Letter from . . . Chicago

Centenary

GEORGE DUNEA

In the course of his efforts to "cure sometimes, relieve often, but comfort always" the modern physician must contend against formidable popular prejudices. He may find his patients quite unimpressed with his cognitive skills, expecting him instead to wave a magic wand, point the bone, or at least dance around the fire in feather garb. He will discover that many patients do not trust his medicines and do not value his advice. Some would not follow his instructions even if he were Freud, Adler, and Jung all rolled in one. Others would ignore him even if, like the great Charcot, he had the kind of dominating personality that made the hysterical anorexics of the Salpetrière eat, the blind see, the lame walk. And he must reckon especially with a deep understanding that questions the value of swallowing tablets—preferring instead a bottle of bitter medicine, a shot of penicillin, a cube that fizzes in a glass of water, a mustard plaster, a leech, cupping, bleeding, plasmapheresis, scarification, electricity, radiology, chiropractic, acupuncture, phrenology, coronary artery surgery, fasting, jogging, hyperalimentation, psychotherapy, making baskets, meditating while standing on one's head, or inserting a soft bullet in a direction retrograde to the course of peristalsis.

Hence the problem of non-compliance—best known to hypertension and tuberculosis doctors, or to naive rheumatologists expecting their patients to take plain aspirin when the man across the street is doing so well taking the latest non-steroidal inflammatory drug. Only once, indeed, have I known a rheumatologist so Charcot like that he could make his patients take 10 aspirins a day year after year. This he achieved by dispensing them himself under a wonderful but fictitious name, emphasising that this unique remedy could not be bought elsewhere—so that 10 years after his death patients still come back to his former office to pick up supplies of the wonder drug.

Compounding the problem with tablets are the recent packaging regulations promulgated in the wake of the Chicago poisonings from Tylenol adulterated with cyanide. These have placed tablets out of the reach of all those who do not combine extraordinary strength with superior intelligence, above average muscle coordination, and ownership of a hydraulic bottle opener. The many steps to analgesia, enough to give one a headache, decidedly eliminate patients with stroke, Parkinsonism, arthritis, or cataracts. Not that it is too difficult, provided you follow instructions: pull off the plastic cover, tear off the aluminium cap—but if you do it wrong the edge will be jagged and you will need a screwdriver. Then align the arrows of the outside and inside containers, whisper the password, take the plastic container out of the aluminium can, and murmur an incantation while facing straight east. Now take the bottle out of the container and open the top after giving the square of the sum of the digits of your mother in law's social security number. Break open the seal, discard the protective fluids, wait 20 minutes for the fluid to dry off, fish out the cotton wool with artery forceps, prize out another plastic cap, and there you are.

But you may decide it is not worth the trouble; hence the recent interest in alternative methods of administering drugs. How much easier to squeeze out a strip of nitroglycerine ointment from one end or the other of a toothpaste like tube—or to stick a patch of nitroglycerine ointment straight over the offending organ, rather like a mustard plaster. Clonidine patches for hypertension, anticancer patches, and hormone patches, are also coming; and one may imagine a nose patch for sinusitis, a scalp patch for headache, a stomach patch for biliousness, perhaps Isolde's heart patch for love sickness. There will also be a new transdermal contraceptive, though we do not know where it will be applied, nor what its complications may be. But already an elderly man with chest pain and headache would have constituted quite a diagnostic problem had his doctor not discovered that one of his wife's nitroglycerine patches had become stuck to his abdomen.[1] And there have been complications from scopolamine patches (widely used to treat motion sickness, dizziness, vertigo, and tinnitus)—namely, a confusional state in one patient and a confusing anisocoria in another. The confused lady responded to 1 mg of pilocarpine given intramuscularly,[2] and the confusing pupil constricted with pilocarpine eyedrops, this indicating that the trouble lay in the eye, not in the brain.[3]

Soon scopolamine will be available for transocular absorption from a system worn in the eye; and protein molecules normally degraded in the stomach will be given by nasal spray; so that some day synthetic vasopressin will be joined by nasal interferon, calcitonin, luteinising hormone, and perhaps even a new insulin to treat diabetes. Other companies are coming up with a soluble aspirin that dissolves instantly, enters the bloodstream in 30 minutes, and causes no gastric irritation. Investigators are also working on polymer bound drugs that may be released in the intestine by ion exchange; by simple dissolution of the polymer matrix; or by having water seep in through a semipermeable capsule, dissolve the drug, and then let it leak out through a microscopic hole created by laser beam. And for patients who like neither pills nor injections there will be implants—computer operated pump implants, subcutaneous ones that release their active ingredient from soluble polymers, or devices in which millions of beads are stirred into motion by an outside magnetic force.[4]

Adequate analgesia

Another obstacle to "relieving always and comforting often" seems to be a reluctance by doctors to prescribe adequate analgesia for patients with postoperative or chronic pain. At least so indicate the reports from conferences of pain experts—not surprisingly perhaps, given that generations of house officers have been indoctrinated that opiates are dangerous because they depress respiration and cause drug addiction. Yet the growing perception that patients suffer needlessly has

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reached even the politicians, some of whom have introduced a Bill to legalise heroin. But the pain experts see the problem not as a lack of heroin but as a lack of understanding of the principles of analgesia. And basic scientists think that more rational treatment would be given if we understood better the physiology of pain. They describe afferent unmyelinated C axon fibres—polymodal nociceptors modulated by prostaglandins and catecholamines, and using substance P as a neurotransmitter; and efferent fibres—with opiate or opioid (endorphin) receptors in the brain producing descending impulses that cause analgesia.[5]

Of more immediate value, however, is an excellent British review on analgesia.[6] This describes the difference between acute pain, with its "fight and flight" response, and chronic pain, with its vegetative features. It emphasises the need to give regular doses of analgesics and provides practical protocols, including 20 points on how to use morphine. It also emphasises that analgesics of different classes may need to be combined or supplemented with "coanalgesics" such as anticonvulsants, steroids, metoclopramide, muscle relaxants, antidepressants, diuretics, or non-steroidal anti-inflammatory drugs.[6]

Similar conclusions were reached last year in a symposium held in Washington and reported more recently in the *Journal of the American Medical Association.*[7] Accompanying this was an editorial decrying "misguided attitudes among health professionals" and a lack of communication between scientists and clinicians belonging to different disciplines.[8] Along these lines one remedy of potential value is a device allowing patients to give themselves predetermined amounts of analgesics through an intravenous set, which may be of considerable value in hospital. But outside hospital the patient with cancer faces different problems. He has trouble in buying narcotics, because the pharmacies no longer stock them for fear of armed robberies. Sometimes his sunken eyes and wasted features may result in his being mistaken for a drug addict.[9] And should he be cured of his cancer, he faces the misery of a life of bias and prejudice, often unable to get a job because prospective employers are afraid they may be liable for future medical bills should the disease recur.

Still on the subject of pain relief, we find that non-steroidal anti-inflammatory drugs are becoming used more widely than ever. They are now often in the news because of their side effects, but also because ibuprofen is about to enter a $1·3 billion a year over the counter painkiller market. This is at present divided among the manufacturers of the various formulations of aspirin and paracetamol, but in anticipation of ibuprofen being approved for sale without prescription, several companies stand poised ready to compete with their own version. The stakes are high because ibuprofen, widely used for menstrual cramps, is already registering sales above $200 million. At our hospital, for instance, the total expenditure for ibuprofen now exceeds that for propranolol. But the drug has also become one of the most frequent causes of a raised blood urea concentration, especially in patients suffering from dehydration or who are taking diuretics.

Serious side effects, however, have been more prominent for benoxaprofen. This agent, now recalled, is thought to have caused some 96 deaths in Britain and 46 in the United States. Among its presumed victims was a woman cut off at the age of 86, for whose loss a jury compensated the son with $6 million. For the other long acting drug, piroxicam, the story is more mixed. On the one hand, there have been questions about its effectiveness; on the other, there have been claims that its prostaglandin inhibiting properties may not only achieve symptomatic relief but actually correct the underlying immunological problem. Then there is the issue of phenylbutazone and oxyphenbutazone, which Mr Ralph Nader's consumer group wants recalled for allegedly having caused 3100 deaths, killing people at a rate of 120 a year, and being prescribed unnecessarily in 99·6% of cases. Many rheumatologists, however, believe that these drugs are being prescribed infrequently, anyway, and that they are useful in ankylosing spondylitis.

Another non-steroidal anti-inflammatory drug, zomepirac, has now also been recalled, after being implicated in five deaths from possible hypersensitivity. I was sorry about this, because the drug had scored highly in my uncontrolled and statistically non-significant trial. I had given out samples of both the small white zomepirac tablet and the more impressive and colourful ibuprofen and indomethacin, and found the patients invariably preferred the former. Not that physician bias in designing this study can be entirely ruled out. For undoubtedly the patients, in their quest for cure, comfort, and relief, must frequently contend with their doctors' inherent prejudices. Which is why some 400 years before this one hundredth Letter from Chicago the wise Montaigne promised that "If your doctor does not think it good for you to sleep, to take wine, or some particular meat, do not worry; I will find you another who will disagree with him."

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MATERIA NON MEDICA

With an umbrella

The rains have come again to the middle hills of Nepal, this year somewhat earlier than usual, much to the local people's satisfaction. Narrow terraces begin to seethe with muddy water, and the rice planting ritual can begin. Men, ploughs, and bullocks labour to and fro, half submerged in mud. The women cower under the local oval "umbrellas" made from bamboo wickerwork, which cover their backs and are worn by a headband, leaving both hands free. Their backs are bent double in the act of planting the rice shoots individually in the quagmire their men have created. From above, it looks as though cockroaches of Himalayan dimensions have taken to the fields.

Today I have completed a short walk, a trivial six hours, between government health posts, whose work we are trying to support. Nobody can claim to have walked in Nepal until they have lost their way in the monsoon and, to regain the path, have traversed the thin mudbanks of the rice paddies, side stepping the young soya plants with all the assurance of a locum tight rope walker. The dilemma that confronts one, whether it is better to fall forwards or backwards, is not attractive.

Back on firm ground, a bird of iridescent blue catches my eye and momentarily my attention is drawn from the leech ridden path; I lose my footing and lurch awkwardly into some nettles—how dare they thrive at this altitude? And leeches, which god thought them up? I can cope with them around my ankles, but dropping from the trees like SAS combat troops seems unreasonable for such brainless creatures. A thump on my umbrella (a standard design, imported from Taiwan), louder than the average rain drop, makes me look up as we pass under some low hanging branches. Aghast, I find towards one edge two inches of sinister blackness adhering to the material above. Furiously I strike it from beneath with the back of my hand. It won't be dislodged. My mind makes the inevitable leap to consider how that thing might have dropped down the back of my shirt if the umbrella hadn't intercepted it. A wave of revulsion results in renewed attempts to rid my umbrella of its unwelcome passenger clinging so firmly to the canvas. Gradually I become aware of my companion staring curiously at this spectacle; he appears to be working out the appropriate dose of chlorpromazine for me. And gradually it dawns on me that I am attempting to dislodge the fastener that I would be able to clip around the furled umbrella, should it ever stop raining.—G TUDOR-WILLIAMS, Save the Children Fund, West Nepal.

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