Annals of the Rheumatic Diseases

A journal of clinical rheumatology and connective tissue research

This journal, founded by the Empire Rheumatism Council, now the Arthritis and Rheumatism Council for Research in Great Britain and the Commonwealth, is also supported by the Heberden Society.

Advice to contributors

Communications This journal exists to publish work on all aspects of rheumatology and disorders of connective tissue. Laboratory as well as clinical studies are welcome. In addition brief communications, for example reports of single cases, will be printed if of exceptional interest.

Papers, which will be accepted on the understanding that they have not been and will not be published elsewhere and are subject to editorial revision, should be addressed to The Editor, *Annals of the Rheumatic Diseases,* Kennedy Institute of Rheumatology, Bute Gardens, London W6 7DW. Each author must sign the covering letter as evidence of consent to publication.

Two copies should be supplied, one a typed top copy. Authors requiring acknowledgement of papers submitted should enclose a stamped addressed postcard or, if overseas, an international reply paid coupon.

Articles must be typewritten on one side of the paper only, in double spacing with ample margins. Only recognised abbreviations should be used.

Tables should be presented on separate sheets apart from the text.

SI units The units in which the work was done will appear first with the other units, i.e. SI or traditional units, appearing after in parentheses. With regard to tables and figures, a conversion factor should be given as a footnote.

References In accordance with the Vancouver agreement references, which must be typed doubled spaced, are cited by the numerical system.

A paper (or book) cited in the text is referred to there by a superscript number. In the list of references the papers (or books) appear in the numerical order in which they are first cited in the text, not in alphabetical order by authors' names. For convenience in preparing the typescript the reference number may be typed between parentheses on the line, not superscript. The titles of journals are abbreviated in accordance with the style of *Index Medicus.* In the typescript they should either be abbreviated in that style or given in full. Three examples follow:

[1] Green A B, Brown C D, Grey E F. A new method of measuring the blood glucose. *Ann Rheum Dis* 1980; **64:** 27–9.

[2] Green A B, Brown C D. *Textbook of Medicine.* London: Silver Books, 1980.

[3] Grey E F. Diseases of the pancreas. In: Green A B, Brown C D, eds. *Textbook of Medicine.* London: Silver Books, 1980: 349–62.

References will not be checked in the editorial office. Responsibility for their accuracy and completeness lies with the author.

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Tables Each table should be on a separate sheet, have a heading, and contain no vertical rules.

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Prescribing Information

Non-steroidal anti-inflammatory agent with analgesic properties.

Indications

'Indocid' Capsules, Suspension, and Suppositories

For the active stages of: rheumatoid arthritis; osteoarthritis; degenerative joint disease of the hip; ankylosing spondylitis; acute peri-articular disorders such as bursitis, tendinitis, synovitis, tenosynovitis, capsulitis of the shoulder, sprains and strains; low-back pain (commonly called 'lumbago'); gout. Also indicated in inflammation, pain and oedema following orthopaedic procedures; and the pain of dysmenorrhoea and in the reduction of associated symptoms.

'Indocid' is not a simple analgesic, its use should be limited to the above conditions, and particularly those cases not responding to conservative measures.

'Indocid' Suppositories may be used where night pain and morning stiffness are prominent. One suppository at bedtime will frequently give relief from pain and stiffness for 13 to 16 hours after administration. 'Indocid' Suppositories may reduce, but not always abolish, gastro-intestinal side effects of indomethacin therapy.

'Indocid'-R

'Indocid'-R may be substituted for all the indications of 'Indocid' except gout, as clinical evidence is not currently available for this dosage form in this condition. Therefore the other forms of 'Indocid' should be used in gout.

Dosage and administration

'Indocid' Capsules, Suspension, and Suppositories

The dosage of 'Indocid' should be carefully adjusted to suit the needs of the individual patient.

Oral therapy

In order to reduce the possibility of gastro-intestinal disturbances, *'Indocid' Capsules/'Indocid'-R Capsules and Suspension should always be taken with food, milk, or an antacid.* (Note, however, that 'Indocid' Suspension should not be mixed with an antacid, but should be taken separately, because indomethacin is unstable in an alkaline medium.) 'Indocid' Suspension should not be diluted.

In chronic conditions, starting therapy with a low dosage, increasing this gradually as necessary, and continuing a trial of therapy for an adequate period (in some cases, up to one month) will give the best results with a minimum of unwanted reactions.

The recommended oral dosage range is 50 mg to 200 mg daily. Paediatric dosage not established.

Suppositories

Adults: 1 suppository to be inserted once or twice a day. One should be used at bedtime. If another is necessary, it should be used in the morning.

Combined therapy. One suppository to be inserted at bedtime, supplemented during the day by capsules or suspension as needed, up to a daily total of 150 to 200 mg indomethacin (including the suppository).

Additional considerations. In conditions where patients initially require a dosage of 150 to 200 mg a day, it is often possible to reduce this gradually to a maintenance level of 75 to 100 mg a day. In patients with persistent night pain and/or morning stiffness, a dose of up to 100 mg at bedtime may be helpful in affording relief. It is rarely necessary to exceed a dosage of 200 mg a day. As dosage is increased to and above this level, a rise in the incidence of side effects, especially headache and gastro-intestinal upsets, may occur, requiring a temporary reduction in dosage.

'Indocid'-R

The sustained-release capsules may be given once or twice a day depending on patient needs and response.

Contra-indications

Children (conditions for safe use not established), active peptic ulcer, recurrent history of gastro-intestinal lesions, sensitivity to acetylsalicylic acid or indomethacin. Safety for use during pregnancy or lactation has not been established. Suppositories contra-indicated in patients with recent history of proctitis.

Precautions

Headache, sometimes accompanied by dizziness and light-headedness may occur, usually early in treatment. Starting therapy with a low dosage and increasing it gradually will minimise the incidence of headache. These symptoms frequently disappear on continuing therapy or reducing the dosage, but if headache persists despite dosage reduction, 'Indocid' should be withdrawn.

Patients should be warned that they may experience dizziness and, if they do, should not drive a car or undertake potentially dangerous activities needing alertness. 'Indocid' should be used cautiously in patients with psychiatric disorders, epilepsy, or parkinsonism, as it may tend to aggravate these disorders.

Gastro-intestinal disturbances may be minimised by giving 'Indocid' orally with food, milk, or an antacid. They usually disappear on reducing the dosage; if not, the risks of continuing therapy should be weighed against the possible benefits. 'Indocid' Suppositories may reduce gastro-intestinal disturbances.

Peptic ulcer has been reported in a small proportion of patients. Haemorrhage and perforation have occurred in a small proportion of patients, usually with a history of peptic ulcer or those receiving corticosteroids or salicylates concurrently. In some cases, however, there was no history of peptic ulcer, or of other agents being used. If gastro-intestinal bleeding does occur, 'Indocid' should immediately be discontinued.

Tenesmus and irritation of the rectal mucosa (sigmoidoscopic examination of a number of patients showed no mucosal changes) have been reported with 'Indocid' Suppositories.

'Indocid' may mask the signs and symptoms of infection, and antibiotic therapy should be initiated promptly if an infection occurs during therapy with 'Indocid'. It should be used cautiously in patients with existing but controlled infection.

During prolonged therapy, periodic ophthalmological examinations are recommended, as corneal deposits and retinal disturbances have been reported.

Patients should be carefully observed to detect any unusual manifestations of drug sensitivity. 'Indocid' should be used with particular care in the older patient, who may be more prone to adverse reactions.

'Indocid' Suppositories should be used with caution in patients with a recent history of rectal bleeding.

'Indocid'-R Capsules are not recommended for the treatment of gout as clinical evidence is not currently available for this dosage form in this condition.

Warnings and adverse effects

Central nervous system: headache, dizziness, light-headedness, mental confusion, syncope, drowsiness, convulsions, coma, peripheral neuropathy, depression and other psychic disturbances such as depersonalisation may occur as transient reactions that often disappear with continued or reduced dosage. However, occasionally, severe reactions require stopping therapy.

Gastro-intestinal: nausea, anorexia, vomiting, epigastric distress, abdominal pain, diarrhoea; ulceration (single or multiple) of oesophagus, stomach, duodenum or elsewhere in the small intestine, sometimes with perforation and haemorrhage (a few fatalities have been reported); gastro-intestinal tract bleeding without obvious ulcer formation; increased abdominal pain in patients with pre-existing ulcerative colitis; intestinal ulceration followed by stenosis and obstruction; stomatitis, gastritis, bleeding from sigmoid colon (occult or from a diverticulum), perforation of pre-existing sigmoid lesions such as diverticula and carcinomata; ulcerative colitis and regional ileitis (causal relationship not established).

Hepatic: rarely, toxic hepatitis and jaundice (some fatalities reported).

Cardiovascular/renal: oedema, elevation of blood pressure, and haematuria.

Dermatological/hypersensitivity: pruritus, urticaria, angioneurotic oedema, angiitis, erythema nodosum, skin rashes, loss of hair, rapid fall in blood pressure resembling a shock-like state, and acute respiratory distress including sudden dyspnoea and asthma. Bronchospasm in patients suffering from, or with a history of, bronchial asthma or allergic disease.

Haematological: infrequently, blood dyscrasias may occur, including leucopenia, purpura, aplastic and haemolytic anaemia, and particularly thrombocytopenia. Rarely, agranulocytosis and bone-marrow depression; anaemia secondary to obvious or occult gastro-intestinal bleeding (appropriate blood determinations are recommended).

Ocular: blurred vision; orbital and peri-orbital pain; corneal deposits and retinal disturbances including those of macula reported in patients with rheumatoid arthritis on prolonged therapy, but similar changes seen in patients with rheumatoid arthritis who had not received 'Indocid'.

Aural: tinnitus, deafness.

Miscellaneous: vaginal bleeding, hyperglycaemia, glycosuria, epistaxis, ulcerative stomatitis.

The following side effects have been associated with use of 'Indocid' Suppositories: tenesmus; proctitis; rectal bleeding, burning pain, discomfort, and itching.

Presentation

Ivory, opaque capsules marked 'INDOCID 25' containing 25 mg indomethacin BP; ivory, opaque capsules marked 'INDOCID 50' containing 50 mg indomethacin BP; ivory, opaque-based, transparent-headed capsules marked 'INDOCID R 693' holding white and blue pellets containing 75 mg indomethacin BP in sustained-release form; a fruit-flavoured suspension containing in each 5 ml, 25 mg indomethacin BP; polyethylene glycol suppositories containing 100 mg indomethacin BP.

United Kingdom basic NHS costs are: 25 mg capsules, £5.40 for 100; 50 mg capsules, £10.40 for 100; 75 mg sustained-release capsules, £18.00 for 100; suspension, £2.80 for 200 ml; suppositories, £2.30 for 10.

Product licence numbers: Capsules: 25 mg, 0025/0111; 50 mg, 0025/0112, 75 mg, 0025/0125. Suspension: 0025/0120. Suppositories: 0025/0062.

Product authorisation numbers: 25 mg capsules, 35/3/1; 50 mg capsules, 35/3/2; 75 mg capsules, 35/3/6; suppositories, 35/3/4; suspension, 35/3/5.

Agents in the Republic of Ireland:
Cahill May Roberts, P.O. Box 1090, Chapelizod, Dublin 20.

Additional information is available to the medical profession on request.

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proportion of its budget is devoted to research, but there are rheumatologists who feel that this aspect requires greater emphasis, particularly if New Zealand is to retain young doctors who wish to train in the specialty.

Wellington is the site of the latest clinical school for undergraduates and its approach to teaching is still evolving. The medical faculty is well endowed with enthusiastic teachers, and rheumatology plays a more important role in the curriculum than in the majority of UK institutions. Dr Burry and his orthopaedic and neurological colleagues have organised a concentrated 4-week course devoted to the locomotor system. It is hardly possible to encompass the whole topic during this period, but it does provide a systematic exposure of all undergraduates to the problems of joint disease. An examination at the end of the course is a serious affair and ensures that classes are well attended. I did sense that students were continually under pressure to attend seminars and lectures in a curriculum which was overgenerous in formal teaching sessions. Medicine was not often taught at the bedside, and the clinical apprenticeship which still forms the basis of teaching in many London hospitals plays little part in the teaching programme.

* * *

As anticipated, the pattern of rheumatic diseases that I encountered was similar to that observed in Britain. The one distinctive feature was the high prevalence of gout among the Maori people and other Pacific Islanders who have settled in New Zealand. It is generally accepted that their susceptibility to hyperuricaemia is to some extent inherited, but the respective roles of nature and nurture are still debated. In particular, the contributions of diet and obesity to their hyperuricaemia are unresolved, and it is of interest that when I embarked on a study of young Maori men in a factory near Wellington, the finding of both hyperuricaemia and obesity was much less than expected. My initial impression may not be substantiated, but it could imply that the latest generation of urban Maoris is more conscious of the health hazards associated with obesity.

There is an increasing awareness of the unique quality of Maori values. Two decades ago the Europeans looked to a future when New Zealand would be represented by a single race, wrought by intermarriage. That view no longer prevails and a burgeoning of Maori culture has followed the recovery of their population which was so sadly depleted in the half-century following European settlement. These warm, spiritual, and friendly people greatly enrich the fabric of New Zealand life, and the social dichotomy and racial tensions which have recently emerged are likely to be constrained by their good sense and pragmatism. New Zealanders frequently refer to their country as 'God's Own.' A land of such unsullied scenic beauty which numbers rugby football among its principal religions is not quite paradise, but is nearer than most.

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Notes

What makes a back ache?

This is the theme of a meeting to be organised by the British Association of Manipulative Medicine on 3–4 April 1981 at the Middlesex Hospital, London. Details from: The Organising Committee, Suite 4, Lister House, 11 Wimpole Street, London W1M 7AB.

Replacement of hip

A symposium on techniques in 'Orthopaedic surgery: selected procedures for total replacement of the hip', at which Sir John Charnley will be guest lecturer, will be held at the Grady Memorial Hospital, Atlanta, Georgia, USA, on 1–3 April 1981. Details from Ronald G Havican, Center for Rehabilitation Medicine, 1441 Clifton Road, N E, Atlanta, Georgia 30322, USA.

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