in our minds, and this is especially true when the same name may be used for very serious conditions. An occasional crop of hives is just as much an allergic phenomenon as a severe urticaria but not by any means of the same clinical importance though it does indicate the same constitutional trend. Not every person but a large number do show allergic manifestations. Vaughan and Pipes⁴ made a survey of 500 persons and found 10.6 were frank major allergics and 49.8 per cent more were minor allergics with mild allergic symptoms in their past history. In the same journal Bret Ratner⁵ states that 7 to 10 per cent of the population are afflicted with allergy. Rowe⁶ found 35 per cent with allergic history or manifestations in a survey he made.

As to the mechanism of allergic reactions only the barest outline is warranted here. There appear to be two major factors. First a deficient or altered constitution on the part of the host which seems to be a derangement of intracellular digestion and second certain specific chemical and

possibly physical stimuli which will precipitate reactions in an individual because of changes brought about by the constitutional deficiency. An allergic individual is in his apparently normal physiological balance as long as contact with the antigenic substances is avoided as for example the freedom of a pure pollen hay fever sufferer at other seasons of the year.

Arthritis is coming to be looked upon more and more as an allergic phenomenon in the skeletal structure as is shown by the tremendous amount of tissue reaction in which only few or no infectious organisms can be demonstrated. Joint reaction to the streptococcus in rheumatic fever is an example of reaction to an infectious agent. The joint manifestations of scarlet fever, typhoid fever and undulant fever are other examples. Non-infectious agents causing joint symptoms may be illustrated by the joint symptoms in serum sickness. Cases are reported where foods cause effusion in joints. In chronic arthritis the agent must be active over a long period of time. Roentgen-ray changes in the bones are often not found when the first symptoms develop and their degree and type depend on the severity and duration of the reaction.

Many authors have looked upon the bowel as the chief focus of infection in arthritis. The contents of the bowel, both food and bacterial and also their breakdown products, offer an unlimited and more or less constant source of antigens for allergic reactions in joints. Normally the mucous membrane of the bowel offers a sufficient barrier to the noxious elements in the intestinal tract so that foreign proteins do not enter the blood stream in amounts in excess of the ability of the body to destroy them. Since arthritics in general show other manifestations of allergy an arthritic probably has a deficient parenteral digestion, but we must also consider whether factors are present in the bowel itself which allow an excess of foreign substances to pass through its mucous membrane to overtax an already deficient though otherwise adequate parenteral digestion. Evidence has been presented of a very high incidence of disturbance of the gastrointestinal tract in arthritis usually with stasis and accompanied by gastrointestinal food allergy.

Rowe⁷ in his book "Food Allergy" (1931) discussed the relation of food to arthritis. He mentions that Talbot (1917) and Cooke (1918) suggested food as a source of arthritic pain in certain patients and that Turnbull in 1924 noted relief of arthritic symptoms on diets based on skin tests. Rowe himself reported three cases. In his discussion he favored the view that arthritis was due to bacterial allergy but felt that in some cases it might be due to foods. More recently, in 1936, W. T. Wootton⁸ suggested that arthritis is an allergic reaction in joints to food or bacterial protein and that elimination diets should be used but states that allergic food reactions are rarer as age advances. G. T. Brown,⁹ in 1934, suggested that the factor of food sensitization should be considered in arthritis but that bacterial allergy was more important. Thus the association of food allergy and arthritis is being recognized.

RÔLE OF GASTROINTESTINAL FOOD ALLERGY

My studies on the 150 cases in this series suggest an explanation of the rôle of food allergy. A survey of the first 50 cases showed that no case that was freed from gastrointestinal symptoms and that regained apparently normal bowel function failed to gain relief from arthritis, and the converse—that those whose gastrointestinal symptoms failed to respond or became worse failed to make much improvement, or progress. Among those who improved were the ones in whom I had recognized food allergy and had eliminated the offending foods from their diet. This observation led me to investigate the problem of food allergy in the succeeding cases.

In working out an elimination diet in an uncomplicated case of arthritis the symptoms due to food allergy will usually clear up in from five to seven days both in the bowel and elsewhere; for example, in the nose, skin, lungs, etc. There is a marked improvement in the constitutional symptoms but usually not much change in the joint symptoms for another five to seven days, but then the muscle soreness and acute inflammation in the joints begin to subside leaving chiefly pain on motion, stiffness from adhesions and weakness due to muscle atrophy. Thus there is a two week cycle. Five to seven days for the bowel to become free from symptoms and five to seven more days for the acute joint reactions to subside. The subsequent introduction of an offending food in the diet is followed in from one to seven days by a return of the allergic symptoms and a few days later after the disturbance in the gastrointestinal tract is established, the joint symptoms increase. This will occur even after the ingestion of the offending food has ceased but before the gastrointestinal symptoms have subsided. Again about five days after the bowel symptoms disappear the rheumatic pain subsides. The observation that exacerbations of the rheumatic symptoms do not occur simultaneously with the development of allergic reactions to foods in other tissues of the body but tend not to appear until a well marked gastrointestinal disturbance is set up and that remissions in the rheumatic symptoms do not occur until after the gastrointestinal symptoms subside, suggest that the rheumatic symptoms are produced by antigens whose access to the joints are conditioned by the allergic reactions elsewhere, presumably the bowel.

An allergic reaction in the bowel is accompanied by disturbed motility and by edema of the mucous membrane. The increased permeability produced by the allergic reactions is suggested by a clinical observation. An individual with a bowel allergy, on a diet that agrees with him, can eat beets without the color appearing in the urine in appreciable amounts. The same individual when having an acute bowel reaction frequently will notice a pink tinge to his urine (on several occasions red enough to engender a phone call to the doctor). This observation suggests that the permeability of the bowel has been altered so that the beet pigment is allowed to pass

into the blood stream or else passes through more rapidly or possibly its digestion in the body is impaired.

Bowel allergy is known to cause constipation and stasis. Constipation and stasis are present in a large proportion of arthritics. That it produces an increased permeability of the bowel is suggested by the beet pigment observation. Thus food allergy may produce both the colonic stasis and increased permeability of the bowel which would make the colon a likely focus for infection.

CONCLUSION

If arthritis is an allergic reaction in joints to foreign protein, living or dead, brought to it from the blood stream, then any portal of entry may theoretically be a focus. It is intended in this paper to imply only that the bowel is the most common focus. Tolerance to an antigen is only relative and probably depends on the efficiency of the mechanism of intracellular digestion. A coexisting food allergy may depress the tolerance to other antigens and it is well known that infection, focal or otherwise, weather, fatigue or menstruation are prone to lower the tolerance of an allergic individual. Again it is not meant to say that food allergy is the only disturbance in the bowel or always the prime one. I have seen one case of pure food allergy, which was freed from symptoms on an elimination diet, return to a regular diet without symptoms after a Jackson's membrane distorting the cecum was severed. Rae Smith in a personal communication to the author stated that adhesions were an important factor in one case in eight of the severe rheumatoid type of arthritis. Dietary deficiencies may play a rôle in the lowering of the resistance of the bowel mucous membrane. My thesis is that food allergy is the most common and in many cases the most important factor in the bowel disturbance that predisposes to chronic arthritis.

SUMMARY

In summary, arthritis is a pathological condition of the joints behind which there is a constitutional background and a widespread disturbance of the general physiology. There is an hereditary tendency to allergy, arthritis, longevity and a hereditary resistance to essential hypertension, and glomerular nephritis. It is a condition where progress may be aggravated by foci of infection in the teeth, tonsils, sinuses, gall-bladder, etc. but where progress may persist in the absence of such foci. The type of reaction in the joint suggests an allergic reaction. This is made more probable by the almost universal presence of manifestations of specific sensitization in other tissues. The presence of disturbances in the bowel due to specific sensitization to food was shown in over 90 per cent of our cases. The clinical course of exacerbations under treatment suggests that these reactions in the bowel make it more permeable and cause the body to be

flooded with an excessive amount of antigens from the bowel to which the joint structures are sensitized.

REFERENCES

1. BIGELOW, G. H., and LOMBARD, H. L.: Cancer and other chronic diseases in Massachusetts, 1933, Houghton, Mifflin Co., Boston.
2. PEMBERTON, R.: Arthritis and rheumatoid conditions, their nature and treatment, 1935, Lea and Febiger, Philadelphia, pg. 48-49.
3. *Ibid.*, pages 234, 235, 236.
4. VAUGHAN, W. T., and PIPES, D. M.: Is there a correlation between food dislikes and food allergy? *Jr. Allergy*, 1937, viii, 257-260.
5. RATNER, B.: Does heredity play a rôle in the pathogenesis of allergy? *Jr. Allergy*, 1937, viii, 273.
6. ROWE, A. H.: Food allergy, 1931, Lea and Febiger, Philadelphia, pg. 19.
7. *Ibid.*, page 271.
8. WOOTTON, W. T., JR.: The rôle of allergy in arthritis, *Jr. Arkansas Med. Soc.*, 1936, xxxii, 119-122.
9. BROWN, G. T.: Allergic phases of arthritis, *Jr. Lab. and Clin. Med.*, 1934-35, xx, 247-249.

LANCASTER PRESS, INC., LANCASTER, PA.