International Social Pharmacy Workshop

Editorial

The Malta College of Pharmacy Practice, will be hosting the 13th International Social Pharmacy Workshop next summer. The concept of social pharmacy is very clearly explained in the article by Professor Ellen West Sørensen and colleagues, who are considered to be pioneers in this field. Malta has successfully hosted a number of pharmacy conferences, however this one is somewhat different and rather special.

It is difficult to describe the feeling at a social pharmacy workshop, because one needs to experience it. This is a meeting of friends, or an extended family, with new friends being always welcome - a situation that lends itself perfectly to our culture and makes Malta the ideal venue for such a meeting. These friends are international leaders, and aspiring leaders in the pharmacy world from academia and other fields of practice, who have recognised the importance of drawing on various non-traditional disciplines to strengthen the profession of pharmacy thereby enhancing patient care. The focus of this meeting is the patient's wellbeing, which necessitates the pharmacist possessing an excellent knowledge in the traditional subjects forming pharmacy's core knowledge base coupled with knowledge from humanistic and social sciences. The strength of this conference lies in the quality of work presented, its multidisciplinary approach and the eagerness of participants to share knowledge. While the formal part of the conference provides the backbone of the workshop, it is in the informal-social part that new ideas start to form, new research projects start to take shape and international pharmacy agendas are influenced. We therefore eagerly look forward to hosting this conference, welcoming our foreign friends and having Maltese participants share this experience.

Our imminent membership of the European Union will influence the profession of pharmacy in a number of ways. An article in a previous edition of the Chronic*ill presented an overview

THE chronic✶ill
Issue 7 Summer 2003

The Official Publication of the Malta College of Pharmacy Practice
c/o Department of Pharmacy, University of Malta, Msida
Tel: (356) 2340 2899
(356) 2134 3764
Fax: (356) 2134 0427

of various relevant issues. The focus in this publication is on consumer medicines information, an area which definitely needs attention in our country. The article by Professor Theo Raynor, who is also very active within the social pharmacy group, provides a highly informative international perspective on consumer medicines information. A significant portion of the article is dedicated to work, that was conducted by his team of researchers in the UK. This work clearly shows that although EU legislation intended to provide consumers with information about their medicines in a clear comprehensive manner, in many cases the leaflets produced fall short of this aim. Professor Raynor's work could well serve as an eye opener to local authorities that would be responsible for adopting and enforcing EU legislation regarding pharmacy in Malta. Professor Raynor and colleagues will be holding a workshop in Malta entitled 'Expressing the risk of side effects to patients-How to get the message across,' during the International Social Pharmacy Workshop next summer.

The other articles in this issue by our local contributors are highly relevant to our practitioners. On a very topical note, Dr Janet Mifsud, who incidentally was the first Maltese pharmacist to participate in the Social Pharmacy Workshops held in the UK in 1992, provides us with practical updated information regarding the use of drugs in sports. From the clinical aspect, Ms Antonella Tonna concludes her series on the management of Diabetes Mellitus, with an overview of insulin use. I would like to take this opportunity to support the sterling work conducted by Ms Tonna and her young and enthusiastic clinical pharmacy team. The need for clinical pharmacists to become integral members of the patient care team is indeed a very real one. The regular presence of clinical pharmacists on our wards would not only contribute to the optimal therapeutic management of patients but would lead to a significant decrease in drug related morbidity and mortality. The provision of a regular clinical pharmacy service would provide Maltese patients with additional safeguards to their health and definitely lead to an improvement in their quality of life.

Finally, I would like to thank the editorial board, the members of the council of the Malta College of Pharmacy Practice and our sponsors for their support. I would like to conclude by encouraging Maltese healthcare professionals to participate, experience and enjoy The 13th International Social Pharmacy Workshop in July 2004.

Maria Cordina
Editor-in-chief

Consumer Medicines Information

An International Perspective

DK Theo Raynor BPharm, MRPharmS, DipEd, CertMan

Professor of Pharmacy Practice, Medicines and their Users, University of Leeds, UK

Email: D.K.Raynor@leeds.ac.uk

Keywords: medicines information, consumers, knowledge

Consumer medicines information is increasingly relied upon to inform and empower consumers regarding their medicines. Legislation and guidelines are now in operation in the US, European Union (EU) countries and Australasia. The lack of an evidence base has led to a variety of approaches to written information provision across the three continents and each has apparent advantages and disadvantages. This review compares consumer medicines information in the three continents and examines the strengths and weaknesses of each system. It also includes an outline of research conducted by Professor Raynor's team on the impact of the EU legislation. This will be of particular interest in Malta, in view of the imminent membership of the EU.

Introduction

Medicines information leaflets are the bedrock of methods used to inform people about their medicines.[1] Previously the focus was on assisting people to take or use their medicines correctly. The focus is now much wider, as it becomes accepted that people need to become more involved in decisions about the medicines that they take. Such patient empowerment is at the heart of a number of policy moves in the countries of the developed world e.g. in the UK.[2] The notion is that people not only have a right to full information about their medicines (to allow them to make informed decisions about how and when they take them), but that adherence with medication will be enhanced if people take part in such decisions about their care and treatments.[3]

There is a relatively small evidence base to inform how written medicines information should be written, designed and delivered.[4] This is unfortunate, and has meant that recent legislation, guidelines or targets in:

- Europe,
- US
- Australia & New Zealand

have had relatively limited underpinning evidence.

The lack of investment in research into consumer medicines information is in stark contrast to the amount of money spent on the discovery, development and testing of the drugs themselves. Paradoxically, the large amount spent on such developmental work is largely wasted if patients do not take their medicines as intended, as a result of the inadequacy of the information supplied.

The term Consumer Medicines Information (CMI) to describe the patient leaflet supplied with medicines was first coined in New Zealand and then adopted by Australia. This review begins with the story of CMI "down under", followed by the US and the Europe.

Australasia

In Australia, the Therapeutic Goods Act requires that CMI is available with all new medicines.[5] It is written by the manufacturer, and the content needs to be consistent with the Product Information (PI) and understandable to the patient. However, there is no strict requirement that every piece of information in the PI must be on the leaflet. Despite this, some laser-printed leaflets run to four or five pages. All existing medicines are required to have such a leaflet available by 2003. The legislation requires that CMI is available for all prescription medications, but there is no legal requirement to provide a CMI with every supply. Australia adopted a collaborative approach to the development of CMI, with a Steering Committee, a Quality Assurance Reference Group (QUARG) and consistency working groups, which developed core CMI's for the major drug groups. The Australian legislation makes an explicit requirement that the written information should be complemented with verbal information.[6]

Evidence-based guidelines on writing leaflets were produced by the Communications Research Institute of Australia[7] and the favoured method of delivery is computer generation in the pharmacy (although package inserts meet the legislative requirements and are still widely used). Computer-generation is the preferred option because it enables the leaflets to be kept up-to-date. There have been a number of problems in Australia relating to computer generation in the pharmacy, due to the cost of buying the printers and supplying the paper. However, community pharmacists have been receiving remuneration for the delivery of CMI from the end of 2002.

New Zealand is working closely with Australia on CMI. The leaflets are not mandatory in New Zealand and there is a system of self-assessment by manufacturers that they need government guidelines. Again, the computer-generated option is preferred. The content of New Zealand leaflets are available on www.medsafe.govt.nz/CMIPage.htm.[8]

United States

In the United States in the mid 1970's there was consumer and professional pressure for legislation which would require package insert leaflets for patients. The commercial sector and some doctors objected and, as a result, a voluntary system was introduced.[9] These voluntary initiatives involved leaflets written and produced by third parties, such as:

- United States Pharmacopeia,
- American Medical Association
- American Society of Health System Pharmacists.

These are single page leaflets, with generally more brief information than contained in the European and Australian leaflets. The method of delivery most commonly used is through computer generation in the pharmacy.[10]

The US Government has set targets for the supply of "useful written information" to patients when they get their first supply of medicine. This was enshrined in Public Law 104-180 (1996), with a first target of 75% by 2000 being achieved. The next target is 95% of patients by 2006.[11] In the US the Food and Drugs Administration states that written information is at the core of its efforts to inform patients. The same law defines "useful written information" as being

- scientifically accurate,
- non-promotional,
- specific and comprehensive and
- understandable and legible

As a result of the legislation, a steering committee was convened in 1996, to facilitate the development of an "action plan" for evaluating and improving the usefulness of written information. The action plan identified the types of information to be included, to meet the criteria for being specific and comprehensive. It also provided general guidelines for evaluating the accuracy, legibility and comprehensibility of written information.[11] An eight-state study in 1999 subsequently evaluated the written information provided by community pharmacies. This found that 87% of new prescriptions had some written information provided (other than the labels or stickers). Most were accurate and unbiased and met a threshold set for information quality. However, certain categories of information fell below the threshold and as a result the authors concluded that the quality was variable and there were many areas for improvement.[12] In 2001 a further study of written information provided in community pharmacies was undertaken.[13] A paper by the same authors used an instrument based on these criteria to assess US leaflets by consumer evaluation of a small subset of leaflets.[14]

One exception to the voluntary code in the United States is covered by recent legislation for medicines which the FDA considers "pose serious and public health concerns".[15] These medication guides (or Medguides) have to be produced by the manufacturer and supplied with every prescription. They can be supplied as hard copy or computer generated and the order and headings of the leaflet are prescribed.

European Union

In the European Union legislation was introduced in the 1990's requiring a comprehensive medicines information leaflet for patients, to be supplied inside the pack of every medicine (EC Directive 92/27).[16] This legislation came into effect on January 1st 1999 across all member states. Subsequently, a Guideline on the readability of the leaflets was published.[17] The leaflets defined by this legislation have to be written and supplied by the manufacturer, according to the detail of the legislation. A key point is that all information in the Summary of Product Characteristics (the PI in the United States) needs to be provided, but in a form comprehensible to the patient. This means that all warnings, precautions and contra-indications have to be included.

Before the EU legislation, package insert leaflets were available in certain European countries, notably in the Netherlands, France and Germany. The content and distribution method of these leaflets varied.[18] In the United Kingdom, before the mid-1980's, few

leaflets were supplied with medicines. Then the pharmaceutical industry sponsored guidelines, based on a two-sided A5 leaflet, which contained brief information on one side and more detailed information on the other. These were based on research carried out by Professor Charles George and colleagues in Southampton.[19] However, in the early 90's this country-based initiative was stalled by the publication of European Union legislation. Current UK leaflets can be viewed on www.emc.vhn.net .[20]

What are the implications of the EU legislation?

The combination of the large amount of information to be included in the leaflets, and the delivery method as a package insert, results in a small, thin and folded leaflet that contains a large amount of information in small type. Research in the UK showed that this method of provision means that the leaflet is perceived by patients to be unimportant,[21] as the leaflets fall out of a pack like they do with many other goods. It is also difficult to incorporate the leaflets into the wider information giving process.[22] When we telephoned people seven days after obtaining a medicine, 83% said they had noticed the leaflet and 74% had kept it. However, only 40% said they had read some and 21% all the leaflet.[21]

In another study based on focus groups of people with asthma, we asked participants to talk about their experiences and views of medicines information. Key points included:

- appearance of the leaflet: "Too small, folded and in the box"
- Order of information: "Things we want to know don't come first"
- Some mistrust of manufacturer's leaflet, thought to be written to protect the manufacturer :"Priorities are those who wrote it, not patients"
- Leaflets can only give general information: "You throw them away don't you", "They don't inspire you", "Never been one for reading the leaflet all the way through"
- Just giving information is not enough: "We need to know 'why'"
- Personal experience was thought to be more important than drug company tests "The people using medicine are best people to know", "People who suffer should help write leaflets"

The EU Readability Guideline 16, issued in 1999 to complement the Directive, included sections on:

- Plain Language
- Good design
- Describing risk
- Testing the leaflets

Guidance on good design and the use of plain language for leaflets in English are on the website www.pecmi.org.[23] PECMI is 'Promoting Excellence in Consumer Medicines Information' a UK group of people with an interest in improving information for consumers around the supply of medicines in the UK, both prescription and self-medication.

In terms of describing risk, the Guideline suggests terms to describe risk as follows:

Very common	10%
Common	1-10%
Uncommon	0.1-1%
Rare	0.01-0.1%
Very rare	0.001%- 0.01%

However, our research in more than 1,000 members of public showed that use of these terms led to gross overestimation of the risk. For example, "Very common" is generally interpreted as being over 50% and "Common" more than 30%.[24,25] More research is needed to determine the best way of expressing the risk of side effects to patients.

An important part of the Guideline is the recommendation for adopting "User Testing" (also known as Consumer or Diagnostic testing to ensure the effectiveness of the leaflets. This process assesses if information in leaflet can be:

- found, and
- understood

Such performance-based testing is different from content testing; it is based on how the leaflet performs, not what it contains.

Typically, 20 consumers in a target group are questioned on 15 key points from the leaflet:

- Can they find information in the leaflet?
- Can they describe it in their own words?

The aim is for 16 out of 20 consumers to be able to do this. We carried out some pilot 'User Testing' on 3 leaflets, which confirmed that 16/20 is a very hard target to meet.[26]

What is the way forward?

It is inconceivable that multiply-folded small print package insert leaflets, with all their disadvantages, will continue to be the mainstay of written consumer medicines information provision in the 21st century. Information technologies will allow computer-generated leaflets to become the norm (as described above, they are already the favoured method in the US and Australia). Computer-generated leaflets can be:

- Generated at point of supply
- Handed to patient and used as aide memoire by the pharmacist
- Given only at first supply
- Updated as required
- Personalisation: include patient's name

In the future, individualisation of the information according to the patient's age, sex, sight loss, level of detail, language etc will become possible. The opportunities for web-based information extend the options still further. However, in the short to medium term, leaflets with medicines will continue to be the mainstay of information provided, and further research is needed to maximise the benefits for patients.

References

1 Raynor DK. The influence of written information on patient knowledge and adherence to treatment. In: Myers L, Midence K, editors. Adherence to treatment in medical conditions. London: Harwood Academic, 1998.

2 The NHS Plan. A plan for investment. A plan for reform. London: Stationary Office, 2000.

3 Marinker M. Writing prescriptions is easy. BMJ 1997;314:747.

4 Anon. Patient pack prescribing and the provision of patient information leaflets. Drug Ther Bull 1995;33:86-88.

5 Parker S. PILs downunder - lessons for the UK. In: Pharmacy Business & Practice. London, NPA, 2001.

6 Dowling H, Consumer product information; where to from here?. Aust. J. Hosp. Pharm. 1996; 13: 293-298.

7 Sless D, Wiseman R. Writing about medicines for people-usability guidelines for consumer medicine information. 2nd ed. Canberra: Australian Government Publishing Service, 1997.

8 NewZealand Medicine and Medical Sevices Safety Authority. Information for Consumers. Consumers Medicine Information available at http://www.medsafe.govt.nz/CMIPage.htm. Accessed June 28, 2003.

9 Nightingale SL. Written patient information on prescription drugs. Int. J. Technol. Assess Health Care 1995; 11: 399-409.

10 Rheinstein PH, McGinnis TJ, Nightingale SL. The patient information and education initiative. Fam. Physician 1995; 52: 2377-2382.

11 Steering committee for the collaborative development of a long-range action plan for the provision of useful prescription medicine information. Action plan for the provision of useful prescription medicine information. Unpublished report submitted to the US Department of Health and Human Services, December 1996. http://www.fda.gov/cder/calendar/meetings/rx2000.

12 Svarstad BL, Bultman DC, Mount JK, Tabak ER. Evaluation of written prescription information provided by community pharmacist: a preliminary study in 8 states. J Am Pharm Assoc (in press).

13 Svarstad BL, Mount JK. Evaluation of written prescription information provided in community pharmacies,2001. Final report submitted to the US FDA.

14 Krass I, Svarstad BL, Bultman D. Using alternative methodologies for evaluating patient medication leaflets. Patient Education and Counseling 2002; 47: 29-35.

15 Anon. Requirements for FDA-approved patient information spelled out in final rule. Am J Health-Syst Pharm 1999;56:107-8.

16 Council Directive 92/27/EEC of 31 March 1992 on the labelling of medicinal products for human use and on package leaflets (OJ No. L 113 of 30.4.1992, p. 8).

17 European Commission, Directorate-General III. A guideline on the readability of the label and package leaflet of medicinal products for human use. Brussels: European Commission, 1998.

18 Dickinson D, Raynor DK, Duman M. Patient information leaflets for medicines: using consumer testing to determine the most effective design. Patient Education and Counseling 2001; 43: 147-159.

19 Gibbs S, Waters WE, George CF, Communicating information to patients about medicines. J. R. Soc. Med. 1990; 83: 292-297.

20 Datapharm Communications Ltd. Electronic Medicines Comperdium. Available aty http://www.emc.vkm.net Accessed June 28, 2003
21 Patient information leaflets: sick notes? London: Consumers Association, June 2000.

22 Raynor DK, Knapp P. Do patients see read & retain the new mandatory medicines information leaflets? Pharm J 2000;264:268-270.

23 Dumar M. PECMI. Promoting Exellence in Consumer Medicine Information. Available at http://www.pecmi.org. Accessed June 28, 2003.

24 Berry DC, Raynor DK, Knapp P, Bersellini E. Patients' understanding of risk associated with medication use. Drug Safety 2003; 26: 1-11.

25 Berry DC, Knapp P, Raynor DK. Provision of information about drug side effects to patients. Lancet 2002; 359: 853-4.

26 User testing for information leaflets - is it more than just a good idea? (Woodland M, Cloherty M, P Knapp, Raynor DK). HSR & Pharmacy Practice Conference, Leeds, April 2002 http://www.hsrpp.org.uk/abstracts/2002_02.shtml.

The Concept of Social Pharmacy

Sørensen EW* MSc(Pharm), **Mount JK+** PhD, RPh, **Christensen ST**** PhD(Pharm)

* **Associate professor, The Danish University of Pharmaceutical Sciences, Dept of Social Pharmacy, Copenhagen, Denmark**
Email: ews@dfk.dk

\+ **Associate professor, University of Wisconsin, Dept of Social and Administrative Pharmacy, Madison, USA**

** **Assistant research professor, The Danish University of Pharmaceutical Sciences, Dept of Social Pharmacy, Copenhagen, Denmark**

The 13th International Social Pharmacy Workshop will be held in Malta in July 2004. The Social Pharmacy Workshops are international conferences for research in social and behavioural pharmacy. Meetings are held every second year and participation has grown steadily since the first Workshop was held in Helsinki, Finland, in 1980. Following the successful 2002 conference in Sydney, Australia, the 2004 meeting in Malta will be the first one held in the Mediterranean area!

Introduction

But what is Social Pharmacy? In this article, we give a brief overview of this field. We identify key questions addressed in Social Pharmacy research and introduce its major theories, concepts, and research methods. Finally, we discuss the future of Social Pharmacy and how it relates to the future of Pharmacy in general.

What is Social Pharmacy?

Traditionally, chemistry, biochemistry, physics and physiology form Pharmacy's core knowledge base. Knowledge of medications and their effects is the basis of the pharmacists' professional expertise. Practising pharmacy, however, is carried out among human beings, the persons referred to as customers or patients or users. They, in turn, are connected with one another in families, organizations and health systems in countries and cultures around the world. Thus, when trying to explain, understand or change pharmacy practice, the natural sciences simply do not provide adequate tools or perspectives. They need to be supplemented with knowledge from the disciplines that deal with people and systems, i.e., the humanistic and social sciences. And this is where Social Pharmacy comes into the picture.

Within Social Pharmacy, the drug/medicine sector is studied from the social scientific and humanistic perspectives. Topics relevant to Social Pharmacy consist of all the social factors that influence medicine use, such as medicine- and health-related beliefs, attitudes, rules, relationships, and processes. One general area of research focus addresses social aspects of drugs themselves including: drug research and development, drug production, drug distribution, drug prescription, drug information and drug control. Examples of questions within this area are:

- How do laws influence development and approval of new drug products?
- What is the influence of a newly developed product on health and health economics?
- How is drug distribution carried out in countries that have different education and availability of pharmacists?
- How do pharmacists perceive and act upon their expanded roles in health care delivery?

The other general area of research in Social Pharmacy addresses user (or patient or customer) perceptions and use of drugs/medicines. Research questions in this area are as diverse as the patients and providers involved in medication use activities, for example:

- Why is the patient taking (or not taking) a medicine as it was prescribed?
- What kind(s) of drug information has the best effect on patient understanding and when should it be provided?
- How can a pharmacist most effectively identify a patient's drug-related problems/side effects?
- How can new pharmaceutical services for the patient/customer be implemented in health care?

Thus, Social Pharmacy can assist anyone who wants to use a scientific approach to describe, explain, understand, and/or change practice. As such, it offers benefits to researchers, policy-makers, and pharmacists as well as other health care providers.

The primary pursuit of Social Pharmacy research is to investigate questions and themes concerning pharmacy practice and medicine use. It is a hybrid field that uses theories and methods from numerous humanistic and social scientific disciplines in order to explore all aspects of pharmacy practice. Because of this interdisciplinary nature, it is necessary to be familiar with diverse disciplines and skilled in applying their methods of inquiry. Social Pharmacy regularly draws upon the disciplines of sociology, social psychology, psychology, political sciences, educational studies, communications, economics, history, and anthropology. It leans more heavily on psychology, social psychology, sociology, political science, and economics, especially as these relate to issues in public health and social politics.

Figure I shows the hierarchy of natural systems, the levels of organisation and the disciplines in the pharmaceutical education. This is the way[a] that we at the Danish University of Pharmaceutical Sciences explain the relationships between the

social pharmacy

exploring theoretical and cultural perspectives

13th international
social pharmacy workshop

19-23 july 2004
malta

Teachers Workshop

19th July

- Plenary session
- 3 concurrent workshops
- Debate dealing with the teaching of Social Pharmacy

Main Workshop

20-23th July

- International, multidisciplinary plenary speakers
- Workshops covering a very broad spectrum of topics
- Oral and poster presentations with opportunity for free communications
- Work in progress sessions for young researchers

social pharmacy
exploring
theoretical and cultural
perspectives
13th international
social pharmacy workshop
19-23 july 2004
malta

General information and conference details:

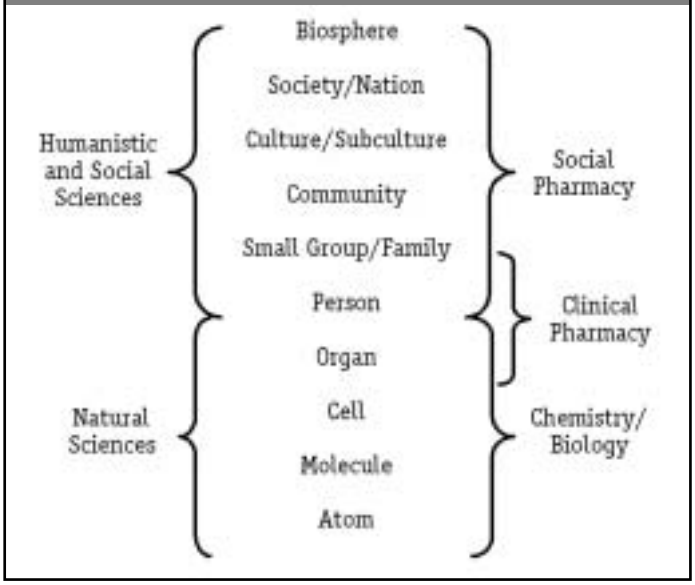
www.mcppnet.org

Malta College
of Pharmacy Practice

different pharmaceutical disciplines. This also illustrates how Clinical Pharmacy serves as a bridge that overlaps with and connects the natural sciences and Social Pharmacy.

Social Pharmacy has strong connections to Pharmacy Practice. In virtually all cases, books[b] addressing subjects, theories and methods of Social Pharmacy associate Social Pharmacy with the term, activities, and/or field of Pharmacy Practise. This is illustrated[c] by Wertheimer and Smith,[1] and Taylor and Harding.[5] In fact, in some countries, Social Pharmacy actually is incorporated under the more general term "pharmacy practice".[4]

Figure I: Levels of Organisation and the Disciplines involved in Pharmaceutical Education



Research in Social Pharmacy

Social Pharmacy/Pharmacy Practice Research is linked to the broad field known as health services research. This linkage emphasises that this is an applied field of research, concerned with both understanding and improving pharmacy practice and medication use. Why is research of this type so important? Increasingly, we recognise that pharmacy practice must be evidence-based and must make use of best practices. Thus, it is important that pharmacy practices be evaluated and that findings of such research be implemented. Much work is still needed in this area. Reviews such as those by De Young,[6] Schumock[7] and Singhal *et al*,[8] conclude that pharmacist consultation and pharmacy-based interventions have positive effects. Applying the strict criteria used to conduct a systematic review, however, Beney, Bero and Bond[9] concluded that more rigorous research is needed to document the effects of pharmacist interventions. Thus, it is important that pharmacist practitioners participate in collaborative Social Pharmacy research or undertake their own research and professional audits.

What topics require investigation?

The Pharmacy Practice and Research Group[10] recommended eight themes and topics for pharmacy practice research:

1. Supply, distribution and availability of services
2. Demand of services
3. Organisation and process of service delivery
4. Effectiveness and outcomes of services
5. Improving quality of services and quality assurance
6. Evaluations of policy and practise experiments and innovations
7. Interface between pharmaceutical and other health services
8. Payment and remuneration for services and pharmaceuticals

Addressing all these topics obviously is a major challenge, one that leads researchers into many different areas of investigation and application. How can such diverse studies be united with one another? By using theories developed in the humanistic and social sciences to guide Social Pharmacy investigations, we are able to develop a more general understanding of social factors that influence pharmacy practice and medicine use.

As a relatively new discipline, though, the theoretical bases of research in the area of Social Pharmacy and Pharmacy Practice still are in the process development.[11] The number and range of theories useful for research, however, are enormous and varied.[12] In the Social Pharmacy research community and at the Social Pharmacy Workshops, we recognize and try to improve upon this; theories are discussed, critiqued, and further integrated into current research. Reflecting the wide array of theories relevant to Social Pharmacy research, a series of articles by Bissell, Traulsen, and Haugbølle[13-15] is being published in the International Journal of Pharmacy Practice. Each article examines an area of sociological theory and its relation to pharmacy practice research. Approaches being examined include: functionalism, marxism, symbolic interactionism and ethno-methodology, feminism, post-modernism and post-structuralism, the work of Michel Foucault and the developing sociology of the body.

Methods

In Social Pharmacy, as in the social and humanistic sciences, there is no one single method of research but several, because the types of question that need to be answered differ. Research is classified into four types in relation to the core questions they can answer, the typical design and research method(s) used, and the different quality criteria for each type.[16] This is shown in Table I.

Research methodology in Social Pharmacy/pharmacy practice is described in by Taylor *et al*[5] and Smith.[17]

Further information about research in Social Pharmacy, may be sought from the following sources:

International journals:

- Journal of Social and Administrative Pharmacy
- International Journal of Pharmacy Practice

Books about Social Pharmacy/Pharmacy Practice:

- Taylor K, Harding G (2001) Pharmacy Practice. London: Taylor and Francis.

National or international conferences:

- International Social Pharmacy Workshop
- Pharmaceutical Care Network Europe (PCNE)
- European Society of Clinical pharmacy (ESCP)

---

a) A similar model is described by Mount in Wertheimer and Smith (1989).[1]

b) This section is based on the following sources: Lilja, 1988;[2] Wertheimer and Smith, 1989;[1] Harding, Nettleton and Taylor 1990;[3] Harding, Nettleton and Taylor, 1994;[4] Taylor and Harding 2001.[5]

c) Language usage reflects social changes. For example, in their 1996 revised edition, Wertheimer and Smith revised the title to Social and Behavioral Aspects of Pharmaceutical Care and Harding and colleagues used the terms Sociology and Social Pharmacy in their earlier textbooks (Harding *et al* 1990; Harding *et al* 1994).[3,4]

- Health Services and Pharmacy Practice Research conferences
- FIP: The International Pharmaceutical Federation
- American Pharmacists Association
- American Society of Health-System Pharmacists

Conclusion: The Future

Social Pharmacy has come to stay, and there are reasons to believe that Social Pharmacy will play an even more crucial role in future pharmacy, i.e. drug engineering based on gene technology and nanotechnology and the increasing reliance on drugs in dealing with human ailments will pose and empower new challenges for pharmacists. The nature of modern and future drugs calls for interdisciplinary approaches in both research and practice in order to fully understand the associated complexity. In the future, health care systems will be stretched far as the "invading nature" of future drugs will have substantial impact on pharmacists' performance, health care policies and expenditures, as well as on the individual user whose life might be altered radically.

Social Pharmacy is the interdisciplinary discipline that enables the pharmacy profession to act, take part and take responsibility in drug matters at a societal level. Being a discipline developing very fast due to social demand, Social Pharmacy is likely to have a central position in the future curricula in Pharmacy Schools.

References

1. Wertheimer AI, Smith MC. Pharmacy Practice: Social and Behavioral Aspects. Philadelphia: Williams and Wilkins; 1989.
2. Lilja J. Theoretical Social Pharmacy: The Drug Sector From a Social Science Perspective. Kuopio: University of Kuopio, Department for Social Pharmacy; 1988.
3. Harding G, Nettleton S, Taylor K. Sociology for Pharmacists: An Introduction. London: Macmillan; 1990.
4. Harding G, Nettleton S, Taylor K. Social Pharmacy: Innovation and Development. London: The Pharmaceutical Press; 1994.
5. Taylor K, Harding G. Pharmacy Practice. London: Taylor and Francis; 2001.
6. De Young M. Research on the effects of pharmacist-patient communication in institutions and ambulatory care sites, 1969-1994, American Journal of Health-System Pharmacy 1996:53 (June 1):1277-91.
7. Schumock GT, Butler MG, Meek PD, et al. Evidence of the economic benefit of clinical pharmacy services: 1996-2000, Pharmacotherapy 2003:23(1):113-32.
8. Singhal PK, Raisch DW, Gupchup GV. The impact of pharmaceutical services in community and ambulatory care settings: Evidence and recommendations for future research, Annals of Pharmacotherapy 1999:33(Dec):1136-1355.
9. Beney, J. Bero, LA. Bond, C. Expanding the roles of outpatient pharmacists. [Systematic Review] Cochrane Effective Practice and Organisation of Care Group Cochrane Database of Systematic Reviews 2003:1.
10. Mays N. Health Services Research in Pharmacy: A Critical Personal Review. Manchester: University of Manchester, Pharmacy Practice Research Resource Centre 1994.
11. Nørgaard LS, Morgall JM, Bissell P. Arguments for theory-based pharmacy practice research. Int J Pharm Pract 2000:77-81.
12. Bissell P, Traulsen MJ, Haugbølle LS. (1) An introduction to sociology - and what it can do for pharmacy practice research. Int J Pharm Pract 2001:9:289-95.
13. Bissell P, Traulsen MJ, Haugbølle LS. (2) An introduction to functionalist sociology: Talcott Parsons' concept of the "sick role", Int J Pharm Pract 2002:10:60-8.
14. Bissell P, Traulsen MJ, Haugbølle LS. (3) How relevant is Marxist sociology for pharmacy practice research? Int J Pharm Pract 2002:10:127-40.
15. Bissell P, Traulsen MJ, Haugbølle LS. (4) The contribution of interactionist sociology to understand experience of health and illness. Int J Pharm Pract 2002:10:213-24.
16. Launsø L, Rieper O. Forskning om og med mennesker. Nyt Nordisk Forlag Arnold Busck, 2000.
17. Smith FJ. Pharmacy practice research methods. London: Pharmaceutical Press., 2002.

Table I: The Main Types of Research[14]

Research Type	Descriptive	Explanatory	Understanding	Action-oriented
Core Question	How is X distributed?	What X causes Y? What Y results from X?	What is X?	How do people involved develop the action on basis of the knowledge gained and communicated during the research process?
Typical Design	Survey	Experimental	Case study	• Action research • Formative evaluation
Dominating Method	Quantitative	Quantitative	Quantitative	Qualitative and quantitative
Quality Criteria	• Reliability • Validity • Precision • Generalisation	• Reliability • Validity • Precision • Generalisation • Prediction	• Validity • Wholeness • Looking-glass • Provocation • Enlargement of meaning	• Validity • Does learning occur? • What direction does change take? • What does change mean?

WHO Special Project for Pharmaceuticals in Newly Independent States (NIS) – Strategic approaches

Nina Saoutenkova

Manager, Special Project on Pharmaceuticals in NIS, Health Technology and Pharmaceuticals

Email: NIS@euro.who.int

The Special Project on Pharmaceuticals in the Newly Independent States (NIS), which includes all former USSR countries except the Baltic countries, was established within the WHO European Office (Copenhagen, Denmark) in 1993 to meet the specific needs of countries in transition from the soviet to the market-oriented economy.

Initiatives taken since 1994

The first phase of the Special Project consisted of fact finding missions to make a proper assessment of the situation. Based on these reports, key problem areas were highlighted and opportunities for successful change and assistance identified.

The second phase provided assistance to Caucasian and Central Asian Republics and at a later stage, to the Russian Federation in a number of key areas, namely:

- national drug policies
- legislation and regulation
- establishment of drug agencies
- quality control
- management of a market oriented supply system
- essential drugs concept
- rational drug use
- education.

Priorities per country differed, depending on the capacities of available counterparts.

The third phase –The Patient in Focus

In the third phase, starting in 1998, the work in countries changed in line with the conclusions of the strategy paper ***The Patient in Focus.*** Deteriorating health status, diminishing budgets and increased poverty levels asked for a larger emphasis on creating sustainable development in a number of areas as illustrated in Table 1.

The WHO Special Project for NIS offers a coherent and well targeted pharmaceuticals programme that is problem oriented, interactive and multidisciplinary, in addressing these huge challenges.

Table 1
The Patient In Focus-Priority Areas

- Access to essential drugs (increase affordability, decrease patient payments)
- Substantial improvements of drug management in hospitals,
- New methods of financing and reimbursement (especially for the poor)
- Evidence based drug selection and use
- Revision of medical and pharmacy education and training.

Major achievements

Within the first five years of its inception, The Special Project for Pharmaceuticals in NIS can boast of number of major achievements:

- The setting up of drug laws and regulatory agencies working in 11 NIS
- National drug policies adopted in 9 NIS
- Essential drugs available in the private sector,
- Improved public-private collaboration,
- Better qualified and skilled sector management capacity
- Improved information on essential drugs
- Tools for appropriate drug treatment
- Changes in drug financing methods initiated in 9 NIS.

A special NIS inter-country project component enabled all NIS to participate and benefit from WHO assistance and learn from experiences in the other countries. Networking, co-operation and problem solving capacity clearly improved.

The future

Over the past five years the Special Project has worked in line with the ***Patient in Focus*** strategy. This has resulted in successful capacity building in different priority areas in separate NIS as well on a Regional and NIS level.

From the first transitional period in which NIS have developed their own pharmaceutical sector systems and infrastructure, the reform process is now moving to an intensified collaboration and networking in several areas. Countries have now gained their own experiences and are becoming more interested and involved in regional collaboration, sharing experiences and information about each-others achievements.

The Special Project approach can now be described as an equal partnership between WHO and NIS countries, where the capacity which has been built in each country is shared within the NIS.

Project on the Reform and development of pharmaceutical Education in Central Asian Republics: Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan

It is recognized that fundamental changes in the education system are necessary as a result of the shift in the pharmaceutical market from supply-oriented to needs-driven. This demands redefinition of healthcare professionals, their tasks and function in the future healthcare and drug supply system.

Since 1996, within the Special Project on Pharmaceuticals in NIS, there exists a Project on the Reform and Development of Pharmaceutical Education in Central Asian Republics (CAR). Changing of education has started within this project with the training and education of decision-makers and academics and the redefinition of curricula. Changes have been made in training curricula of physicians and pharmacists first of all in areas of drug selection and drug prescribing. Educators have been trained in problem-based pharmacotherapy teaching and have extended their experience to all educational institutions of the CAR region.

Close relationships among CAR countries and constant migration of population demands mutual recognition of diplomas at least within CAR Region. In spite of governmental agreements, the mutual recognition could not have been achieved without harmonization of curricula. This year, during the 7th meeting of the Network on the Reform and Development of Pharmaceutical Education, all participants have agreed to adopt a credit system in line with European standards. It will allow countries to achieve mutual recognition as well as to integrate international educational systems. One of the major resolutions of this meeting is the setting up of an institute for the advancement and harmonisation of pharmaceutical education in CAR countries. The Special Project is currently seeking funding for the setting up of this institute. The milestones achieved by the Project on the Reform and Development of Pharmaceutical Education in Central Asian Republics, qualify as yet another major accomplishment for the Special Project on Pharmaceuticals in NIS.

Funding and collaboration

The project has been able to achieve the above mentioned goals through funding by major donations from the United Kingdom-Know How Fund (UK KHF) now DFID, by the United States International Development Agency (USAID), and the European Union (ECHO). Other contributors are the German Government and the Government of Norway. The Special Project works in close collaboration with the World Bank, UNICEF and TACIS projects.

The Special Project on Pharmaceuticals in NIS looks forward to meeting the challenges ahead and to achieving further significant goals. In order to keep up this intensive work, the Special Project is continuously seeking financial support from organisations willing to make donations. This is the main means by which the Special Project on Pharmaceuticals in NIS can continue to support pharmacy in these countries and in so doing, enrich the international pharmacy community.

Paediatric Cancer in Malta

Dr Victor Calvagna MD, MRCP, MRCPCH

Consultant paediatric oncologist
President, Puttinu Cares Children's Cancer Support Group

The illness we call cancer has extraordinarily diverse features including its causation, underlying pathology, clinical symptoms, therapeutic response, and outcome or chance of cure. It is a collection of many disorders of cell and tissue function that have one special biological property in common - the territorial expansion of a mutant clone. Cancer develops as a chromosomal gene disorder in single cells. That cell or those cells with the right mutation or combination of mutations will form the winning clone that will acquire the ability to proliferate uncontrollably and spread locally and distantly in spite of the body's natural defence mechanisms against such rogue cells.

An overview

Around one in three of us will at some time have an unwelcomed diagnosis of cancer. In the developed world with the eradication of infection and malnutrition as major causes of mortality, cancer has largely by default, become more prominent as a life-threatening illness in children, although its frequency in the young remains very low. About 1% of all cancers diagnosed up to the age of 75 years occur in children and the incidence of the disease worldwide is 110 - 130 per million children per year. The relative risk for a child to get cancer up to the age of 15 years is 1 in 600. Compare this to the risk of 1 in 3 for an adult up to the age of 75.

The spectrum of the disease is different in children when compared to that in adults. Epithelial cancers or carcinomas like those found in the breast, lung, colon, prostate, cervix, uterus and skin are extremely rare in the paediatric age group. The most common cancers in children are the acute leukaemias and lymphomas, brain tumours, the various sarcomas and the embryonal tumours particular to children. These cancers are as a group more responsive to chemotherapy and radiotherapy than the epithelial cancers found in adults with the corresponding better survival and cures in the paediatric age group.

Nowadays with modern combination chemotherapy combined with modern surgical techniques and radiotherapy more than two thirds of children with cancer can be cured. In fact in the western world about 1 in every 1000 adults is a survivor of childhood cancer. This improvement in survival is also due to better supportive care, the treatment of children with cancer in specialised units and the ongoing national and international trials that try to answer questions about the disease and its treatment and which have inevitably resulted in better cure rates with the least harm.

The local scene

Cancer in Malta affects around ten children under the age of fourteen years every year. A third of these will have leukaemia and another third will have a brain tumour, the rest will have one of the sarcomas or embryonal tumours particular to the paediatric age group. The treatment of children with cancer in Malta has over the last ten years undergone some fundamental changes that have made our cure rates comparable to those of the rest of Europe and the treatment itself less hard for the family and child.

More than ten years ago the treatment of children with cancer used to be

The twelve major diagnostic groups of cancer in children are:

Leukaemia	39.8%
Lymphoma	11.3%
Brain and spinal	27.0%
Sympathetic	8.8%
Retinoblastoma	3.7%
Kidney	7.6%
Liver	1.2%
Bone	5.1%
Soft tissue sarcoma	7.7%
Gonadal and germ cell	3.7%
Epithelial	3.3%
Other	0.4%

undertaken, as used to happen in other more developed countries, by adult oncologists in conjunction with paediatricians. The treatment, although based on the best protocols available at the time, was usually carried out on a general paediatric ward by persons with little training and experience in the care and management of children with cancer. In many of the cases the patient had to be sent abroad for treatment in centres that specialised in the treatment of paediatric cancer. This, together with the diagnosis of cancer and the uncertainties of the child's future, brought a lot of hardship and anguish to the families concerned. The success of treatment does not depend only on the protocols and chemotherapy used but to a large extent on a multidisciplinary team that is specialised in the treatment of paediatric cancer working in a centre that has a modern diagnostic and therapeutic infrastructure.

Although we cannot be expected to provide all the care locally, especially the more specialised cancer treatment, because of the small number of cases involved, in most instances the treatment is carried out by local paediatricians and nurses trained in the care of children with cancer in a dedicated area away from the busy general paediatric wards. The advent of paediatric surgery, neurosurgery and modern radiotherapy techniques on the island together with modern laboratory and radiological diagnostic methods combined with efficient and state of the art blood transfusion and pharmacy departments has meant that most of the children with cancer can now receive all of their treatment on Wonderland Ward at St Luke's Hospital.

As already mentioned not all the children can have their entire treatment locally mainly because the speciality does not exist or the necessary supportive care is not available. One case in point is bone marrow transplantation or very high dose chemotherapy treatment requiring Peripheral Blood Progenitor Cell rescue. Others include specialised cancer surgery, especially in certain areas of the brain and abdomen, and certain specialised radiotherapy techniques. However in most cases the diagnostic workup and the conventional treatment essential and prior to such aggressive and specialised treatment is carried out locally, therefore minimising the hardships for the patient and his or her family.

One must also mention the valuable foreign contacts that have catalysed and made possible the present state of affairs. Our long and precious friendship with specialists from paediatric oncology centres in the Royal Marsden Hospital and Great Ormond Street Hospital have resulted in the various local specialists who are now working as a team in the field of paediatric oncology. The modern advances in information technology have made it possible to discuss difficult cases with foreign specialists in a short period of time to the benefit of our young patients.

What else?

Cancer does not occur in a vacuum but usually affects a child who up to a few months or weeks before was a healthy member of one of the various family units that nowadays are the norm in our society. The parent or parents will be working hard to raise and support the family and to give the best education and upbringing to the affected child and his or her siblings. The grandparents look at their children and their families with satisfaction and joy. All this collapses when cancer is diagnosed. The child is admitted to hospital for tests and treatment for periods ranging from a few days to weeks and sometimes months. One of the parents will have to take time off from work or resign from his or her job completely. The other siblings are quite frequently neglected because most of the attention is now focused on the affected child. There is a lot of anxiety and fear that shakes the whole family unit and permeates through the rest of the extended family. Feelings of guilt increase the tension within the family and past problems between family members resurface and threaten to break up the family. It is especially hard for single parent families and for low-income families. Life will never be the same for the parents and the rest of the family of the affected child. Sometimes treatment has to be given in a specialised centre abroad and, although the government pays for all the medical treatment, the financial burden on the family will still be substantial. When this is combined with the lack of close family ties in foreign countries the strain on these families will be tremendous. The child may miss out on school at a critical stage of his formative years.

It is for these reasons that the Puttinu Cares Children's Cancer Support Group was formed. It is composed of professionals working in the field of paediatric cancer, parents of children that have received treatment for the disease and persons who voluntarily lend their support and time to improve the plight of children with cancer. The aims of the support group are:

1. To advocate on behalf of affected children and families by representing their needs.
2. To campaign for the provision of a coordinated network of care and support.
3. To promote models of good care and practice.
4. To support families with a national information service.
5. To enhance the knowledge and skills of professional carers by providing specialist literature and education opportunities.

Since its setting up, towards the end of 2001, the support group has actively participated in the following projects:

1. The renovation of Wonderland Ward. This included the redecoration of the single rooms, new furniture, television and Playstation equipment, extra wall mounted beds for the parents and air-conditioning equipment.
2. A modern pantry where the parents can do most of their cooking if they wish too.
3. A new automatic washing machine and dryer.
4. A new playroom.
5. The support group is at present in the process of completing a classroom in

Wonderland Ward equipped with computers for the use of the children on the ward.

6. The group has also advocated for the children and their families who come from Gozo or need to go abroad for treatment so that the cost of travelling would be given at a special reduced price.
7. The group has also organised several recreational activities for the children and their families. These included Christmas and other parties, BBQs and boat trips.
8. Some of the children and their families have also benefited from leisure trips abroad free of charge or at special reduced prices.
9. The group has also obtained the services of social workers, psychologists and a spiritual counsellor to tackle some of the difficult social and emotional problems that the families present with.

The support group meets regularly, at least once a month, to plan new projects and assess the ongoing ones. Obviously none of this is possible without the generous help of sponsors like the HSBC, through its Help the Children Fund, and others that are too numerous to mention individually. In fact one of the group's main functions is to obtain funds and other resources from the various sponsors and most members of the group have at one point or another taken part in fund raising activities. The group also aims to create more awareness about cancer in children, not just the ugly side of the disease but also the fact that in most cases it is a curable illness. The support group also aims to remove the stigma of doom and death attached to the word cancer. It is true that cancer is a ruthless disease that is in most cases difficult to cure and may affect people in their most productive or formative years. However for the past twenty years or so, a lot of advances have been made in its treatment especially in the field of paediatric cancer. Consequently a number of members from the support group have appeared on the media to promote its activities, create more awareness about the disease and its treatment and most important of all to advocate for the patients and their families.

Puttinu Cares Children's Cancer Support Group contact details:

Dr Victor Calvagna
Email: victor.calvagna@gov.mt
Tel: 2125 5670

Ms Toots Birch
Email: pandtbirch@onvol.net

Ms Rennie Zerafa
Tel: 7980 9778

Drugs and the Athlete:
What is the price for winning at any cost?

Dr Janet Mifsud BPharm(Hons), PhD(QUB)

Senior Lecturer, Department of Clinical Pharmacology and Therapeutics, University of Malta, Msida, Malta MSD06
Member, Medical Sub Commissions, Malta Sports Council, Malta Football Association.
Email: janet.mifsud@um.edu.mt

Key words: Drug doping, athletes, sports medicine, anabolic steroids, ergogenic aids.

Man has always sought to go faster, higher, quicker and has embarked on all kinds of means in order to achieve these aims. The first use of performance enhancing compounds can be traced back to the ancient Olympic Games, but the first list of banned ergogenic aids was only issued in 1967. Yet athletes are still being found positive. They should be educated that these drugs are not only on the list because they are illegal means of achieving results, but all of them have side effects which can lead to severe short-term and long-term health problems for athletes. Drug doping in Maltese sports could become a major ethical, educational, financial, and health management problem. Community pharmacists have an important role to play in advising athletes, sportsmen and women about which drugs or OTCs can or cannot be taken during sports events.

Introduction

Man has always sought to go faster, higher, quicker and has embarked on all kinds of means in order to achieve these aims.[1] The first use of performance enhancing compounds can be traced back to the 300 BC, at the ancient Olympic Games, when mushroom and plant extracts were used. The first reported death associated with drug use by a sportsman is in 1866, when European cyclists took *'caffeine based sugar cubes dipped in nitroglycerin and vin mariani, a mixture of ground coca leaves and wine.'* The issue of drugs in sport was brought to public awareness after several events, including amphetamine use by US troops in World War II, widespread allegations of drug abuse at the 1964 Tokyo Olympics and the televised death of Tom Simpson in the 1967 Tour de France.[1]

In 1967, the International Olympic Committee (IOC) Medical Commission was formed, which published a banned list of performance enhancing drugs. As testing technology developed more drugs were added to the list of banned substances.[2] Yet still today, at each major event, athletes are still being tested positive and some athletes have even withdrawn from competition rather than risk being tested.[3] In the 1983 Pan American games, 19 athletes tested positive for anabolic steroids, while Ben Johnson made headline news following his disqualification in 1988 Olympics in Seoul for taking stanazolol[4].

Yet steroids are not the only culprits and several OTC preparations may also be guilty parties.[5] In the 2000 Summer Olympics, a Romanian female gymnast was stripped of her gold medal when tested positive for pseudoephedrine, from a Nurofen Cold and Flu® preparation, a medication prescribed by a physician for a common cold.[1] Even locally in this season, at least two

footballers playing with the Maltese football league, were found positive after taking anti-cold medication intended for their children, which they had no idea was prohibited.

Community pharmacists have an important role to play in advising athletes, sportsmen and women about which drugs or OTCs can or cannot be taken in sports events. It has become even more important with the publication of the recent Sports Law, which will open the way for a Legal Notice on drug doping in sports, making positive results a criminal offence.

What is drug doping in sports?

Doping is defined as *'the use of an artifice, whether substance or method, potentially dangerous to athletes' health and/or capable of enhancing their performances, the presence in the athlete's body of a substance, the ascertainment of the use of a method, as per the list annexed to World Anti-Doping Code'.*[2]

The List includes a whole range of drugs including:

- Therapeutic drugs used to treat legitimate illness or injury (prescribed or OTC)
- Social drugs of abuse
- Ergogenic drugs (licit and illicit)
- Drugs used to mask the presence of other drugs in urine

In fact, virtually all drugs in the banned list have legitimate therapeutic indications (table 1).

Prohibited doping methods include blood doping and pharmacological, chemical, and physical manipulation. These methods attempt to mask the use of the prohibited substances listed above. Blood doping is the administration of blood, red blood cells, artificial oxygen carriers (substances that substitute blood), and/or related red blood products to an athlete for athletic performance enhancement.[2]

There may also be pharmacological, chemical and physical manipulations, and attempts to alter the integrity and validity of samples used in drug testing. Examples of such methods include the use of diuretics, catheterisation, inhibition of renal excretion, sample substitution, and sample tampering.[3]

Table 1: Partial list of banned drugs according to WADA[2]

STIMULANTS
- amphetamines and derivatives
- cocaine
- ephedrine
- caffeine
- phenylephrine
- beta 2 agonists e.g. clenbuterol

DIURETICS
- spironolactone
- bumetanide
- frusemide
- amiloride

NARCOTIC ANALGESICS
- dextropropoxyphene
- methadone
- morphine
- pethidine

PEPTIDE HORMONES AND ANALOGUES
- HCG
- corticotrophin
- growth hormone
- erythropoetin

ANABOLIC STERIODS
- danazol
- methyltestosterone
- stanazolol
- oxymetholone
- nandrolone

BETA BLOCKERS
- atenolol
- labetolol
- nadolol
- propranolol

Misc & MASKING AGENTS
- epitestosterone (if urine conc of test:epitest > 6)
- probenecid

What are the main effects of drugs on athlete?

Athletes should be educated that these drugs are not only on the list because they are illegal means of achieving results, but all of them have side effects which can lead to severe short-term and long-term health problems for athletes.[5]

One common health problem has been defined as the *female triad*. This is the result of extended eating disorders combined with intensive training, consisting of disordered eating, amenorrhoea (cessation of menses for at least 3 to 6 months) and premature osteoporosis.[6]

Anabolic Steroids

Non-medical use of anabolic steroids is illegal and banned by most, if not all, major sports organisations. Still, some athletes persist in taking them, believing that these substances provide a competitive advantage. But beyond the issues of popularity or legality is the fact that anabolic steroids can cause serious physical and psychological side effects.[4]

Anabolic steroids - or more precisely, anabolic-androgenic steroids - are the synthetic derivatives of the naturally occurring male anabolic hormone testosterone. Both anabolic and androgenic have origins from the Greek anabolic, meaning "to build," and androgenic, meaning "masculinizing." Testosterone's natural androgenic effects trigger the maturing of the male reproductive system in puberty, including the growth of body hair and the deepening of the voice. The hormone's anabolic effect helps the

body retain dietary protein, which aids in the development of muscles.[8]

Steroids can be taken orally or they can be injected. Those that are injected are broken down into additional categories, those that are very long-lasting and those that last a shorter time. In recent years, use has shifted to the latter category - shorter-lasting, water soluble injections. These have a shorter half life, are excreted more quickly but these C-17-alkylated derivatives are more hepatotoxic. Most healthy males produce less than 10 milligrams of testosterone a day.[4] Females also produce testosterone but in minute amounts. Some athletes however, may use up to hundreds of milligrams a day, far exceeding the normally prescribed daily dose for legitimate medical purposes. Anabolic steroids do not improve agility, skill or cardiovascular capacity.[8]

Although anabolic steroids are derived from a male sex hormone, men who take them may actually experience a "feminisation" effect along with a decrease in normal male sexual function. Some possible effects include, reduced sperm count, impotence, development of breasts, shrinking of the testicles, and difficulty or pain while urinating.

On the other hand, women often experience a "masculinisation" effect from anabolic steroids, including facial hair growth, deepened voice, breast reduction and menstrual cycle changes.[6] Abuse of such steroids turned East German female swimmers into "lumbering beauties" in 1970s/1980s.[4]

Steroids have very severe side effects such as aggressive behaviour and rage, headache, acne, altered libido, euphoria and appetite, liver complications, hepatitis, hepatic tumours, non specific elevations in Liver Function Tests (LFT), irreversible viriluzation, hirutism, baldness, coarse voice, gonadotrophin suppression, glucose intolerance and altered thyroid and Low Density Lipopration (LDL), reports of Myocardial Infarction (MI), left ventricular hypertrophy, hypertension, teratogenic, uterine and breast atrophy.[4]

Recent evidence suggests that long-time steroid users and steroid abusers may experience the classic characteristics of addiction including cravings, difficulty in stopping steroid use and withdrawal symptoms. Adolescents may also experience premature closure of the growth centers of long bones, which may result in stunted growth.[7]

Beta-blockers

Beta-blockers that lower blood pressure are also on the banned list as they assist in keeping the hands of the athlete steadier when used in archery and pistol shooting. The side effects include bradycardia, heart failure peripheral vasoconstriction, bronchoconstriction (care in asthmatics), depression, lethargy and nightmares.[9]

Diuretics

Diuretics have important therapeutic indications for the elimination of excess fluid from body tissue in certain pathological conditions, which requires strict medical supervision. Diuretics are abused by athletes to reduce weight quickly in sports where weight categories are involved and to reduce the concentration of prohibited substances by diluting urine.[3] Reducing weight in a short period of time has the potential for serious health side effects. Also, using diuretics to deliberately cheat drug tests is ethically unacceptable. They cause dehydration and muscle cramps, dizziness, high potassium and calcium levels, low blood sugar levels, headache and nausea, vomiting and drowsiness.[8]

Anti-Asthma preparations

Highly trained athletes are repeatedly exposed to cold air and to many pollen allergens in spring, while competitive swimmers are exposed to chlorine derivatives from swimming pool disinfectants which may lead them to greater susceptibility to asthma. In the last Olympic Games, about 10% of athletes showed evidence of asthma or used antiasthmatic medication.[9] Antiasthmatic preparations e.g. salbutamol and terbutaline by aerosol or inhalent route are now permitted if the prescribing physician sends recent evidence of bronchial challenge tests just prior to the holding of the event to IOC. This new regulation is causing a great deal of controversy since many are claiming that such tests could be detrimental to their well being and physical fitness.[6]

Clenbuterol (Clenasma®), a beta-2-agonist used for chronic obstructive airways disease is on the banned list as it has a unique anabolic effect. In fact, it is used as a veterinary agent to increase lean weight in livestock and poultry.[9]

Stimulants

Stimulants such as amphetamine, caffeine, cocaine, and ephedrine, increase alertness and reduce fatigue. Stimulants alter cardiovascular cooling that may predispose athletes to heat exhaustion. They also may increase competitiveness, hostility, and the chance of injury from accidents caused by the user's poor judgment. Addiction is also possible with the use of stimulants. Caffeine, which is found in many energy drinks, sport gels, alcoholic beverages and diet aids, is considered illegal when present in urine at a concentration of greater than 12mg/L which is the equivalent of drinking around eight cups of coffee in a three hour period.[3] It does not improve maximal oxygen capacity

directly, but could permit the athlete to train at a greater power output and/or to train longer. It causes jitters, insomnia, and inability of focus.[10]

Blood doping

Blood doping is the administration of blood to raise the blood's oxygen carrying capacity, thus enhancing aerobic athletic performance. Athletes may use their own blood or someone else's blood. Erythopoetin increases oxygen absorption, reduces fatigue, and improves endurance by increasing the rate of red cell production. It can lead to increased thickening (blood viscosity) of the blood which may cause high blood pressive, stroke and heart failure.[6]

Hormones

Hormones, including human chorionic gonadotrophin (hCG) and corticotrophin, (ACTH, tetracosactide), are used in sports for a variety of effects. HCG and other related compounds lead to increased rate of production of endogenous androgenic steroids. Corticotrophin has been used to increase the blood levels of endogenous corticosteroids to obtain the euphoric effect of this hormone. The use of growth hormones can cause many serious side effects, including diabetes and Creutzfeldt-Jacob disease.[2]

Narcotic analgesics

Narcotic analgesics mainly function as painkillers but also may produce euphoria or psychological stimulation, false feelings of invincibility, and illusions of physical prowess. These drugs also increase the pain threshold, which can cause greater injury because an athlete may not be aware of the original injury. Use of narcotics can also lead to physical dependence.[3]

Food and other supplements

Vitamins and mineral supplements

Vitamins and mineral supplements provide no ergogenic benefits and athletes who have a well-balanced diet will not need additional vitamins.[1] Excess vitamin C may lead to the formation of kidney stones and vitamin B6 can induce liver and nerve damage. No physiological benefits have been proven with Pangamic acid or "vitamin B15". Low iron stores may be observed in female athletes and long distance "endurance" athletes.

Chromium has a role in insulin production and protein synthesis and strenuous exercise may lead to a deficiency. Coenzyme-Q is a vital component in energy production; aerobic power and exercise performance was improved after ingestion.[8]

Increased protein intake

Increasing protein intake is unlikely to result in additional increases in muscle tissue synthesis because there is a limit to the rate at which protein tissue can be accrued. Branched-chain amino acids may enhance endurance performance by delaying the onset of central nervous system fatigue. Glutamine is a non-essential amino acid which helps augment protein synthesis and prevents breakdown.[1]

Creatine

Creatine, which is found naturally in meat and fish, is the latest ergogenic aid. It causes an increase in body mass and is useful in team sports. It is not illegal but more research is needed to look at its long-term effects such as muscle cramping, nausea and seizures, serious kidney problems.[8]

Conclusion

Sports in Malta has recently been given a new dimension with physical education now being an official SEC subject and a new Minister for Sports. As athletic competition continues to intensify, even local athletes will strive for higher levels of performance to achieve success. Drug doping in Maltese sports could become a major ethical, educational, financial, and health management problem. This brief review of the major banned groups of drugs illustrates that while there may be some benefits to taking drugs for sport, they are often outweighed by the risks which can be permanent and fatal.[5] The pressures to win may, at times, be large enough to drive athletes to drugs, but is it worth it considering the humiliation they face if they are found out? The Maltese athletes, coaches, trainers and managers too should be educated and community pharmacists certainly have an important role to play in this respect.

References

1. Silver MD. Use of Ergogenic aids by athletes. J Am Acad Ortho Surg 2001; 9:61-70.
2. WADA, World Antidoping Agency Medical Commission. The World AntiDoping code, WADC E version 2.0, 2003. Available at: www.wada-ama.org. Accessed June 28, 2003.
3. Epstein S, Eliakim A. Drug Testing in Athletes. IMAJ 1999; 1: 79-82.
4. Kutscher EC, Lund BC, Perry PJ. Anabolic Steriods. Sports Medicine 2002; 32: 285-296.
5. Kanayama G, Gruber AJ, Pope HG Over the counter drug use in symnasiums: an unrecognized substance abuse problem. Psychother Psychosom 2001; 70:137-140.
6. Honours JW. Steroid abuse in female athletes. Current Op in Obs & Gyn 1997; 9:181-186.
7. Blue JG and Lombardo JA, Steroids and Steroid Like compounds. Clinics and Sports Medicine. 1999; 18:667-689.
8. Kennedy MC. Newer Drugs to enhance sporting performance. MJA 2000;173: 314-327.
9. Helenius I, Rytila P, Sarna S, Lumme A. Effect of continuing or finishing high-level sports on airway inflammation, bronchial hyperresponsiveness and asthma. J Allergy Clin Immunology 2002; 109:962-968.
10. Graham TE. Caffeine and Exercise. Sports Medicine, 2001;31:785-807.

The Psoriasis Association of Malta

Josette Camilleri B.Sc
Secretary Psoriasis Association of Malta

The Psoriasis Association of Malta was the brainchild of leading dermatologist Dr. Joe Pace. In January 1994 he invited many of his patients who had this condition, to get together to work out how the association was to function.

Since then we have met several times. Our meetings usually take the form of a talk by a qualified speaker followed by refreshments. Sometimes we have a question and answer session which many members look forward to. We have been helped in this respect by Dr. Joe Pace and Dr. Dino Vella Briffa several times. Patients always find it reassuring to have their queries answered by a qualified dermatologist. Being in a group seems to give them more courage to ask questions they would be afraid to ask otherwise.

Except in a few extreme cases, when it appears in conjunction with Psoriatic Arthritis, Psoriasis is more of a social and therefore psychological problem than a medical one. Even if the condition is mild, the patient feels uncomfortable when having to expose imperfect skin to others. Simple activities can sometimes turn into nightmares. Problems arise at hairdressers , dressmakers, when shopping for clothes, at the beach and especially round swimming pools. For this reason the association worked hard for the first few years to create an awareness of this condition with radio talks and television appearances of members of the committee.

Psychologically, meeting others who can understand what they're going through makes patients feel less isolated. That is why there is always time at meetings for members to discuss their problems and share their experiences.

Since Psoriasis is, to some extent, stress related, some of our meetings were focused on stress reducing techniques. One interesting session was on the benefits of Yoga exercises in this respect. Another highlighted the use of aromatherapy.

Another role of the association is to let members know when new products are available. Pharmaceutical companies approach us when something new appears on the market and they are then invited to give a presentation about their product to our members. The most recent one was held at the plush Hotel Intercontinental last February on the occasion of the European Academy of Dermatology and Venereology International Spring Symposium. Members were able to learn about the new preparations and were given samples to try out.

Anybody interested in obtaining more information about the Psoriasis Association of Malta may contact me on tel: 21317338.

Diabetes Mellitus: Insulin Use

Part 3

Antonella Tonna B.Pharm. (Hons), MSc (Aberdeen)

Senior Clinical Pharmacist
St. Luke's Hospital, G'Mangia

Email: antonellatonna@hotmail.com

Insulin is required for normal carbohydrate, protein and fat metabolism. Patients with Type I diabetes depend on exogenous insulin for their survival while Type II diabetics may require insulin at a later stage of their disease.

A history of insulin

The discovery of insulin in 1921 by Banting, Collip, MacLeod and Best was one of the medical breakthroughs of this century. These first insulins were of animal origin, excreted from the pancreata of cows and pigs. Addition of protamine and zinc allowed the development of longer acting insulins that were developed by 1951. By 1972, insulins were purer and this made them less immunogenic with a more reliable onset and duration of action. In the early 1980s, genetic engineering allowed the production of insulin identical to human insulin by bacteria and yeast.[1,2]

Indications for insulin therapy

All patients with Type I diabetes require replacement insulin therapy upon onset of the disease.[3,4] Most patients with Type II diabetes initially secrete enough insulin to be treated with diet, exercise and oral hypoglycaemic agents. However as the disease progresses, the secretory capacity falls making insulin treatment necessary. About 50% of patients require insulin due to beta-cell exhaustion. Other indications for insulin include pregnancy, ill health precluding oral treatment, during and after major surgery, any illness that may place the body in a stress situation, fasting blood glucose of more than 17mmol/l on diagnosis and diabetic ketoacidosis or hyperosmolar coma.[3,5,6]

The aims of treatment with insulin, are whether Type I or Type II diabetes mellitus are:

a) to achieve optimum metabolic control by mimicking production of endogenous insulin as closely as possible
b) to avoid experience and risks of hypoglycaemia.[4]

Types of insulin

Since insulin is a protein that is acted upon by the gastrointestinal enzymes, it must be administered parenterally. Insulins may be classified depending on their pharmacokinetic profile into three types - short, intermediate and long acting.

Regular insulin is a soluble, short-acting insulin and since it is the only one available in solution, it is the only insulin that may be administered intravenously.[6,7] Intermediate and long acting insulins are suspensions of insulin that have been modified to prolong absorption from the site of administration. This is achieved by producing insulin-protamine or insulin-zinc mixtures. Insulin zinc mixtures may be amorphous or crystalline, with the latter having a longer duration of action.[6,7] The insulins available within the Government Health Services (GHS) together with a comparison of their pharmacokinetic characteristics are summarised in Table 1. When applying data linked to pharmacokinetics, one must keep in mind that most data were obtained through assessment in healthy volunteers or in well-controlled diabetics under specific metabolic conditions. In actual fact, there is wide inter and intra subject variation in response to insulin.[8,9] Since many patients require a combination of intermediate or long acting insulin with short acting insulin, ready mixed insulin in the form of biphasic insulins are available.[6]

Fast acting analogues (insulin lispro, insulin aspart), have been developed in an attempt to mimic physiology more closely. Conventional soluble insulin forms hexamers when in solution. These need to dissociate before absorption and this delays the onset of action. The newer analogues are monomeric insulins and do not associate. These insulins start to act within 15 minutes of injection, peak at 50 minutes and have a duration of action of 3-5 hours, which more closely resembles human insulin. They are therefore administered immediately before a carbohydrate meal and this is likely to enhance patient compliance.[2,6,16]

All insulins available within the GHS are human in origin. The two forms of biosynthetic recombinant DNA insulins using Eschericia coli (Lilly) and Saccharomyces cerevisiae (Novo-Nordisk) are therapeutically equivalent.[17] One should also keep in mind that insulins from foreign countries may be of animal origin. It is important that there is no inadvertent exchange of insulins. When in doubt, human insulin should be used.[18]

All locally available insulins are of the 100 unit strength implying that they contain 100 units of insulin per millilitre (ml). Therefore care must be taken to instruct the patient about the correct dose in units and not in millilitres (mls) of insulin. One must also exercise caution when instructing tourists since different strengths of insulin may still be available internationally - 40 units/ml or 500 units/ml.[17]

Designing insulin regimens

There is no generally accepted approach to initiating insulin therapy and much depends on the preferences of the diabetologist. An empiric way of calculating the dose may be the following:[7]

A) Type I: Initial dose: 0.5-0.8U/kg
B) Type II: With ketosis, during illness: 1-1.5U/kg
C) Type II: Adolescents in growth phase: 1-1.5I/kg
D) Type II: With insulin resistance: 0.7-2.5U/kg

Different dosing regimens may be administered and these are tailored according to the patient's motivation, the ability to monitor control and adjust doses and the level of control desired.[17] Factors

that may alter the onset and duration of insulin action need to be considered. This includes the site of injection (absorption is fastest from the abdomen and slowest from the thigh), ambient temperature (heat increases the rate of absorption) and massage of the local area (increases rate of absorption).[7] Table 2 offers a comparison of possible insulin regimens.

Administration of insulin via a continuous subcutaneous infusion offers intensive glycaemic control but requires training, motivation and compliance together with supervision from an experienced healthcare team. Such a system provides a basal amount of insulin (0.5-1 unit/hour) and patient-activated pulsatile doses of insulin to cover meals. Pump therapy may increase patient flexibility but it is coupled by numerous problems such as mechanical failure and hypoglycaemic and dermatological complications. Besides, there is no evidence that this intensive insulin therapy offers better control than multiple dosing.[7] Patient selection criteria are therefore cardinal to ensure safety and success of treatment.

The sliding-scale method of insulin dosing is sometimes used in a hospital setting where insulin requirements may vary drastically over a short period of time due to stress, variable calorie intake or inactivity. Capillary blood glucose concentrations are measured every 4-6 hours and insulin administered accordingly as prescribed. Sliding scales vary from institution to institution and according to the patient response. One needs to ensure that the personnel involved are adequately trained in bedside blood glucose monitoring and that meters are properly maintained and calibrated. Strips should be kept in tightly sealed containers to prevent deterioration.[7]

A dosage regimen may involve combination of insulin with oral agents and this may be an option in Type II diabetics where glycaemic control is not adequate. Insulin is normally administered as a dose at night to suppress the hepatic glucose output.[5] The reader is referred to part 2 of this series for a more detailed discussion.[19]

Patients may present to the pharmacy with nausea and vomiting due to conditions such as viral gastritis. It is very important to advice the patient to maintain the same dose of insulin despite minimal food intake and advise the patient to seek specialist medical advice immediately. At no point should such a patient be advised to stop insulin since this may precipitate ketoacidosis.

Adverse effects associated with insulin therapy

Particular problems that one needs to look out for include:

- Hypoglycaemia may be a particular problem in drivers and other high risk occupations. Patients usually become aware of dysfunction when glucose levels fall below 3.5mmol/l. This may be avoided by individualising the dosage regimens, educating the patient and regularly reviewing drug regimens. Patients should be educated to avoid factors that may increase the risk or degree of hypoglycaemia such as missing meals, having smaller meals than usual, increasing alcohol intake or a sudden increase in physical exercise. They should also be instructed on management including the ready availability of oral glucose if still conscious and administration of glucagons by relatives or companions if unconscious.[4,6] Hypoglycaemic unawareness may be a problem in patients who have been on insulin for a long time or are on beta-blocker treatment. Such patients should be encouraged to monitor blood glucose frequently. Despite reports that this phenomenon is increased when changing from animal to human insulin, there is no evidence to support this.[4,7]
- Dermatological complications include lipoatrophy (more common in women), lipohypertrophy (more common in men) and local skin reactions. Rotation of injection site, use of human insulin and use of a pure form of insulin reduces such complications.[7,17]

Newer therapies

Research is currently underway to exploit different delivery routes for insulin. Inhaled insulin is an option where insulin is absorbed over the lung alveolar surface. However the bioavailability is only 10% making this an expensive alternative. Absorption is also very erratic with considerable variation between individuals.[2,21] The possibility of delivering insulin transdermally is also being researched.[22]

Table 1: Characteristics of insulins currently available within the Government Health Services [6,7]

Type	Brand name	Active Ingredient	Manufacturer	Onset (hr)	Peak (hr)	Duration (hr)	Appearance
Short Acting							
	Actrapid (10)	Soluble insulin	Novo Nordisk[1]	0.5-1	2-4	5-7	Clear
	Humulin R (11)	Soluble insulin	Lilly[2]	0.5-1	2-4	5-7	
Intermediate							
	Monotard (12)	Mixture of Zinc amorphous & crystalline particles ratio 3:7	Novo Nordisk	within 0.5	7-15	24	Cloudy
	Humulin N (11)	Crystalline suspension of human insulin with protamine and zinc	Lilly	within 0.5	4-12	24	Cloudy
	Insulatard (13)	Isophane insulin	Novo Nordisk	within 0.5	4-12	24	Cloudy
Long Acting							
	Ultratard (14)	Suspension of insulin zinc crystalline particles	Novo Nordisk	4	8-24	28	Cloudy
Biphasic							
	Mixtard 70/30 (15)	70% isophane 30% soluble	Novo Nordisk	within 0.5	2-8	24	Cloudy
	Humulin 70/30 (11)	As above	Lilly	within 0.5	2-8	24	Cloudy

[1] All Novo products - biosynthetic recombinant DNA origin produced in Saccharomyces cerevisiae

[2] All Lilly products - biosynthetic recombinant DNA origin produced in Escherichia coli

Table 2: Comparison of methods of insulin dosing [2,5,6,17]

Time of insulin administration	7am: before breakfast	11am: before lunch	6pm: before dinner	Comments
Single injection - Intermediate acting	Total dose			Least efficient to control glucose. Most likely to result in hyperglycaemia before dose, and hypoglycaemia at peak insulin effect. Should be reserved only for elderly patients.
Two daily injections of intermediate acting	2/3		1/3	Better than above. Assumes that 2/3 of calorie intake at breakfast and lunch.
Two doses of fixed biphasic insulin	2/3		1/3	Provides average control. Usually 70/30 mixture of intermediate/short acting used. Allows change in units but not ratio.
Two doses of biphasic insulin where ratios may be altered	2/3		1/6 short acting 1/6 intermediate	Provides above-average control. Allows change in both units and ratio of mixture of insulins used.
Split regular with long acting	1/5 short	1/5 short	1/5 short 2/5 intermediate or long	Provides excellent glucose control but requires patient motivation. Use one or two intermediate long acting doses to provide background levels and regular insulin doses before each meal.

The role of transplantation in Type I diabetes is an interesting feature with the first pancreatic transplantation being carried out in 1996. An overall one-year patient survival rate of 90% and graft survival rate of 82% has been reported. Selective Islets of Langerhans cell transplantation is another option that appears more attractive since it involves only a minor surgical procedure. The number of cells available would be larger than a whole pancreas.[2,5,7] Problems associated with transplantation include lack of pancreatic donors, the need for lifelong immunosuppression and the use of steroids in the post-transplant period. Transplantation is therefore limited to Type I diabetics only when conventional therapy significantly fails.

Though there have been numerous developments to produce newer insulins and alternative therapies that are more convenient for the patient to use, it appears that more progress is required to make optimal use of the insulins that are currently available.

References

1. Discovery of insulin.com website. www.discoveryofinsulin.com. Accessed on March, 3rd, 2003.
2. Amiel Stephanie. Is there anything new about insulin therapy? In: Amiel S, editor. Horizons in Medicine. Number 13. London. Royal College of Physicians; 2002.
3. Bahttacharyha A. Aetiology and Pathology of Type 2 Diabetes Mellitus. Hospital Pharmacy 2001: 8:5-9.
4. International Diabetes Federation on behalf of the St. Vincent Declaration initiative of IDF (Europe)/WHO. Consensus Guidelines for the Management of Insulin-Dependent (Type I) Diabetes. Available at: www.staff.ncl.ac.uk/philip.home/iddmch3.htm. Accessed on March, 3rd, 2003.
5. Bahttacharyha A. Treatment of Type 2 Diabetes Mellitus. Hospital Pharmacy 2001: 8: 10-17.
6. British Medical Association and Royal Pharmaceutical Society of Great Britain. British National Formulary. September 2002. Available at: www.bnf.org. Accessed on: March, 3rd, 2003.
7. Koda-Kimble Mary Anne, Carlisle Betsy A. Diabetes Mellitus. In: Young LY, Koda-Kimble MA. Applied Therapeutics: The clinical use of drugs. 6th edition. Vancouver. Applied Therapeutics. 1995.
8. Binder C. Insulin Pharmacokinetics. Diabetes Care. 1984; 7:188.
9. Zinman B. The physiologic replacement of insulin. An elusive goal. NEJM. 1989; 321:363-70.
10. Electronic Medicines Compendium for the Professional. Specific Product Characteristics. Actrapid. 2001. Available at: www.emc.vhn.net/professional. Accessed on: March, 12th, 2003.
11. Drug Information by RxList - Drugs and Medications. www.rxlist.com/cgi/generic/huminsr.htm. Accessed on March, 12th, 2003.
12. Electronic Medicines Compendium for the Professional. Specific Product Characteristics. Monotard. 2001 Available at: www.emc.vhn.net/professional. Accessed on: March, 12th, 2003.
13. Electronic Medicines Compendium for the Professional. Specific Product Characteristics. Insulatard. 2001. Available at: www.emc.vhn.net/professional. Accessed on: March, 12th, 2003.
14. Electronic Medicines Compendium for the Professional. Specific Product Characteristics. Ultratard. 2001. Available at: www.emc.vhn.net/professional. Accessed on: March, 12th, 2003.
15. Electronic Medicines Compendium for the Professional. Specific Product Characteristics. Mixtard 70/30. 2001. Available at: www.emc.vhn.net/professional. Accessed on March, 12th, 2003.
16. Campbell KR., Campbell LK, White JR. Insulin Lispro: its role in the treatment of diabetes mellitus. Annals of Pharmacotherapy. 1996; 30: 1263-1269.
17. White John R., Campbell KR. Diabetes Mellitus. In: Herfindal ET, Gourley DR. Textbook of Therapeutics: drug and disease management. 6th Edition. USA. Williams and Wilkins. 1996.
18. American Diabetes Association: Clinical Practice Recommendations. Insulin Administration. Diabetes Care. 2001; 24 (S1).
19. Tonna A. Management of Type II Diabetes Mellitus - Part 2. The Chronicill. 2002;6: 5-9.
20. Dixon N. Pharmacists as part of an extended diabetes team. PJ. 2002; 268: 469-470.
21. White JR, Campbell KR. Inhaled insulin: An overview. Clinical Diabetes 2001;19: 13-16.
22. Medicine in the making: Insulin via a skin patch? Health Horizons 1996; 27:18.

Dermal Fillers

The solution for lines, wrinkles, lip enhancement and facial contouring.

Alister Mallia BPharm (Hons)

Email: alistermallia@hotmail.com

Keywords: dermal fillers, tissue augmentation, hyaluronic acid, collagen replacement therapy, polymethylmethacrylate (PMMA) microspheres .

Tissue augmentation is a specialist area of bio-engineering which has been the subject of intrinsic research over the last twenty-five years, and represents a marriage of innovative pharmacology and chemical applications as diverse as reconstructive surgery, cosmetology, ophthalmic/ ENT and orthopaedics. In the field of cosmetic surgery, dermal filling is one of the most performed procedures. The earliest skin tissue expander or filler was autologous-fat which is today undergoing a revival, as extraction and injection methods improve.

The greatest research and successes, however, relate to connective tissue matrix material mainly collagen and hyaluronic acid, derived from non-human sources. Synthetic or semi-synthetic materials, notably polymethylmethacrylate (PMMA), gore-tex and, more debatably, silicone, also have a niche application. These latter products are marked by superior persistence and longevity in the body but carry attendant risks of complications, notably rejection, granuloma formation and scarring.

This article seeks to present a balanced review of the state of the art of some of the most commonly used fillers, namely, the two temporary fillers, namely bovine collagens and avian hyaluronic acid (HA), and the semi-synthetic semi-permanent filler PMMA - Collagen . The chemical properties, clinical applications and cautionary features of each product are described.

1 Hyaluronic acid (HA)

It is perhaps, the extradinary biocompatibility of the hyaluronan molecule that distinguishes it so markedly from other classes of materials used in soft tissue augmentation. Hyaluronan exhibits no species or tissue specificity because the chemical structure of this polysaccharide is the same throughout nature. This property has enormous benefits with respect to immunological compatability. Until recently, the most successful dermal soft tissue implants have been derived from bovine collagen whose use, because of species and tissue specificity, may be impeded by clinical reactions due to immunological incompatibility. The concept of using a hyaluronan derivative - hylan B gel (produced by a bis-ethyl-sulfonyl-crosslinking process that links every hyaluronic acid molecule into a continuous cross-linked polymer network such that the individual molecules are no longer freely soluble)[1] - for soft tissue augmentation was developed by Balazs and co-workers as a result of years of research. They established that insoluble, injectable, cross-linked hylan gels made from hyluronan exhibited a prolonged residence time in soft tissues and were as biocompatible as natural hyaluronan.

HA is injected into the dermal tissue to provide a space-occupying viscoelastic supplement for the intercellular matrix of the connective tissue. This viscosupplementation or augmentation of the dermal tissue can result in the correction of skin contour deficiencies caused by wrinkles and depressed scars.

Indications for using HA

- Nasolabial folds - the lines extending in an arc from the corners of the mouth to each outside edge of the nose.
- Oral commissures (Marionette Lines) - the lines extending down from the corners of the mouth to the jaw.

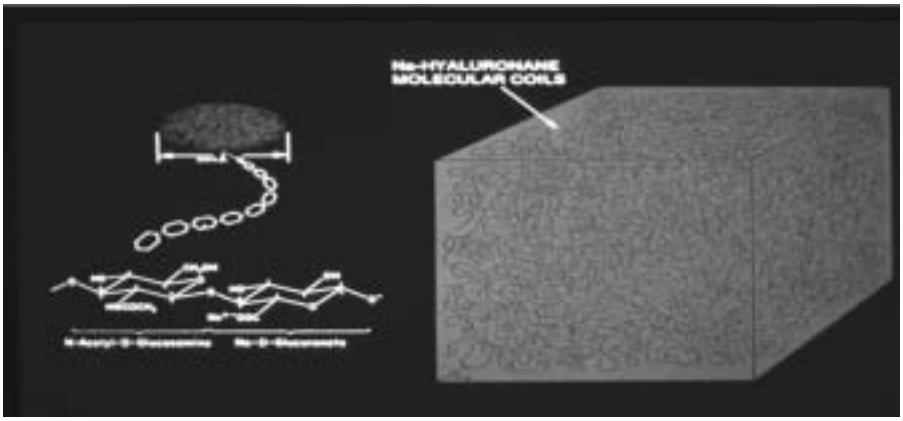


Figure 1: Hylan B gel Molecule (reproduced, with permission, from Piacquadio et al, 1998).[1]

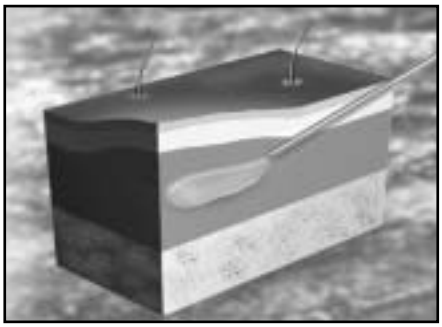


Figure 2: Tunnelling injection technique using HA (reproduced, with permission, from Piacquadio *et al*, 1998).[1]

Figure 3: Lip Augmentation using Hylan B (reproduced, with permission, from Balazs and Leshchiner, 1989).[3]

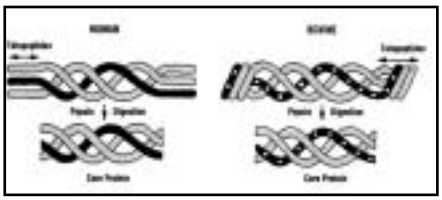


Figure 4: Similarity between human and bovine derivative (reproduced, with permission, from Balazs 1991).[5]

- Glabellar furrows (Frown Lines) - the vertical lines directly above the top of the nose and in between the eyebrows.
- Lip border - the border around the lips
- Peri-orbital - lines at the corner of the eyes
- Peri- oral - lines on the top of the upper lip.[2]

Depending on type of skin and lesion, best results are obtained in areas where these defects are readily distensible and where the correction can be visualised by manual manipulation (stretching) of the skin.

Injection procedure.

The patient has to sit upright for injection. Gravity will let the skin fall naturally so that the doctor can identify and treat the appropriate lines. The skin is stretched to provide a firm surface for injection. When injecting, the defect should not be over corrected; it should be raised to the desired level of correction. For fine wrinkles and scars it is best to place the filler in the papillary dermis. For deeper lines, the material is best placed in the reticular dermis. This can be followed by a more superficial injection into the papillary dermis to complete the treatment if needed.

For lip augmentation, the material should be injected into the apparent space between the body of the lip and the dermis of the upper lip (vermillon border) to create fuller lips (Figure 3).

Contraindications

Hylan B is contraindicated for breast augmentation, for implantation into bone, tendons, ligament or muscle. It must not be injected in patients with any acute or chronic skin disease in or near the intended area of correction.[4]

Cautions

Hylan B must not be injected into blood vessels. It may occlude the vessels, and could cause infarction or embolization.

2 Collagen

Collagen - which means glue in Greek - is a naturally occurring protein found in all mammals. It provides structural support for the bones, skin, tendons, ligaments, blood vessels, and almost every internal organ. Collagen has been used as a biomaterial in medicine and surgery for almost a century in sutures, haemostatic agents, wound dressing and heart valve replacement.

Structure And Chemical Composition

The strength and resilience of collagen is derived from the arrangement of the molecule, a rigid, triple-stranded helical structure, consisting of three polypeptide chains of 1000 amino acids wound around each other in a regular helical configuration. At both ends of the helical structure, there are short non-helical amino acid sequences known as telopeptides.

Bovine Collagen

Bovine collagen is derived from the hide of cows and is very similar in chemical composition to human collagen. The telopeptides are the regions of greatest chemical variability from species to species and consequently these sites are most likely to elicit an immune response when implanted in a foreign host. To reduce the risk of an immune response the telopeptides are removed from the bovine collagen using a protease enzyme, pepsin.

Collagen is licensed as a medical device to correct lines, wrinkles or scars. The practitioner injects small amounts of collagen directly into the dermis where the body's own collagen has been weakened by disease, trauma, atrophy, or age. The treatment restores the contour of the skin, minimising lines and wrinkles, and is often referred to as collagen replacement therapy.

Composition

Collagen is composed of highly purified sterile bovine collagen suspended in saline and 0.3% of the local anaesthetic lignocaine.

Collagen Replacement Therapy

As collagen is a naturally occurring product, it is metabolised over time. In 70% of patients the treatment has to be repeated every six to twelve months. However, 30% of patients maintain full correction for up to 12 months. For some patients this can be perceived as an advantage, as they do not have to commit to a surgical procedure that is permanent. Unlike surgery, the recovery time after collagen replacement therapy ranges from a few hours to a few days with minimal side-effects.[5]

Benefits of collagen

Collagen offers the following benefits:

- It is a simple and relatively painless procedure
- Results are almost immediate compared to other methods of skin rejuvenation and dermal correction techniques

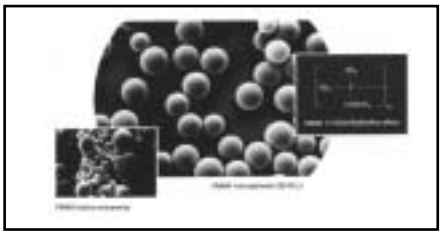


Figure 5: PMMA molecule (reproduced, with permission, from Klein, 1992).[7]

- It is associated with a low incidence of adverse reactions provided the recommended screening procedures are followed
- There is a high level of patient satisfaction with the aesthetic result

Indications for collagen replacement therapy

Collagen can be used to correct a range of facial deficiencies ranging from fine lines to deep scars and furrows. Collagen replacement therapy can also be used in combination with other treatments, such as topical retinoids, chemical peels and facial surgery and will produce excellent results.[6]

Hypersensitivity

Hypersensitivity is by far the most common adverse reaction to collagen replacement therapy, occurring in approximately three per cent of patients undergoing a test implant. A hypersensitivity reaction is characterised by erythematous, oedematous pruritic areas limited to the site of injection.[6]

Complications

These include:

- Cyst and abscess formation
- Necrosis
- Autoimmune diseases.

3 Homogenous non-biodegradable polymethylmethacrylate (PMMA) microspheres filler

Composition and mode of action

This filler is suspended in 3.5% bovine collagen and an average concentration of 0.3% lidocaine hydrochloride. The collagen serves as a vehicle for injection and is eventually degraded, leaving behind permanent implantation of the beads. All microspheres will be totally and evenly encapsulated by a fine fibrous capsule with minimal inflammatory reaction.[7] Since the PMMA microspheres are non-biodegradable, and too large to be phagocytosed or to migrate, the resulting tissue augmentation will be long lasting, if not permanent. Patients must be tested for allergy to bovine collagen prior to administration. Before using this filler, a skin test is optimally carried out 14 to 21 days prior to injection to determine the sensitivity for bovine collagen.

Injection Technique

The mixture is injected without overcorrection subdermally, that is, into the border of dermis to subcutaneous fat to treat deeper rhytids and scars. While injecting the needle should be drawn forwards and backwards (tunnelling technique) while maintaining constant pressure throughout the procedure, filling the channels thus created with the filler.[8] The injection pressure is correct if the implant flows slowly but evenly and without great exertion. The gray of the needle should never shine through the skin,

Contraindications and cautions

Contraindications to using this filler include sensitivity to bovine collagen, a history of keloids or atrophic skin diseases and patients with thin, flaccid skin because of the risk of permanent surface irregularities.[9]

The Future of Dermal Fillers

From the above, it would appear that the ideal dermal filler should:

- Be chemically and immunologically inert
- Have a space occupying effect lasting between 1-5 years, beyond which body contours are likely to alter as part of the aging process, so that the expander effect becomes less desirable
- Be easy to administer with minimal local tissue trauma

The industry is already perfecting its search for the above fillers and the most recent offerings are tissue expanders of human origin, either cadaveric or bio-engineered. Human collagen has recently obtained FDA approval and has entered clinical use this year.

References

1. Piacquadio DJ, Larsen NE, Denlinger JL and Balazs EA. Hylan B gel (Hylaform) as a soft tissue augmentation material. In: Klein AW, editor. Tissue augmentation in clinical practice: procedures and techniques. New York: Marcel Dekker, Inc.; 1998. p. 269-291.
2. Larsen NE, Pollak CT, Reiner K, Leshchiner E and Balazs EA. Hylan gel biomaterial: dermal and immunologic compatibility. J Biomed Mater Res 1993;27:1129-1134.
3. Balazs EA, Leshchiner EA. Hyaluronan, its crosslinked derivative - hylan - and their medical applications. In: Inagaki H, Phillips GO, editors. Cellulosics utilization: research and rewards in cellulosics. Proceedings of Nisshinbo International Conference in Cellulosics Utilization in the Near Future; 1989. New York: Elsevier Applied Science; 1989. p. 233-241.
4. Balazs EA. Matrix engineering with viscoregulation: why hylans are versatile tools. In: Price H, editor. The Biotechnology Report. London: Campden Publishing Ltd.; 1995. p. 81-82.
5. Balazs EA. Medical application of hyaluronan and its derivates. In: Gebelein CG, Cheng F, Yang V, editors. Cosmetic and pharmaceutical application of polymers. London. Plenum Press; 1991. p. 293-310.
6. Balazs EA, Leshchiner E, Larsen N, Band P. Hyaluronan biomaterials: medical applications. In: Wise DL, editor. Handbook of biomaterials and applications. New York: Marcel Dekker Inc.; 1995. p. 1693-1715.
7. Klein A. Injectable collagen gives good cosmetic results in soft-tissue augmentation. Cosmetic Dermatol 1992;5(7):42-3.
8. Keefe J, Wauk L, Chu S, DeLustro F. Clinical use of injectable bovine collagen: A decade of experience. Clin Materials 1992;9:155-62.
9. Lemperle G, Ott H, Charrier U, Hecker J, Lemperle M. PMMA microspheres for intradermal implantation: Part I, animal research. Annals of Plastic Surgery 1991;26:57.
10. Lemperle G, Hazan-Gauthier N, Lemperle M. PMMA microspheres (Artecoll) for lomg lasting correction of wrinkles: Part III, Refinements and statistical results. Aesthetic Plastic Surgery 1998;22:356.
11. Grubmeyer HH. The use of Artecoll (polymethylmethacrylate) for tissue augmentation in the face. 8th Congress of the European section of IPRAS; Lisbon, 1997.

Instructions to Contributors

1. Type of Manuscripts

The Chronic*ill publishes review articles in any field related to pharmacy. Manuscripts should not exceed 1500 words (approximately 5 double-spaced typewritten pages), excluding references. The total number of figures and tables should not exceed 4 and the number of references should not exceed 50. Authors are encouraged to consult with the Editor-in-Chief if they require an exception to these limits.

Manuscripts will be reviewed by at least two anonymous independent referees. Authors may suggest names of expert reviewers, but selection remains a prerogative of the Editors. Authors may include supplementary material to facilitate the review process. If a paper is cited in press and is required for evaluation of the submitted manuscript, authors should, upon request by the Editor-in-Chief, be able to provide three copies for use by the referees.

Manuscripts will be processed on the understanding that they have not been previously published in any language anywhere and are not under simultaneous consideration by another publisher. Authors are responsible for all statements in their work, including changes made by the copy editor after a manuscript is accepted.

2. Manuscript Submission

Manuscripts should be submitted in quadruplicate (original plus three copies), together with one copy on computer disk to:

The Editor-in-Chief
The Chronic✶ill
Department of Pharmacy
University of Malta
Msida MSD 06, Malta
Tel: (+356)2340 2899
Fax: (+356)2134 0427
Email: maria.cordina@um.edu.mt

together with a covering letter from the corresponding author.

The computer disk should either be a 3.5" diskette or a CD-ROM, and should be labelled with the following information: (a) word processor used, version number and whether Macintosh or PC edition, (b) name of disk file, (c) title of paper, and (d) name of corresponding author. The disk file must be the one from which the accompanying manuscript was printed. The Editor-in-Chief cannot accept a disk without its accompanying, matching hard-copy manuscript.

3. Copyright transfer and conflict of interest

A statement transferring copyright from the authors (or their employers, if they hold the copyright) to The Malta College of Pharmacy Practice will be required before the manuscript can be accepted for publication. The Editors will supply the necessary forms for this transfer.

Every author of each manuscript is responsible for disclosing any commercial or other association that might pose a conflict of interest related to the subject of the review. A statement to this effect is to be signed by each author on an appropriate form.

4. Permission for reproduction of tables and illustrations

The inclusion of any table or illustration, which has been directly reproduced from another source, should be accompanied by a letter from the original copyright owner, indicating that permission has been granted for publication of this item in The Chronic*ill. If the source comprises material which is still in press, unpublished data or personal communication, permission should be obtained from the main author. The reproduced material should be appropriately labelled 'reproduced with permission', and the relevant source cited. The responsibility of obtaining the relevant permissions remains with the authors of all work submitted to The Chronic*ill.

5. Organisation of Manuscript

The manuscript should be typed using 12pt font size and double-line spacing on one side only on A4 paper with 2.5cm margins all around. The manuscript should comprise, but not necessarily be limited to, the following sections: Abstract (not more than 100 words), Introduction, Discussion, Conclusion, Acknowledgements, Notation, References, Appendix, Tables, Figure-caption list, and Figures.

6. Title Page

The title page should include (a) the full title of the article, (b) the full name and surname of each author (including qualifications), (c) the affiliation of each author, and (d) a suggested running head. The affiliation should comprise the department, institution, city, and state (or country) and should be typed beneath the author's name. The suggested running head should be less than 50 characters (including spaces) and should comprise the article title or an abbreviated version thereof. For office purposes, the title page should include the name and full mailing address, telephone number, fax number, and email address (if available) of the author designated to review proofs.

7. Keywords

A list of 4-6 key words for indexing purposes is to be provided on the title page.

8. Abbreviations

Abbreviations should be used sparingly. A notation section, listing all nonstandard abbreviations used, should be provided on a separate page before the references section. The metric system is to be used for all measurements. Metric abbreviations should be expressed in lowercase letters without periods (cm, ml, sec). All symbols used in equations and formulae should be defined. When symbols are used extensively, a list of all symbols in the notation section should be included.

9. Acknowledgements

All acknowledgements (including those for financial support) should be typed in one paragraph on a separate page.

10. References

References should be typed double-spaced on a separate page and numbered consecutively in the order in which they are cited in the text. Citations in the text should be indicated by the appropriate Arabic numeral as superscript. References to unpublished personal communications should be avoided. Abbreviations for journal names should conform to those of the United States National Library of Medicine (available upon request). The style and punctuation of the references should conform to the Vancouver style outlined below (more details available on request).

Journal Article

1. Author's surname Author's first name or initial. Title of article. Title of the Journal Year of publication; Volume Number (Issue number): Page numbers of article.

1. Withrow R, Roberts L. The videodisc: Putting education on a silver platter. Electronic Learning 1987: 1(5):43-4.

Book

2. Author's surname Author's first name or initial. Title of the Book. Edition [if not first]. Place of publication: Publisher's name; Year of publication.

2. Groenewegen D. The Real Thing?: The Rock Music Industry and the Creation of Australian Images. Golden Square, Victoria: Moonlight Publishing; 1997.

Contribution to a Book

3. Author's surname Author's first name or initial. Title of chapter. In: Editor's surname Editor's first name or initial, editor. Title of the Book. Edition [if not first]. Place of publication: Publisher's name; Year of publication.

3. Blaxter P. Social health and class inequalities. In: Carter C, Peel J, editors. Equalities and Inequalities in Health. 2nd ed. London: Academic Press; 1976.

11. Tables

Tables should be numbered using Roman numerals and referred to by number in the text. Each table should be presented on a separate sheet, and should not exceed 120 characters per line, including spaces, with column delimiters being counted as 4 characters . The title should be centred above the table, and any explanatory text (indicated by superscript lowercase letters) should be typed below the table.

12. Illustrations

Illustrations (photographs, drawings, diagrams, and charts) should be numbered consecutively using Roman numerals in the order in which they are cited in the text. The captions for illustrations should be typed on a separate sheet of paper. Photographs should be glossy high contrast monochrome prints, and will be reduced to fit double column (12 cm) or triple column (18 cm) width. Drawings should be prepared using indian ink, or high quality laser printing. Either the original drawing or good-quality glossy photographic prints are acceptable. The artwork for each figure should be supplied on a separate sheet of paper. Identify illustrations on the back with author's name and number of the illustration marked lightly in pencil. Mark the top part of the figure with the word 'top,' unless obvious.

13. Footnotes

Footnotes should be avoided. When their use is absolutely necessary, footnotes should be numbered consecutively using Arabic numerals and should be typed at the bottom of the page to which they refer. Place a line above the footnote, so that it is set off from the text. Use the appropriate superscript numeral for citation in the text. ✶