give rise to misunderstandings. They emphasise the importance of clear explanation as the examination proceeds and the potential consequences of failures of communication (Medical Defence Union, Medical Protection Society, personal communications). Furthermore, complaints of indecent assault have been made by patients of both sexes and are not limited to allegations against a doctor of the opposite sex.

The numbers of cases dealt with by the defence organisations are too small to draw conclusions about other risk factors, but evidence exists that young, medically inexperienced women consulting unfamiliar doctors are more likely to accept the offer of a chaperone,⁵ and it may be prudent for trainees and locums to consider their use in these circumstances. Beyond this, the exercise of wisdom, discretion, and even intuition is likely to represent a more effective strategy than a belief that a chaperone is never appropriate.

When a chaperone is used, she is likely to be a practice nurse, although receptionists, dispensers, and practice managers may also take this role, an arrangement likely to surprise some patients. Unsatisfactory tactics, such as leaving the surgery door ajar or keeping the intercom open between surgery and reception, have also been described.⁸ Doctors and, to a lesser extent, patients have stated that the presence of a third party can compromise the doctor-patient relationship and hamper communication; conversely, some patients may be more likely to discuss their fears and concerns with a nurse, although other members of the practice team might be less able to provide this support.

What should our patients expect? Principally that any consultation or examination is carried out in an atmosphere of care, confidentiality, and trust with the general practitioner of their choice, where anxieties are sought and addressed and where explanation and understanding are assured. This involves sensitivity to patients' social and cultural back-

grounds and to their abilities to understand the information we provide. Patients should also expect that an examination will be expertly performed so that it is as physically and mentally comfortable as possible, although this cannot be taken for granted.⁹

Considerable literature exists about patients' preferences for the gender of their general practitioner,^{10,11} but our knowledge of their preferences regarding chaperones is slight, and more information would be useful. The offer of a chaperoned examination is likely to be acceptable to most patients, but accepted by a minority; equally, few patients are likely to object to the routine presence of practice nurses, particularly when they provide support for the patient and assistance to the doctor. The challenge is to create a climate of trust and honesty within which patients who may be confused or upset about events occurring in the surgery are able to articulate their concerns and obtain explanation and reassurance where appropriate.

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Melatonin

Hormone of darkness

A recent review of melatonin was entitled "Time in a Bottle," and there could be no more apt description of this old hormone with its newly discovered function.¹ Just imagine it; we can now use melatonin to help coordinate, regulate, and, if necessary, readjust the body's internal biological clock.

Annual biological rhythms are probably not very important in human affairs, although long winter nights produce seasonal affective disorder in some people. Bright lighting, which inhibits melatonin secretion, may be an effective treatment. But what of those 24 hour circadian rhythms that have much greater effects on our lives, such as the rhythms of sleeping and waking, body temperature (highest in the afternoon), cortisol (highest at dawn), prolactin (highest during the night), melatonin (absent during the day), and intellectual performance (best at midday)?

Normally they are in synchrony with one another; but perturb the system by working night shifts and attempting to sleep by day, or by crossing time zones and succumbing to "jet lag," or by going blind, and you soon become aware of what it is like to live in a state of desynchrony. A growing body of clinical evidence exists to show that timed melatonin administration is of considerable benefit in allowing the re-entrainment of these disturbed rhythms.²

Recent research has begun to show how melatonin produces its entraining effect. The body's 24 hour "clock"

seems to reside in the suprachiasmatic nucleus of the hypothalamus, one of the few sites in the brain to have high affinity melatonin receptors. Keep a rat in constant dim light and its 24 hour rhythms of eating, sleeping, feeding, and drinking become disrupted, but give the rats a daily injection of melatonin at the same time each day and all these rhythms will become reentrained.² The metabolic activity of the suprachiasmatic nucleus is altered by melatonin administration,¹ suggesting that it is the hormonal transducer of darkness. Melatonin transmits information to the inner depths of a brain that lacks the ability to tell the difference between night and day.

In humans melatonin is produced at a rate of about 30 µg/24 hours, almost all of it being secreted by the pineal gland during the hours of darkness.³ When physiological amounts of melatonin are given to subjects, there is a fall in basal body temperature comparable to that normally seen during sleep.⁴ This fall may affect other bodily rhythms—for example, intellectual performance and body temperature tend to go hand in hand.

In humans, large doses of melatonin, ranging from 5 mg to 5 g have a marked short term hypnotic effect. One group in the Netherlands have started phase 3 clinical trials of a contraceptive pill containing 75 mg melatonin and 500 µg norethisterone. The group hopes that this will put women

into a state akin to the seasonal anoestrus of animals and, as melatonin can suppress the growth of human breast cancer cell lines in vitro, protect them from breast cancer at the same time.⁵ Presumably the pill must be taken in the evening because of the profound hypnotic effects of such a massive dose of melatonin. The induction of sleepiness alone could make it a very effective contraceptive.

Further work is under way to isolate and characterise melatonin's receptor in the hope of designing synthetic agonists and antagonists. A simple derivative of tryptophan and serotonin, melatonin is cheap enough to make, but unfortunately it will still cost millions of dollars to complete the acute and chronic toxicity tests required by drug regulatory authorities. The evidence that taking melatonin benefits jet lagged travellers, shift workers, blind people, and elderly

people with sleep disturbances becomes stronger by the day.^{1,2,5} Let's hope that we will soon see it on the market.

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Outcomes in intensive care

Are related to case mix, but we still need much better measures

This issue of the *BMJ* includes two papers that examine aspects of intensive care in the United Kingdom and Ireland.^{1,2} They represent the first large collaborative study of intensive care activities and outcome to have been conducted in these two countries, and the results have implications for medical audit in general as well as for intensive care. What are these implications, and what do the studies tell us about intensive care practice?

That differences in case mix should influence outcome of medical care is not surprising. Case mix refers to factors that characterise the patient population in terms of diagnosis, age and sex, severity of illness, and available treatment. The influence of case mix on medical outcomes is well recognised,^{3,4} but it is not easy to measure. In an era of managed health care in which budgets and contracts govern medical activities, intensive care units (and other disciplines) will find it reassuring to be able to measure the impact of case mix on outcome rather than having substantial variations attributed to differences in quality of care.

The interrelations between different components of case mix need to be explored in detail. For example, increasing age may inherently include other risk factors such as pre-existing chronic disease. The reported impact of age on outcome varies among countries,⁵⁻⁷ suggesting that it is biological age, not chronological age, that is important. International and intranational comparisons may have to wait for the development of better measures of physiological reserve and population health. Multivariate analysis will help to clarify some of these issues, but statistical manipulation of biological variables is less complex than measuring them in the first place, and Rowan and her colleagues are right to draw attention to the need to standardise terminology on case mix. Severity of illness is a good place to start.

The American APACHE II system had a considerable impact on intensive care because it described the important but nebulous concept of severity in terms of homeostatic disturbance by attaching numerical values to physiological variables and chronic health status.³ In conjunction with weighted coefficients for specific diagnoses these values could then be used to calculate the risk of death for groups of patients. By comparing predicted with actual outcomes (the standardised mortality ratio), comparisons could be made between different treatments, and indeed between different intensive care units,⁸ by controlling for the main components

of case mix. Can this tool be used to assess intensive care performance in the United Kingdom?

Rowan *et al* have shown that, when a large cohort of patients is examined in this way as a group, the APACHE II system fits the United Kingdom and Irish data almost as well as the American data from which it was derived. Indeed, for 22 of the 26 contributing intensive care units, if we assume that mortality ratios are normally distributed, the APACHE II system seemed to be able to account for all the observed differences in mortality. This is impressive.

Nevertheless, significant differences appear between predicted and actual outcomes when certain subgroups—for example, those defined by age or diagnostic category—are tested. The authors discuss possible causes for these discrepancies, but the importance of this finding is that the same unmeasured factors may also be responsible for the differences in mortality ratios in the remaining four intensive care units, three of which “performed” significantly better, and one worse, than the majority. Are these differences real or is the measuring device poorly calibrated?

Indeed, could the score be manipulated to give an unfair advantage? If in future such data were to be collected for resource allocation and contracting it might be possible to select values for physiological variables that would result in attractively low standardised mortality ratios: in a competitive health care system commercial advantage may not necessarily respect scientific truth. Physiologically based systems are also susceptible to treatment, and while this feature can be used to improve predictive ability,⁹ it may also be a source of significant error in comparisons of performance if patients receive substantial physiological support before admission,¹⁰ a phenomenon known as lead time bias.

The revised APACHE II system adjusts for this effect as well as incorporating new variables and diagnostic coefficients, but the improvement in predictive power is modest and the coefficients and equation for calculating risk are not in the public domain.¹¹ Automated systems facilitate collection of certain physiological variables but will not replace manual verification of all data. Binary methods (requiring yes/no responses) like the mortality prediction model¹² may well be useful adjuncts to physiologically based systems because they are independent of treatment and can be used to stratify patients before admission to intensive care and could therefore provide a form of cross referencing. Once again, however,