Neuropsychiatric Reactions to Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)
The New Zealand Experience

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Summary
The New Zealand Medicines Adverse Reactions Committee has been monitoring reports of adverse drug reactions (ADRs) since 1965. We wished to determine the numbers of voluntary reports of different types of ADR to all nonsteroidal anti-inflammatory drugs (NSAIDs) over a long time period and relate these to age. As the elderly are known to suffer from neuropsychiatric adverse effects of many drugs, we investigated neuropsychiatric reactions to NSAIDs to determine whether these were more commonly reported in the elderly. We counted all reported ADRs suspected to be associated with NSAIDs as well as selected types of ADRs reported from 1970 to 1989. These were divided into 5-year periods and 10-year age groupings.

In each consecutive 5-year period there was a progressive increase in the numbers of all ADRs reported for all NSAIDs. This was particularly marked above 50 years of age, but the numbers were reduced above 80 years. Reports for females accounted for about two-thirds of all reactions. Not unexpectedly, alimentary and dermatological ADRs accounted for most reactions and were more common in the group above 50 years.

Overall, neuropsychiatric reactions were the third most common ADR type reported. Their numbers increased with age and peaked in the 50 to 59 age group, with a sharp decline after 69 years. This age distribution paralleled that for all ADRs to NSAIDs. Although neuropsychiatric reactions to NSAIDs were reported in all age groups, they were not reported more commonly in the elderly. This study suggests that neuropsychiatric reactions to NSAIDs may be more frequent than is commonly believed.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed group of drugs worldwide. About 21% of adverse reactions reported to the US Food and Drug Administration (FDA) and 25% of reactions reported to the UK Committee on Safety of Medicines (CSM) are associated with NSAID use (Johnson & Day 1991). Dermatological and alimentary reactions are particularly well recognised, with elderly patients suffering from a high occurrence of serious gastrointestinal reactions (Beard et al 1987). Many other types of adverse effects have been attributed to NSAIDs (for reviews see Fowler 1987; Henry 1988; Johnson & Day 1991), with neurological and psychiatric reactions reported occasionally, particularly in the elderly (Carney 1977; Thornton 1980).

In New Zealand, adverse drug reactions (ADRs) have been spontaneously reported to the New Zealand Medicines Adverse Reactions Committee (MARC) since 1965, using notification cards. We have investigated ADRs to NSAIDs reported in New Zealand with the intention of determining
whether there have been any changes in the number and type of adverse reactions reported over the last 20 years. As NSAIDs are prescribed more frequently to the elderly who are sensitive to many drugs (Ghose 1991), we particularly wished to identify the types of adverse reaction suffered by this group. Neurological and psychiatric reactions are less commonly recognised adverse reactions to NSAIDs and, as these may occur frequently in the elderly, we have looked into this by categorising the frequency and type of these reactions in relation to age.

**Methods**

Using a mainframe computer, ADRs to all NSAIDs reported to the New Zealand MARC were counted between 1970 and 1989.

These were analysed separately in each 5-year period and were further divided into 10-year age groups. Only those reactions where an NSAID was suspected by a medical assessor as a probable or possible cause of the reaction were counted. Reactions that occurred while a patient was taking an NSAID but where a different type of drug was suspected of causing the reaction were excluded.

Particular classes of adverse reactions were further analysed, using the WHO classification as modified and previously published in New Zealand ADR reports (Edwards et al. 1988). These were alimentary, dermatological, renal, haematological, neurological and psychiatric reactions. Because of obvious overlap in categorising neurological and psychiatric reactions, these were combined as neuropsychiatric reactions for some analyses. The individual types of neurological and psychiatric reactions reported below 20 years and above 80 years, as well as in the 10-year age groupings between, were examined separately.

**Results**

Figure 1 summarises the number of adverse reactions for all NSAIDs reported over the period 1970 to 1989. There was an increase in the number of reactions up until age 60 to 69 after which there was a decrease. Two-thirds of the reactions occurred in women.

There was an increase in the number of ADRs for NSAIDs in each of the separate 5-year periods examined up until the age of 50 to 59 or 60 to 69 years. After this, there was a decrease in the numbers of reactions reported, especially in the above 80 group (fig. 2). As expected, alimentary and dermatological reactions were the first and second most frequent reactions, but neuropsychiatric reactions accounted for the third most common type of reaction overall.