

The report presented findings that the prescribing information of eight proprietary medicines containing codeine or other opioid-like compounds as published in *Master Index of Medical Specialties* (MIMS),<sup>2</sup> a popular prescribing handbook in Hong Kong, did not include age-adjusted dosages for children and did not warn against their use in young children. As such, the authors warned medical practitioners and pharmacists of this 'prescribing pitfall' and recommended improvements to the prescribing information of cough and cold medicines.

On behalf of the publisher and editors of MIMS (Hong Kong edition), I should like to clarify the concept of MIMS, as an abbreviated drug directory of locally approved medicines. Our guiding principle is to present the information succinctly without compromising the content of the original prescribing information approved by the local health authority. Thus, common practical considerations, such as dosage adjustments based on age-group, size or pathophysiological condition (eg renal impairment), are not included in each abbreviated monograph.

*Taber's Cyclopedic Medical Dictionary*<sup>3</sup> defines paediatric age-groups as follows: neonate or newborn—up to 1 month of age; infant—from 1 month up to 12 months of age; children—after infancy to puberty (ie from 1 year to 12 years of age). Where 'Childn' (abbreviation for children) is specified under 'Dosage Information' in MIMS, the medicine is intended for use in children (1 year or older), not infants. This applies to cough and cold medicines: Bromhexine Compound Vida, Cosyr (reformulated), DEC, Ephedryl, and Uni-Pholco. If no age-group is specified, then the medicine is intended for adult use only. This applies to DM-Cordyl, Marsedyl, and Vida Brown Mixture.

While MIMS does not explicitly caution about the use of codeine or opioid-like cough preparations in children or infants, this is a widely published and recognised medical axiom. The authoritative United Kingdom drug reference, *British National Formulary*, recommends that codeine preparations may be used only in children of 1 year or older, while the *American Hospital Formulary System* and *Lexi-comp's Pediatric Dosage Handbook*, both well-known United States drug references, advise its use only in children of two years or older.

The MIMS Editorial team will, however, undertake to further clarify special precautions on the use of medicines in infants, to promote awareness among medical practitioners and pharmacists, and facilitate the use of professional and clinical judgement in this regard.

I am pleased to address any further queries or issues that may pertain to our MIMS publications.

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# Prescription of codeine in young infants

*To the Editor*—We read with great concern the case report "A case of probable codeine poisoning in a young infant after the use of a proprietary cough and cold medicine" by Lee et al.<sup>1</sup> As quoted by the authors without elaboration, we reported a similar case in 2001. It involved a 17-day-old Chinese baby girl. She was given phensedyl linctus 2.5 mL 3 times daily and chlorpheniramine 0.5 mg 4 times a day by a private doctor to treat a mild cough and nasal blockage. The daily dosage of codeine was 6.6 mg/kg. She developed three episodes of cyanosis secondary to central hypopnoea. Cardiopulmonary resuscitation was performed by the mother, a registered nurse, for the first episode. The next two episodes responded to oxygen. Investigation revealed a codeine level of 0.24 µg/mL in the blood sample taken 9 hours after the last dose of codeine. The estimated peak level was about 1 µg/mL, which is lower than the reported range of concentration of codeine that causes intoxication and death in adults (1.4-5.6 µg/mL).<sup>2</sup> As far as we know, the

mother of our reported patient did not launch a formal complaint against the prescribing doctor.

The half-life of codeine in young infants is much longer than that in older children because of immaturity of the hepatic glucuronidation system and they are also more sensitive to the respiratory suppression effect of codeine as illustrated by our reported case. Even if one adjusts the codeine dosage according to body weight as recommended for older children, the risk is still high because the recommendation is based on older children who metabolise codeine quicker.

As Lee et al<sup>1</sup> stated in his case report that paediatric prescribing information were not available in most proprietary products, prescription of such products by paediatricians should be extremely cautious. For dispensing of paediatric medication, we personally recommend the

*Pediatric Dosage Handbook* published by the American Pharmaceutical Association to be far superior to *Master Index of Medical Specialties* (MIMS). In a review of management of upper respiratory tract infection,<sup>3</sup> we found that codeine was not recommended in those younger than 2 years. Up till now, there is still no evidence that codeine is more effective in reducing cough than a placebo in children.<sup>3</sup>

From the authors' personal observation, it is common for infants to be prescribed codeine and not uncommon for young infants less than 3 months old to be given codeine. The cough for infant could only be one of two things: mild or not mild. If it is mild, it should not be treated with codeine—this is not recommended and dangerous as illustrated. If it is not mild, for example, pertussis, gastroesophageal reflux or bronchiolitis, codeine would only delay proper treatment and potentially aggravate the situation as in codeine and bronchiolitis. In the lay press coverage of Lee et al's report,<sup>4</sup> a medical practitioner was quoted as saying that codeine is acceptable for those under 1 year old. This suggestion is rather unfortunate in view of the fact that among the five case reports of six young infants, defined as 3 months old or younger, who suffered adverse effects associated with codeine used as a treatment of cough retrieved from our search in Medline (Ovid) from 1970 to 2004 using the following key words: codeine, child, and newborn infant, two were reported from Hong Kong.<sup>1,2</sup> This disproportionate over-representation (33%) of Hong Kong in the published evidence of the adverse effect of codeine is in line with our observation that

the practice of codeine prescription is common in Hong Kong. It is often argued that experienced medical practitioners observe no problems in infants who are given codeine. However, this statement must be viewed with extreme caution because those with problems might not inform the prescribing doctors, as in our case. In conclusion, we would urge all medical practitioners not to prescribe codeine-containing medications to infants as the benefit, if any, is not worth the risk and better alternatives are available<sup>3</sup> unless and until we have solid evidence that Chinese young infants tolerate codeine well and all the previous cases are unrepresentative.

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## Suicides in general hospitals

*To the Editor*—The article by Ho and Tay<sup>1</sup> draws our attention to a very important problem in hospital practice. A number of important factors relevant to suicide have been pointed out and discussed. To this list I would like to add two points in patient management which might induce suicidal tendency.

The first is drug-induced suicidal tendency. Theoretically all drugs causing depression can cause it, eg *Harrison's Principles of Internal Medicine* has listed beta blockers, reserpine, methyl dopa, clonidine, glucocorticoids, levodopa, and even amphetamine (withdrawal) to this effect.<sup>2</sup> Many years ago, as a junior trainee, I had the unpleasant task to certify the suicidal death of seven patients within 3 months in a chest unit. The alarm was raised and the culprit was traced to cycloserine which was being tried on tuberculous patients resistant to standard treatment. Stopping cycloserine put an end to the suicide epidemic.

The second is the attitude of the health-care personnel. At the same unit mentioned, we had a patient with chronic empyema who broke hospital discipline on some trivial matter.

He was summoned to the astute nursing officer in charge of the floor, and given a no-nonsense reprimand. In the end he turned around, rushed to the window and climbed out. I had to use all my strength to pull him back (not the safest procedure for both doctor and patient)! Later we transferred him to another hospital and operated on his empyema successfully.

Happily, I am sure that both drug safety and the attitude of hospital staff are vastly improved nowadays.

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