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## Lesson of the week

### Colchicine in acute gout

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We describe three histories of patients with gout who were treated with doses of colchicine as advised by the *British National Formulary* (BNF)—that is, 1 mg initially followed by 500 µg every 2-3 hours until relief of pain is obtained or vomiting or diarrhoea occurs or until a total dose of 6 mg has been reached; the course should not be repeated within three days.<sup>1</sup> All three patients developed nausea or diarrhoea with this regimen. We consider that an alternative low dose schedule should be used to avoid such adverse events.

#### Case reports

*Case 1*—A 91 year old woman with a history of ischaemic heart disease and non-insulin dependent diabetes developed an ulcer over the right first metatarsophalangeal joint, which was discharging a white toothpaste-like material containing urate crystals. She was given 1 mg colchicine and then 500 µg every three hours, but she developed diarrhoea, and colchicine was stopped. After three days, the toe was still painful, and the course was repeated. She developed severe diarrhoea again and became dehydrated and unwell. We rehydrated her intravenously and gave her meloxicam. After the first few days we started her on colchicine 500 µg daily. She tolerated this well and it helped with pain relief.

*Case 2*—An 88 year old woman with a history of ischaemic heart disease, atrial fibrillation, congestive cardiac failure, chronic renal failure, hypertension, and osteoarthritis was admitted with pain in her right knee. Investigations led to a diagnosis of acute gouty monoarthritis (serum urea 27.1 mmol/l, serum creatinine 236 µmol/l, and serum uric acid 920 mmol/l). She was given 1 mg colchicine and then 500 µg every eight hours (a reduced dose because the BNF advises caution with renal and cardiac impairment). Within two days she developed nausea and vomiting. We stopped colchicine for 24 hours and then resumed with 500 µg twice a day. This improved her right knee pain without further nausea.

*Case 3*—A 56 year old man in general good health with recurrent acute gout found that non-steroidal anti-inflammatory drugs were ineffective and productive of severe indigestion; therefore he was given 1 mg colchicine and 500 µg every three hours for acute attacks. With this regimen, he had diarrhoea and sickness, and the acute attacks of gout continued. We reduced colchicine to 500 µg two or three times a day, which was effective without adverse event.

#### Discussion

The current BNF recommends a regimen for colchicine which is unchanged since the 1966 edition. The same regimen was also expressed in grains in Hollander's *Textbook of Rheumatology*, 1960. (The BNF is an authoritative guide on drugs and their use. In a recent survey of general medical staff in our hospital, of the 17 respondents, 12 said they would follow the BNF's advice, three gave no indication as to what dose they would use, one suggested an improbably large dose, and one would never use colchicine.)

The BNF states that colchicine is probably at least as effective as a non-steroidal anti-inflammatory drug in an acute attack of gout (although to our knowledge only one double blind placebo controlled study has been done with colchicine in gout,<sup>2</sup> and none has been done for NSAIDs and gout). The BNF also states that colchicine does not induce fluid retention and can therefore be used in heart failure, and it can be given to patients on anticoagulants. Thus the non-specialist is encouraged to use colchicine, especially when other treatments such as non-steroidal anti-inflammatory drugs or sometimes steroids (whether local or systematic) are inappropriate or ineffective. The BNF cautions about gastrointestinal disease, cardiac, hepatic, and renal insufficiency, but the only contraindication noted is pregnancy.

Although non-specialists are likely to prescribe the regimen as given, many rheumatologists have never used such high doses because they were trained to use

**In acute gout, lower doses of colchicine are effective yet less toxic than traditional regimens**

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low dosages even in acute gout. Low dosages were first advocated for the long term treatment of gout in the 1930s and are now used as prophylaxis while treating with allopurinol or uricosuric agents (using a lower dosage of colchicine during induction of urate reducing drugs is already mentioned in the BNF).<sup>3</sup> Even though lower doses of colchicine for acute gout were advocated in the *ABC of Rheumatology* in 1995,<sup>4</sup> a recent editorial in the *BMJ* still advocated the traditional high dose regimen.<sup>5</sup>

Empirical studies by rheumatologists over many years have shown the effectiveness of low doses of colchicine for acute gout without adverse events. We do not advocate an increase in the use of colchicine because non-steroidal anti-inflammatory drugs are usually highly effective, but we think lower dosages of colchicine should be publicised as being effective and much less likely to produce side effects than traditional high dose regimens. The side effects of nausea, vomiting, or diarrhoea are particularly difficult to endure in patients who are in pain, incapacitated, and immobile from acute gouty arthritis.

We suggest that in acute gouty arthritis colchicine should be used at a dose of 500 µg three times a day or less frequently, especially in those with renal impairment. In the absence of any other recent studies the BNF should provide this information which would benefit many patients.

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### When I use a word

#### Anecdote

Anecdotal reports are classified at the bottom of the recognised hierarchy of evidence that should be used to mould clinical practice, a list that is topped by large randomised clinical trials and systematic reviews. Nevertheless, I have elsewhere argued, in relation to suspected adverse drug reactions and interactions, that there are several important reasons for publishing anecdotes (*BMJ* 2002;326:1346). Indeed, nearly a third of the total literature on such reactions is in the form of anecdotal reports, although such reports often fall short of the standard of reportage that they deserve. However, this is not perhaps surprising. Anecdotes were never meant to be published.

The word anecdote comes from the Greek word ἀνεκδοτος (anekdotos), which means unpublished, or literally “not-out-given” (an-ek-dotos). Originally, the word was used in the neuter plural form, anekdota, meaning “secret, private, or hitherto unpublished narratives or details of history” (*Oxford English Dictionary*).

When the sixth century gossip Procopius wrote his scurrilous memoirs of life at the court of the Roman emperor Justinian and his wife Theodora (which incidentally includes another form of the giving word, and means “gift of God”), he called them “Anekdota,” which is sometimes translated as “Secret Histories” but which might be better rendered as “Unpublished Gossip.” The title is not as oxymoronic as it appears, for it is unlikely that the memoirs were published until after Procopius had died, and certainly not in Justinian’s lifetime.

And so anecdotes, which were originally unpublished, and indeed sometimes unpublizable, became gossipy stories ripe for circulation, and hence any stories, scandalous or not. This reminds me of

“confidential,” which in Oxford refers to something you may reasonably tell to a roomful of people, and “strictly confidential,” which refers to something you may tell only one person—at a time.

A collection of gossip was at one time known as an ana. But this word has nothing to do with anecdotes; it comes from the neuter plural form of the Latin suffix -anus, which meant “belonging to.” This survives as a suffix in words such as Victoriana and cricketana.

However, it is not generally appreciated (and not mentioned in the dictionaries) that anekdotos had an anterior meaning in Greek. A dowry is something that is given with a girl who is getting married, from the Greek dotos (granted) via the French douaire. And anekdotos meant “not given in marriage,” usually, in the feminine form ἀνεκδοτή (anekdote), referring to a girl; in other words, one who has not been betrothed. Which may reflect the anecdote’s position at the bottom of the evidence hierarchy.

Finally, an anekdotos was also a secret remedy. Perhaps one that had a lot of adverse effects?

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We welcome articles up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. Please submit the article on <http://ssubmit.bmj.com>. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for “Endpieces,” consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.