FEATURE REVIEW

Personalized Medicine

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The following true story, although pertaining to a rare condition, is typical of medicine practised in hospitals and doctors' surgeries every day all over the world. Mrs M's district nurse phones me - she is with Mr and Mrs M at their house dressing a leaking exophytic chest wall lesion. She can see a 'liver like substance' extruding from a small inferior wound, there is some fresh blood, and she is concerned that Mrs M may bleed suddenly and profusely. I ask her to send Mrs M to Casualty. Mrs M agrees, but on the condition that she is not admitted to hospital. Mrs M has mesothelioma and for several years, has only had a 'few months left to live'. She presented thirteen years ago with a pleural effusion, for which no cause was found for seven years. A pleural biopsy finally showed mesothelioma, and she underwent chemo and radiotherapy. Unusually for this type of cancer, Mrs M's months turned into years and she is now experiencing late manifestations of her disease, not often seen. Some months ago she noticed growth of hard lumps under her right arm, over her shoulder blade, behind her right breast and above her right clavicle. Stoical to the utmost, she bought new clothes and got used to bumping her chin on the lump above her clavicle every time she turned her head to the right. She adapted to using her left hand more - for holding the telephone and stirring soups. Mrs M's oncologist started her on Thalidomide, an experimental drug in an oncology setting, with the hope that these uncomfortable lesions might die away as they are starved of their blood supply. Within weeks, what were hard lumps turned to boggy masses. Ultrasound confirmed a number of large fluid filled spaces, some of which were amenable to drainage. So, we drained off two litres of highly viscous blood stained fluid from the lesion on her back, and two weeks later another litre from the lesion anteriorly. The lump on which she hit her chin had also become cystic, so we drained off as much as we could from there too. I prescribed antibiotics (whatever the viscous material was, it was likely to get infected), asked her to check her temperature at meal times and let us know if she became febrile, and sent her home for her District Nurse to review regularly. Six days later I received the phone call. One of the lumps had become cystic and had burst through the skin. Her response to the thalidomide treatment was turning out to be phenomenal - contrary to all expectations.

'Mrs M has arrived - let's go down and see her', I say to my colleague. On the way down, I give him a brief history, but it is difficult and he clearly has no idea what to expect. She is in her cubicle with her husband, perfectly dressed. She transfers to the bed and I undo the dressing, but before that I get prepared with a pad and two sick bowls. Nothing fancy. Immediately, as I peel back the dressing. the familiar cystic fluid pours out of the small wound inferiorly. I hold a bowl beneath it, none spills. My colleague goes pale, and rushes to put up drips and to attach monitors. The bowl fills up and the wound stops draining. I ask Mrs M to sit up, this time, however, I'm too slow in reaching for an empty bowl and it pours into her lap, which she handles with good grace. She does not look and protests good naturedly when her husband attempts to give a running commentary. Completely detached, Mrs M appears remarkably unaffected by this illness, which thirteen years ago was only going to give her 'a few more months to live'. We talk about other things - about her grandchildren coming over the next day for cooked English breakfast, about the merits of single sex education, about how she and her husband met, about the National Heath Service, about all sorts of things. She tells me how nice it is that since last week she can turn her head without hitting her chin, and she thanks me for it, because she knows I missed lunch for it. The 'lump' has drained dry and loose skin hangs where it had been tense. She has a change of clothes and the nurses re-dress the wound. She is ready to go home, but she agrees to a blood test, and a blood transfusion

if her haemoglobin is low. I don't expect it to be, there was no fresh blood. My colleague is dumbfounded - he had just watched two litres of what looked like blood pour out of Mrs M's chest wall and I was sending her home. The decision to send her home was highly personalized - I knew her condition and what to expect, moreover she had a breakfast to cook for her grandchildren the next day.

'Personalized medicine' is, however, the term used for treating patients according to their genes, or, in oncology, according to their tumour's genes and is far removed from the type of medicine described in Mrs M's story. Personalized medicine involves all three aspects of health care: prevention, detection and treatment. Personalized medicine uses genetic information to tailor strategies for these three cornerstones of health care at the level of the individual. The rapid advances in genomic sequencing and bioinformatics are making these dreams come true. Patients sensitive to drugs such as Azathioprine can now be identified pre-treatment and their doses adjusted accordingly - before they experience potentially life-threatening myelosuppression1. Thousands of cancer patients are benefiting from targeted drugs such as Gleevec (for Philadelphia chromosome positive chronic myeloid leukaemia), Iressa and Tarceva (for certain patients with non-small cell lung cancer) (2). Many more such 'designer drugs' are emerging from the research and development pipelines. Last year, the US Food and Drug Administration approved the first test to use genetic information to allow doctors to choose the most appropriate drugs and doses for their patients. The AmpliChip test analyses for common variants in two cytochrome P450 genes (CYP2D6 and CYP2C19) which play a major role in the metabolism of 25% of all prescription drugs. The test results place individuals into one of four categories: 'poor', 'intermediate', 'extensive', or 'ultra rapid' metabolizers. A similar 'p53 chip' is under development for prognostication in oncology (3).FDA approval of the original AmpliChip test means approval for this and several other chip-based testing kits is likely to be rapid.

These new developments must be seen in the context of present day life. Holidays, mobile phone tariffs, pay-back schemes, you name it, everything these days can be tailored to your needs. As in the market place, so in medicine: patients will jump at the opportunity to be treated in a personalized fashion. As Dr Francis S Collins, director of the National Human Genome Research Institute writes:

> To realize the full potential of personalized medicine, we must venture beyond the fields of science and medicine and into the ethical, legal, and social arenas. For example, without legislative protections against genetic discrimination in health insurance and the workplace, many people will be reluctant to undergo potentially life-saving genetic tests or to participate in the clinical trials needed to develop genetically targeted therapies. In February, the Senate passed the Genetic Information Nondiscrimination Act of 2005 by a vote of 98-0. The president has indicated strong support, but the bill remains before the House of Representatives, with no hearings scheduled. Given that more than 800 genetic tests are now available and hundreds more are on the horizon, we need this legislation.
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> Other tough questions that we as a society need to ask ourselves are: Will access to genomic technologies be equitable? Will knowledge of human genetic variation reduce prejudice or increase it? What boundaries will need to be placed on this technology, particularly when applied to enhancement of traits rather than prevention or treatment of disease? Will we succumb to genetic determinism, neglecting the role of the environment and undervaluing the power of the human spirit?' (4)

Advances in technology will ultimately lead to truly individualised therapy. However, as clinicians, we must not lose sight of personalised medicine in every sense (technology and humanity). It is our role to guide patients through these advances and translate their test results into meaningful messages for them. I see clinical practice in the near future to be an arena where both personalized and personal medicine co-exist and complement one another to the benefit of both patients and society.

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