THE EFFECT OF PENICILLIN ON RHEUMATOID ARTHRITIS *

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The cause of rheumatoid (atrophic) arthritis is unknown. Of the many aetiological theories the
microbic hypothesis is still the most widely accepted, and of the many different bacteria which have been
incriminated, haemolytic streptococci have been, since 1929, most under suspicion. Haemolytic
streptococci from time to time have been recovered from the synovial fluid and blood, from foci of in-
fec tion, and occasionally from synovial membrane, blood, and lymph nodes of patients with rheumatoid
arthritis. The blood of the majority of patients who have this disease contains antibodies against haemo-
lytic streptococci—that is, agglutinins, generally in high titre, and precipitins for the C substance of
haemolytic streptococci. Although the concentra-
tion of antistreptolysins and antifibrinolysins in the
blood is not increased, except in some early or acute
cases, the skin of patients with rheumatoid arthritis
often is found to be hypersensitive to extracts of
haemolytic streptococci. Such is the direct and in-
direct evidence on which the argument against
haemolytic streptococci has been based. But since
many patients with unmistakable rheumatoid
arthritis do not present such evidence, the hypothesis
has been presumptive only.

Ever since it was announced that penicillin was
extremely effective against a variety of infectious
agents, including haemolytic streptococci, many
physicians and a host of rheumatic patients have
been hopefully awaiting news that penicillin might
prove effective against rheumatoid arthritis, although
the sulfonamides, also effective against haemolytic
streptococci, have proved useless against this disease.
Hence this investigation.

Plan of Investigation

Two chief policies governed our investigation.
1. Policy Regarding Selection of Cases.—The
only cases chosen for trial of treatment with penicillin
were those in which the disease had advanced
far enough to be diagnostically unmistakable but
not far enough to have produced irreversible changes
(destruction of cartilage and subchondral bone,
notable flexion deformities), the presence of which
might have made difficult a clear-cut evaluation of
results.

2. Policy Regarding Dosage.—We decided to give
penicillin long enough and in large enough doses so
that, were our results negative, it could not well be
said that our patients had not received sufficient
amounts of the material. Ten patients have been
treated intensively; all were male soldiers recently
on active duty; their ages were from 23 to 45. The
average duration of the disease was 7-4 months.

* Abridged from a paper in the Journal of the American Medical
Association (1944, 126, 820-823), by courtesy of the Editor.

The sedimentation rates varied from 21 to 55
(Wintrobe).

Summary of the Results

1. Penicillin was given to ten soldiers with early
but progressive rheumatoid arthritis.

2. Large doses of penicillin were given intramu-
cularly every three hours day and night. The
daily doses of penicillin were from 120,000 to 320,000
Oxford units; total doses were from 1,800,000 to
3,250,000 units within fourteen to twenty days. Such
large doses are known to be adequate—indeed,
perhaps more than adequate—against even severe
infections (with or without bacteriaemia) from
haemolytic streptococci, staphylococcus aureus, and
so forth.

3. Our clinical results from penicillin, given in the
doses stated over a period of fourteen to twenty-one
days, were essentially negative. In 7 of the 10 cases
there was no significant subjective or objective
improvement. One patient felt worse but did not
appear to be in worse condition than before treat-
ment. In one case there was slight subjective, but
no objective, improvement. One patient experi-
enced moderate objective and subjective improve-
ment in some, but not in all, of his joints; the
sedimentation rate increased slightly during treat-
ment, and he was by no means cured or even
decidedly improved. In view of the capricious
nature of rheumatoid arthritis the improvement in
these two cases must be regarded as unrelated to the
penicillin.

4. There was no definite evidence of improvement
as measured by laboratory tests. There was no
significant improvement in sedimentation rates or
in the comparative leucocyte counts on synovial
fluid made before and after treatment.

5. Definite improvement in appetite was noted by
6 of the 10 patients. It may have been unrelated to
treatment with penicillin or it may have been a
general side effect thereof.

Conclusions

1. Our results offer no support to the idea that
haemolytic streptococci may be aetiologically related
to rheumatoid arthritis.

2. In view of these negative results with rather
large doses of penicillin, it seems reasonable to
assume that rheumatoid arthritis is not caused by
any of the bacteria which are already known to be
rapidly affected by penicillin.

3. From these negative results we would conclude
that penicillin probably should not be used for the
further clinical treatment of rheumatoid arthritis,
at least until the material is available in something
approaching inexhaustible quantities.
Effect of Penicillin on Rheumatoid Arthritis

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