**Lecture 8 Dr. Haider Raheem**

**Ethical Problems in**

**the Pharmacist's Clinical Practice (continued)**

**Ethics and the Promotion of Prescription Drugs**

Health care professionals question the ethics of accepting gifts from drug companies. Gifts ranging from low cost items such as pens, notepads, clothing, textbooks, and meals to high-cost gifts such as all-expense-paid trips to luxury resorts and cash gifts used to be common. Pharmacists attending national pharmacy association meetings often attended industry-sponsored continuing education presentations, receptions, and parties and collected bags of gifts from pharmaceutical industry exhibitors.

 The ethical issues are complex and grow out of the unique relationship between the pharmaceutical industry and health care professionals. Unlike other types of advertising, pharmaceutical advertising targets health care professionals, who influence drug selection, and not patients, the ultimate consumers of the products. Acceptance of these gifts carries ethical implications, no matter the monetary value of the gift.

 The ethical implications of accepting gifts from the pharmaceutical industry involve issues of justness and obligations. The cost of pharmaceutical gifts and other forms of advertising is included in the price of medications. Therefore, some argue that spending patients’ money without their knowledge or consent and without direct benefit is unjust. Gift giving also implies obligations on the part of the recipient. The obligations may be subtle, but even the appearance of an obligation may alter society’s trust in the profession.

 Guidelines regarding the relationships between health care professionals and the pharmaceutical industry continue to evolve. Although most of the discussions have targeted physicians, the ethical issues, and therefore the guidelines, are applicable to other health care professionals. In 1992 the ASHP board of directors approved and published the ASHP guidelines on pharmacists’ relationships with industry. The guidelines address the issues of gifts and hospitality, continuing education, consultancies and advisory arrangements, clinical research, and disclosure of information.

 Guidelines regarding the relationships between the pharmaceutical industry and health professionals also are evolving. The Pharmaceutical Research and Manufacturers of America (PhRMA) first adopted a voluntary Code on Interactions with Healthcare Professionals in 2002; an updated and enhanced code became effective January 1, 2009. The code addresses the interactions between pharmaceutical and biotechnology companies and health care professionals, including industry-sponsored informational presentations, educational meetings, consultancy arrangements, and the use of non–patient identified prescriber data. Common practices of the past, such as sponsoring dinner at a local restaurant, paying for gasoline or a round of golf at a local golf club, or giving gifts such as golf balls or mugs imprinted with a drug name, are no longer acceptable. The code allows companies to offer gifts that are primarily for patient education (e.g., anatomic models, educational posters) if the gift is not of substantial value ($100 or less) and does not have value beyond the health care professional’s professional responsibilities. Companies can provide modest meals with presentations if the presentation is at the health care professional’s office or hospital.

**The pharmaceutical manufacturing industry**

Since the latter part of the nineteenth century, the provision of medicines has shifted progressively from extemporaneously prepared pharmacopoeial medicines or specialities to large-scale industrial proprietaries for either over the counter sale or for supply on prescription. The modern pharmaceutical industry, largely dominated by Western European and North American manufacturing companies, is the principle source of the vast majority of research, development and clinical evaluation of new medicines.

**Ethical issues**

While responsible for introducing a great many prophylactic and therapeutic compounds that have saved or improved countless lives, the industry often attracts highly critical comment from the media and others regarding excessive profits and questionable promotional practices (misleading advertising; inducements encouraging GPs to prescribe or to increase numbers of prescriptions written; funding for conferences or attendance; pressure on researchers to manipulate results; failure to act promptly or acknowledge (even suppress) reports of adverse effects).

 In 2006, the multinational pharmaceutical company Merck, Sharp & Dohme was suspended from the Association of the British Pharmaceutical Industry for malpractice. The malpractice involved an offer of assistance to GPs with blood pressure monitoring and control, but only to those GP practices that regularly used the company’s antihypertensive drug Cozaar® (losartan). This is the second suspension since the introduction of a more rigorous Code of Practice at the beginning of 2006.

**Global availability of medicines and developing countries**

Most of the major international pharmaceutical companies are now truly multinational or global, with subsidiaries in both developed and developing countries. The ethical problems of pharmaceutical advertising and promotion are further complicated by market conditions and indigenous culture. But perhaps the most important consideration is the extent to which ‘Big Pharma’ has an obligation (if any) to make products available at a price locally affordable in developing countries. The question has both commercial and humanitarian implications. The commercial aspect centres on profit maximization (a duty to shareholders). The wider the distribution, the greater are potential sales and profits. But most developing counties are unable to afford to pay Western market prices for their medicines. Some pharmaceutical companies do charge significantly lower prices in some of these markets, presumably a lower profit margin can be sustained and there is net marginal value. The economic term ‘Ramsey-Pricing’ is often used to relate ‘the set of price differentials that yield the highest possible social welfare, subject to a specified target profit level for the producer, usually a normal, risk-adjusted return on capital’.

**Orphan diseases, orphan drugs**

The term orphan disease is used to describe those ailments of a chronic or life-threatening nature that are so rare that drug development is not commercially viable using the usual criteria. In Europe, the term is applied to indications with an incidence of no more than 5 in 10 000 persons. Some, possibly many, so-called tailor-made pharmacogenetic medicines would fall into this frequency category, although it is not suggested that all orphan drugs are of a pharmacogenetic nature.

 To some extent, those who suffer from orphan diseases can be considered to face a double jeopardy – the disease itself and a dearth of possible treatments. Irrespective of this, the fairness and possible exploitation of subsidising orphan drug development costs have been questioned: ‘Special status in resource allocation will avoid difficult and unpopular decisions, but it may impose substantial and increasing costs on the health care system. The costs will be borne by other, unknown patients, with more common diseases who will be unable to access effective and cost effective treatment as a result.’

**AIDS and the regulation of medicines**

One of the most significant, devastating and wide-reaching influences of the latter part of the twentieth century was the appearance of the human immunodeficiency virus (HIV), leading to the development of AIDS, early in the 1980s. The success of the pharmaceutical industry in creating effective anti-AIDS drugs was notable for becoming the arena for a pivotal political battle between AIDS activists and drug regulators.

 The AIDS lobby in the USA – large in number, knowledgeable, politically astute and legally well represented – argued that for many of those with AIDS time was of the essence. They were literally dying and wanted rapid access to experimental drugs even though these were not properly validated and approved, and they were prepared for the possibility that treatment might do more harm than good. AIDS sufferers considered that the cautious step-by-step processes of evaluation and regulation, and in particular blinded placebo-controlled studies, were inappropriate.

 So successful was lobbying in the USA, that arrangements were made to permit use of experimental drugs at various stages after phase I trial for those facing imminent death, not only for AIDS sufferers but eventually also for those with advanced breast cancer, Parkinson’s disease, Alzheimer’s disease and juvenile diabetes. The average delay between application and approval by the Food and Drug Administration was reduced from an average of 34.1 months in 1986 to an average delay of 12.6 months in 1999.

 The conventional wisdom of drug regulation had been successfully challenged by the AIDS lobby and, by default, on behalf of others with terminal illnesses. However, apart from fostering a fundamental review of regulatory requirements and procedures, medicines for treating nonlife-threatening conditions would seem to be generally well served by the classical slow and steady approach. Paradoxically, the well-known serious cardiovascular problems associated with the cyclo-oxygenase 2 inhibitor Vioxx (rofecoxib), and terrible problems experienced by volunteers in the phase I assessment of TGN1412, tend to reinforce the case for having a robust regulatory system, but nevertheless one that is continuously under review and learns from mistakes.

**Stem cell research**

Pharmacists are unlikely to have direct involvement with stem cell medicine, at least for the foreseeable future. Nevertheless, some understanding of the ethical and legal background is advantageous. Stem cells are ‘pluripotent’, undifferentiated cells carrying the genetic potential of all the specialised cell types of the body (there are 216 potential cell types). These cells can be directed into development pathways for different cell types with different specialized functions. Such cells are present in the early embryo, in the fetus, in the blood of the umbilical cord and are also present in adult tissues. Just how the development of these stem cells is controlled is not fully understood, but there is considerable interest in the therapeutic potential to use them to repair and restore tissues and organs (for example in heart disease, blood and neurological diseases and damage). Diseases such as Parkinson’s disease, diabetes and Alzheimer’s disease are important candidates. Research that might bring these possibilities closer to fruition is at a very early stage.

**Ethical issues**

The major ethical questions concern the supply of research material and research funding. In July 2006 in the USA, the American president vetoed a congressional act that would have provided federal funding to enable research on stem cell lines in frozen embryos marked for destruction. Currently, the primary sources of human stem cells are human embryonic or cadaveric fetal tissue. The Warnock Committee Report (1984), which substantially informed the 1990 Human Fertilisation and Embryology Act, recommended that research on embryos should be limited to 14 days following fertilisation – the time at which generation of the nervous system ‘primitive streak’ begins. In the future, it may be possible to derive adult stem cells from a patient’s own somatic cells (using the ‘Dolly the sheep’ technique of somatic cell nuclear transfer), which would have the important advantage of avoiding rejection problems.

 In principle, stem cells could be obtained from embryos or fetuses that arise either contingently (‘spare’ embryos or fetuses’) or deliberately ‘created’ for the purposes of research by somatic cell nuclear transfer. The North East England Stem Cell Institute has been granted a licence from the Human Fertilisation and Embryology Authority (July 2006) that will allow women to receive a 50% reduction on the cost of fertility treatment in exchange for donating ‘spare’ embryos for research. This represents a departure from previous policy, which prohibited direct payment for eggs.





