Rheumatoid (ankylosing) spondylitis.—Although adequate trials are lacking, indomethacin appears to be as effective as phenylbutazone in ankylosing spondylitis. For patients in whom aspirin is ineffective, some clinicians prefer indomethacin to phenylbutazone because its side effects, while frequent, are not likely to be as serious as they may be with phenylbutazone; many deaths from blood dyscrasias have followed prolonged or repeated use of that drug.

Gout.—Indomethacin is often effective in the treatment of acute gouty arthritis (P. L. Boardman and F. D. Hart, Practitioner, 194:560, 1965), with some reports indicating that it acts more rapidly than colchicine or phenylbutazone. Some clinicians prefer a brief course of phenylbutazone, and consider both drugs preferable to colchicine because of the frequency and severity of gastrointestinal side effects with colchicine. Trials comparing indomethacin with phenylbutazone are too few to permit a confident choice between the drugs.

Osteoarthritis.—The manufacturer claims that indomethacin is effective in osteoarthritis of the hip. While the evidence is not conclusive, one controlled short-term trial does support this claim (J. Wanka and A. St. J. Dixon, Ann. Rheum. Dis., 23:288, 1964). Present evidence does not adequately support the results of early studies showing the drug to be effective in other joints affected by osteoarthritis.

Adverse effects.—The incidence of adverse effects has varied, in different studies, from a few per cent to about three-quarters of the patients. Gastric side effects have been less frequent with the capsule formulation which replaced the early tablet formulation. Most of the studies have shown a high incidence of such side effects as headaches, vertigo, and gastrointestinal disturbances, including nausea and vomiting. Peptic ulceration has occurred, sometimes with bleeding, and cholestatic jaundice has been reported. Mental depression has also been reported (M. Thompson and J. S. Percy, Brit. Med. J., 1:80, 1966). There have been a few reports of leukopenia, thrombocytopenia, and agranulocytosis. A number of deaths have been associated with the use of indomethacin, some of them the result of ulceration and bleeding. Both the incidence and the severity of side effects have usually been dose-related. Indomethacin may interfere with resistance to infection, particularly in children (J. C. Jacobs, JAMA, 199:932, 1967), or may activate latent infections. For the persent, indomethacin should not be administered to children.

Dosage.—The manufacturer recommends an initial dosage of 50 to 75 mg a day with gradual increases up to 200 mg a day. Because of the high incidence of adverse effects at 200 mg many clinicians limit dosage to 100 to 150 mg a day.

Conclusion.—Indomethacin appears to be no more effective than aspirin in the treatment of rheumatoid arthritis; all Medical Letter consultants agree that aspirin is the drug of choice and that indomethacin should be used only in patients who cannot tolerate aspirin. There is some belief that the combination of indomethacin and aspirin may be beneficial in a few patients with rheumatoid arthritis not satisfactorily controlled on aspirin alone, and that a trial of the combination in such patients is worthwhile. Indomethacin appears to be as effective as phenylbutazone in the treatment of ankylosing spondylitis and is probably less hazardous. It is also effective in acute gouty arthritis, and it may be helpful in the treatment of osteoarthritis of the hip. Despite frequent minor side effects and occasional serious effects, indomethacin appears to be less hazardous for long-term use than corticosteroids, gold, or phenylbutazone.

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INDOCIN

Indomethacin (Indocin—Merck) is a nonsteroid indole derivative offered for the treatment of rheumatoid arthritis, ankylosing (rheumatoid) spondylitis, osteoarthritis and gouty arthritis. Like other drugs used in arthritis—aspirin, phenylbutazone, and the corticosteroids—indomethacin has analgestic and anti-inflammatory effects. The drug is not free of serious side effects, and its effectiveness is much more limited than many of the early claims would indicate; nevertheless, it appears to be a useful addition to the group of drugs available; for the treatment of arthritic disorders.

Rheumatoid arthritis and spondylitis.—In a number of clinical trials, mostly uncontrolled, about 40 to 50 per cent of patients with rheumatoid arthritis showed some improvement when given indomethacin. In one study, doses of 150 to 200 mg of indomethacin daily were found to be effective in most patients with mod-