

any of the chemical elements of the blood. Notably, we could not find any consistent elevation of the BUN. All liver function studies remained normal during therapy and there were no evidences of any ill-effects on the kidneys or lower urinary drainage structures. No cardiovascular effects could be detected. The drug did not have any reproducible effect on the Latex Fixation Test nor was there any significant effect on the Sedimentation Rate regardless of the clinical response. No effects on the skin were observed and there were no changes in the lower bowel or the bowel habits. The drug had no apparent effects on appetite or on muscle strength.

In summary, "Indochin" would appear to be an excellent therapeutic vehicle for treating rheumatoid spondylitis. In the very few cases where it was tried, it seemed to have a beneficial effect on acute attacks of gout. It did not seem to influence materially cases of generalized chronic fibrositis or acute localized periarticular fibrositis nor did it have any beneficial effect on back problems, especially posterior cervical fibrositis. In one case of chronic gouty arthritis, it has proved to be dramatically but consistently beneficial to a very high degree over a period of nearly two years. "Indochin" has an "excellent" beneficial effect in some cases of peripheral rheumatoid arthritis but only a "good" effect in a larger percentage and there is complete failure or ineffectiveness in a distressingly high percentage of such cases. In most of these latter cases, it was our feeling that the failure was due largely to the inability to break through the therapeutic ceiling maintained by the cerebral toxicity.

I hope the enclosed summarized data will be helpful to you.†

Cordially yours,

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AN EXTENDED STUDY OF INDOMETHACIN*

II. CLINICAL THERAPY

(By Norman O. Rothermich, M.D.)

A new antirheumatic drug, indomethacin, was evaluated over a long period of observation (42 months maximum). Clinically satisfactory results listed as both good and excellent were obtained in a high percentage of patients with ankylosing spondylitis, gouty polyarthritis, psoriatic arthritis, and other miscellaneous benign (nonfatal) rheumatic diseases. In rheumatoid arthritis, indomethacin produced good and excellent results in a lesser, though appreciable, percentage of cases and may be regarded as another valuable drug to be added to the overall program of therapy in this notably difficult disease. As indicated in the previous report, the experimental nature of this study required that in some cases the dosages be increased to and beyond tolerance. Therefore, therapy in private practice may not yield as high a percentage of favorable results as indicated in this report.

The present treatment of rheumatoid arthritis still leaves much to be desired. Virtually all therapeutic agents which are believed to have beneficial effect in this disease have limitations on their utility and efficacy because of harmful side effects, usually dose-related. The development of an antirheumatic agent with little or no clinical hazards would be very desirable. In a previous publication,¹ it was reported that indomethacin was not hazardous, except for the possibility of gastric-ulcer formation.

Previous reports have indicated that indomethacin produces significant benefit in certain rheumatic diseases.^{2,3,4,5} These reports were based largely on com-

†Retained in committee files.

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¹Rothermich, N.O.: A Report of 42 Months Experience With Indomethacin: I. Clinical Pharmacology, *JAMA*, to be published.

²Norcross, B. M.: Treatment of Connective Tissue Disease With a New Nonsteroidal Compound (Indomethacin), *Arthritis Rheum* 6:290 (June) 1963.

³Smyth, C. J.; Valayios, E. E.; and Amoroso, C.: Indomethacin in Acute Gout Using a New Method of Evaluating Joint Inflammation, *Arthritis Rheum* 6:299 (June) 1963.

⁴Rothermich, N. O.: Indomethacin: A New Pharmacologic Approach to the Management of Rheumatic Disease, *Arthritis Rheum* 6:295 (June) 1963.

⁵Hart, F. D., and Boardman, P. L.: Indomethacin: A New Nonsteroid Anti-inflammatory Agent, *Brit Med J* 2:965-970 (Oct 19) 1963.