Journal of the
CHAMBER of
PHARMACISTS
APRIL 1989 No. 20

EDUCATION AND TRAINING OF PHARMACISTS

CPA EUROPEAN REGION WORKSHOP

THE PHARMACIST

AUGMENTIN

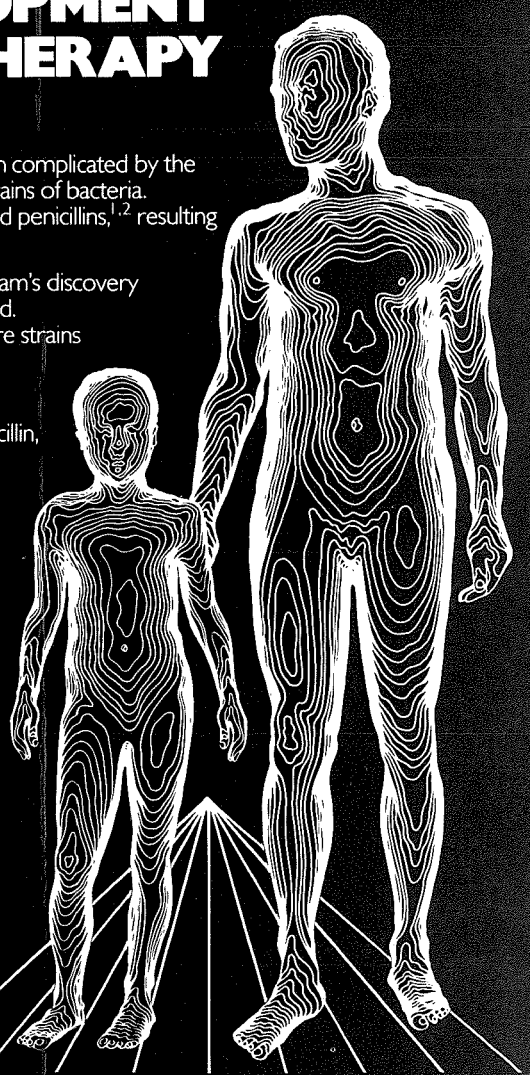
clavulanate-potentiated amoxycillin

A MAJOR DEVELOPMENT IN ANTIBIOTIC THERAPY

In recent years, the treatment of infection has been complicated by the increasing prevalence of ß-lactamase producing strains of bacteria. ß-lactamase destroys many oral cephalosporins and penicillins,[1,2] resulting in treatment failure.

AUGMENTIN is the first antibiotic to utilise Beecham's discovery of the powerful ß-lactamase inhibitor, clavulanic acid. This neutralises the bacterial defence, bringing more strains and species within the scope of oral therapy.

- **AUGMENTIN – Broader in spectrum** than oral cephalosporins, co-trimoxazole, ampicillin, tetracycline or erythromycin.
- **AUGMENTIN – Outstanding success** against today's infections.



Adult infections	No. of patients assessed	Clinically cured/ improved	Clinical success
Upper respiratory tract[3]	146	141	**97%**
Lower respiratory tract[3]	98	89	**91%**
Urinary tract[3]	175	167	**95%**
Skin & soft tissue[3,4]	81	75	**93%**

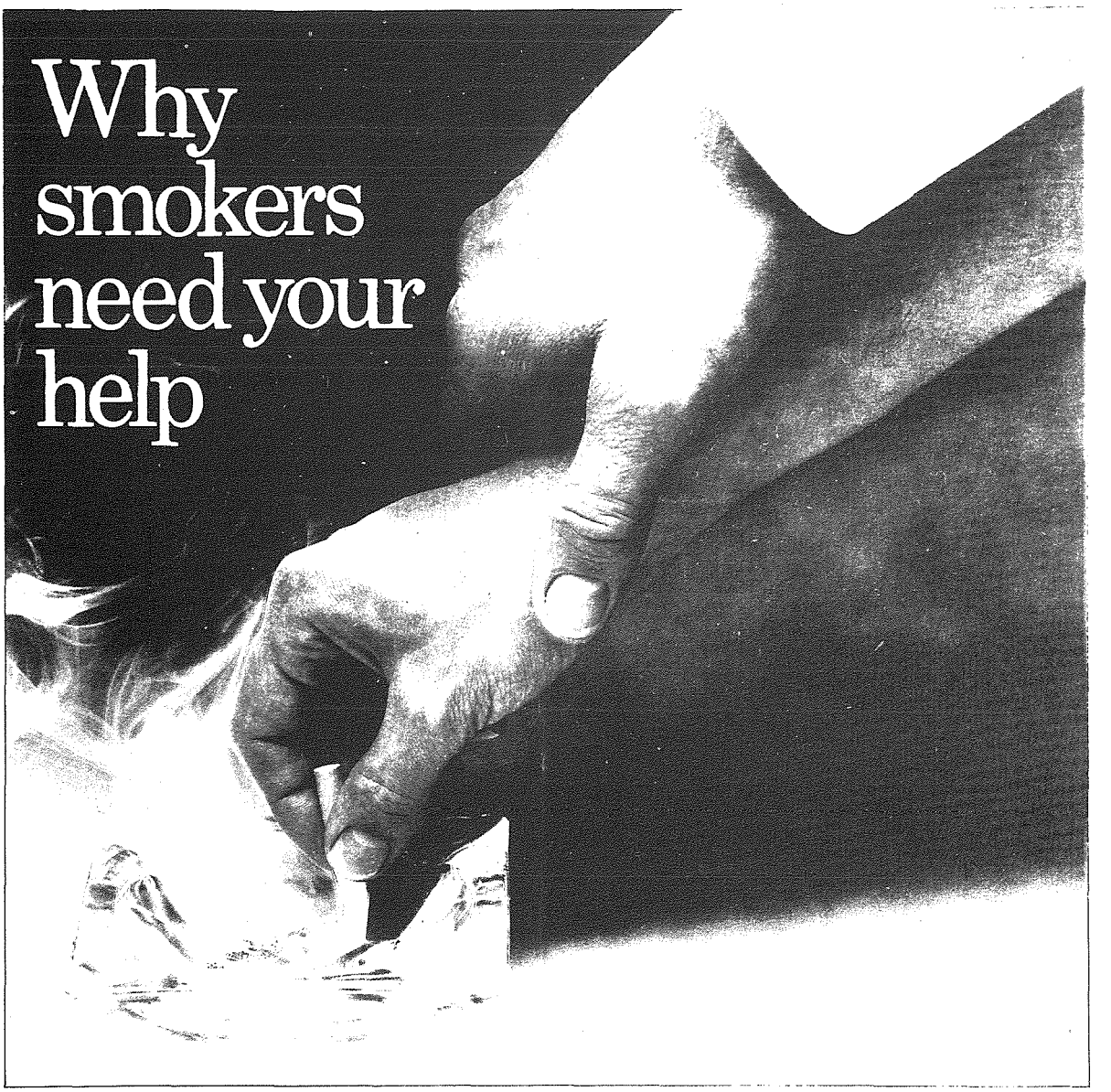
Paediatric infections	No. of patients assessed	Clinically cured/ improved	Clinical success
Upper respiratory tract[5,6]	70	70	**100%**
Lower respiratory tract[7]	28	27	**96%**
Urinary tract[6,7,8]	61	57	**93%**

PRESCRIBING INFORMATION

INDICATIONS: Chest, ear, nose, throat, genito-urinary, skin and soft tissue infections including those caused by ß-lactamase producing organisms. **DOSAGE: Adults and children over 12 years** one AUGMENTIN tablet (375mg) three times daily. **Children 7-12 years** 10ml AUGMENTIN syrup (312mg) three times daily. **Children 2-7 years** 5ml AUGMENTIN syrup (156mg) three times daily. **Children 9 months-2 years** 2.5ml AUGMENTIN syrup (78mg) three times daily. In severe infections these dosages may be doubled. Treatment should not be extended beyond 14 days without review. **CONTRA-INDICATION:** Penicillin hypersensitivity. **PRECAUTIONS:** Safety in human pregnancy is yet to be established. Oral dosage need not be reduced in patients with renal impairment unless dialysis is required. **SIDE-EFFECTS:** Uncommon, mainly mild and transitory, eg diarrhoea, indigestion, nausea, vomiting, candidiasis, urticarial and morbilliform rashes. If gastro-intestinal side-effects do occur they may be reduced by taking AUGMENTIN at the start of meals. **PRESENTATIONS:** 375mg AUGMENTIN tablets each containing 250mg amoxycillin (1) and 125mg clavulanic acid. (2) 156.25mg AUGMENTIN syrup. Powder for preparing fruit flavoured syrup. When dispensed each 5ml contains 125mg amoxycillin (1) and 31.25mg clavulanic acid. (2) Not all presentations are available in every country. (1) as the trihydrate, (2) as the potassium salt.

Further information is available from:
Beecham Research Laboratories
Brentford, Middlesex, England.
AUGMENTIN and the BRL logo are trademarks.

References 1. Proc. Int. Symp. on AUGMENTIN, Excerpta Med. (1980), **ICS 544**, 173. 2. Excerpta Med. (1980), **ICS 544**, 19. 3. Excerpta Med. (1980), **ICS 544**, 187. 4. Scot. Med. J., (1982), **27**, 335. 5. Proc. Europ. Symp. on AUGMENTIN, Excerpta Med. (1982), **CCP4**, 341. 6. Excerpta Med. (1982), **CCP4**, 347. 7. Excerpta Med. (1982), **CCP4**, 325. 8. Excerpta Med. (1982), **CCP4**, 334.



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Nicorette abbreviated prescribing information

Presentation: chewable nicotine resin complex containing 2mg or 4mg nicotine
Uses: an aid to smoking cessation.
Dosage and administration: Adults only over 15 years: each piece should be chewed for about 30 minutes, with a pause every few minutes. Maximum daily consumption is 15 pieces of 4mg Nicorette.
Contra-indications: pregnancy and breast feeding.
Adverse reactions: occasional hiccups, mild throat irritation, mild indigestion, heartburn.

1. SK&F data on file

SK&F
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Prescribing Information

AMOXIL is a broad spectrum antibiotic suitable for a wide range of infections caused by susceptible organisms.

Indications
Respiratory, ENT, genito-urinary and skin and soft tissue infections.

Dosage
Children: Oral and injectable – up to 2 years: 62.5mg-125mg every 8 hours. 2-10 years: 125mg-250mg every 8 hours. Based on bodyweight (including neonates) 35-100mg/kg/day. Adults: Oral – 250mg-500mg every 8 hours. Injectable – I.M. 250-500mg every 8 hours or more frequently if necessary. I.V. 500mg-2g every 4-6 hours. (Doses in excess of 1g should be given by infusion over 30 minutes).

Presentations
Capsules: maroon and gold capsules, each containing 250mg or 500mg amoxycillin.
Syrup: 125mg amoxycillin per 5ml in 60ml or 100ml bottles.
Syrup Forte: 250mg amoxycillin per 5ml in 60ml or 100ml bottles.
Paediatric drops: 125mg amoxycillin per 1.25ml in 10ml bottles with calibrated dropper.
Injection: Vials containing 250mg or 500mg amoxycillin.

Precautions
Reduced dosage is required in patients with impaired renal function.

Contra-indications
Penicillin hypersensitivity.

Side-effects
Side-effects, as with other penicillins, are usually of a mild and transitory nature; they may include diarrhoea, indigestion or an occasional rash, which may be either urticarial or erythematous. in either case it is advisable to discontinue treatment.

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A Division of Beecham Pharmaceuticals, Brentford, England.
Full information is available on request from the company.

THE PHARMACIST

JOURNAL OF THE CHAMBER OF PHARMACISTS — TRADE UNION

THE **PHARMACIST** is published by the Chamber of Pharmacists, 1, Wilga Street, Paceville. It is sent free to all Pharmacists and distributed to doctors. Others may subscribe at an annual subscription of Lm1.50 or obtain copies from Sapienza's Library, Valletta.

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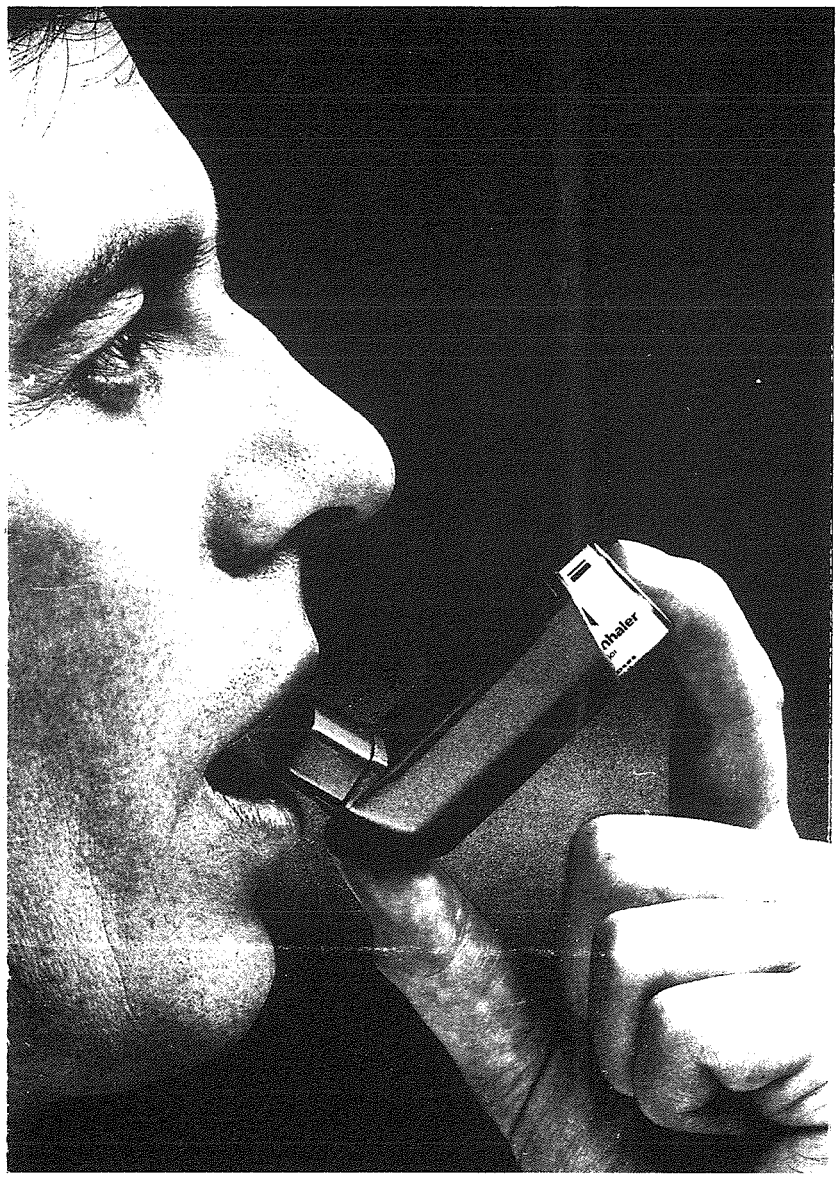
Cover

Front Cover was created on a Macintosh with Mac Paint by Charles Cassar and printed with the Apple Laser Writer.

Cover photos:

The participants at the CPA European Regional Workshop on Education and Training of Pharmacists held at the Royal Pharmaceutical Society of Great Britain on the 10th and 11th November 1988.



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EDITORIAL

Professional Service and Control in Community Pharmacy

The Pharmacist — the specialist on medicines — is the ideal person to ensure that medicines are used correctly. The development of medicines with increasingly potent and subtle effects, unexpected risks and often with a narrow therapeutic index, makes this even more essential.

The Government is committed to decentralize the distribution of medicines in the National Health Scheme. The patient will be able to obtain his medicines of proven quality, safety and efficacy from the community pharmacist of HIS choice.

This will create the right environment for a closer relationship between the pharmacist and the patient. The role of the pharmacist as a patient counsellor and educator will become even stronger, thus improving patient compliance.

The Chamber of Pharmacists has prepared a report entitled "The Distribution of National Health Service Medicines" (which is being printed in full as a supplement to this issue), in which the necessary changes to the current system of distribution of free medicines are being proposed.

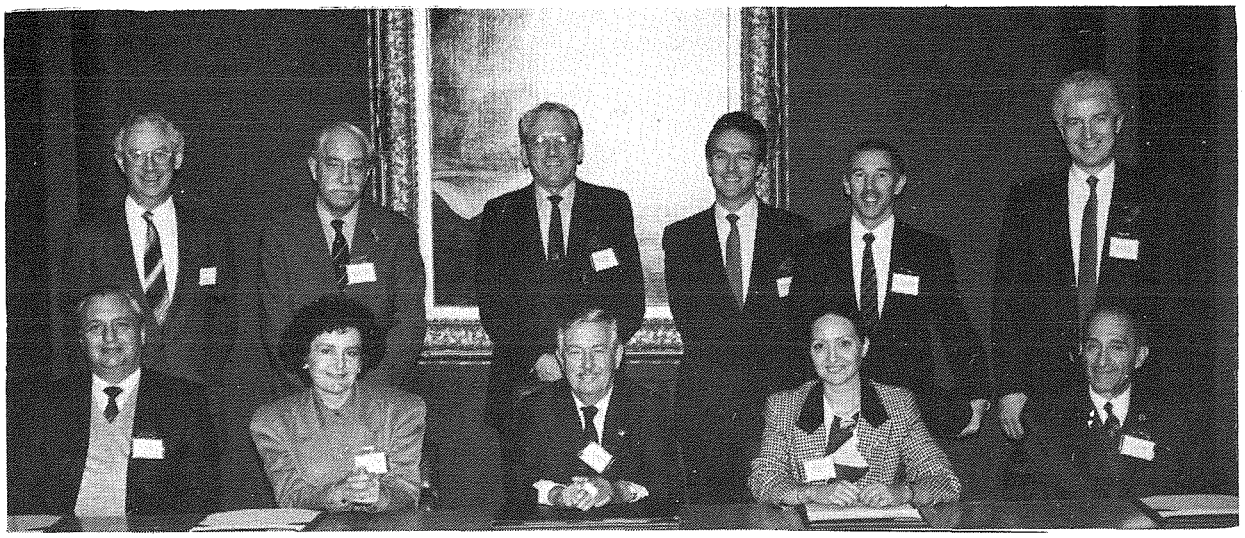
However these 'personalizing' changes which will be brought about through the decentralized way in which the distribution of medicines is envisaged will not materialize, unless *all* the community pharmacies are professionally run. Unfortunately, although the legislation regulating the proper running of pharmacies exists, the will to enforce it is lacking.

For this reason, the Chamber of Pharmacists has chosen to discuss "Professional Service and Control in Community Pharmacy" during the Congress being held on Sunday, 30th April 1989. The Congress is part of the Pharmacy Week which is being organised by the Chamber of Pharmacists on the occasion of the holding in Malta of the Executive Committee Meeting of the Commonwealth Pharmaceutical Association.

The Chamber of Pharmacists now awaits the recommendations of this seminar which will be published in full in a special edition dedicated to Pharmacy Week, and looks forward to the day when all community pharmacies will be providing an optimal service to the community. Anything less than this means that medicines are sold as ordinary items of commerce by unqualified persons without advice. This certainly is not the service that the community deserves!

EDUCATION AND TRAINING OF PHARMACISTS

CPA EUROPEAN REGION WORKSHOP



Present at the meeting were (standing from left): Mr. Raymond Dickinson, Secretary CPA; Professor Patrick D'Arcy, CPA council member (Northern Ireland); Professor T.G. Booth, Past President, Royal Pharmaceutical Society of Great Britain; Mr. Nicholas L. Wood, Chairman, Education Committee, Royal Pharmaceutical Society of Great Britain; Dr. Dean W.G. Harron, observer, Queen's University, Belfast; Mr. R. Clarke, Past President, Pharmaceutical Society of Northern Ireland; (sitting from left): Mr. Eric Zammit, CPA council member (Malta); Miss Mary Anne Ciappara, Secretary Chamber of Pharmacists (Malta); Professor Arnold H. Beckett, Vice President CPA; Mrs. Mary Ann Sant Fournier, President, Chamber of Pharmacists (Malta); Mr. C.M. Ioannidos, President, Pancyprien Pharmaceutical Association and CPA council member (Cyprus).

A delegation from the Chamber of Pharmacists led by the President, Mrs. Mary Ann Sant Fournier, B.Pharm., M.Phil., and including the Secretary, Ms. Mary Anne Ciappara, B.Pharm., and the CPA Council Member Mr. Eric Zammit, B.Pharm., has participated in the Commonwealth Pharmaceutical Association, European Region Workshop on Pharmacy Education and Training held in London on the 10th and 11th November, 1988.

The workshop was attended by representatives from the Pharmaceutical Associations of Great Britain, Northern Ireland, Cyrus and Malta. It was chaired by Professor A.H. Beckett, who is the representative of the Royal Pharmaceutical Association of Great Brtain, on the CPA Council and a CPA Vice-President.

All countries participating prepared a detailed report on current pharmacy practice in community, hospital, industry and wholesaling, expected developments in practice, current education and training and education needs.

These reports will be compiled as a final document on the current Pharmacy Practice and Education of all member countries of the Commonwealth. These reports set the stage for plenary discussions. Emphasis was made on the main problem which the Profession of Pharmacy in Malta is facing including the Education and training of Pharmacists and on Pharmacy Practice and Legislation. The Working Group noted and supported the proposal made recently by the Chamber of Pharmacists for a reorganization of the Pharmacy degree course and for the establishment of a Faculty of Pharmacy.

The workshop evaluation revealed that the meeting had been useful in so far as exchange of experiences is concerned.

The Executive Committee of the Commonwealth Pharmaceutical Association will be meeting in Malta on the 1st and 2nd May 1989 where it is expected that the recommendations of the European Working Group will be considered together with those of other regional working groups on the same topic. During this meeting the actions that can be taken by CPA towards meeting identified needs will be discussed.

PHARMACY WEEK

29th April - 6th May 1989

This Pharmacy Week is being organised by the Chamber of Pharmacists on the occasion of the holding in Malta of the Executive Committee Meeting of the Commonwealth Pharmaceutical Association.

PROGRAMME

Saturday, 29th April 1989

Pharmacists in Art

An exhibition of Contemporary Paintings, Photographs and Poems by Pharmacist-Artists at the Cathedral Museum, Mdina.

Sunday, 30th April 1989

Chamber of Pharmacists (Malta) Commonwealth Pharmaceutical Association Congress 1989 at the Aula Magna, Foundation of International Studies, University of Malta, Valletta.

9.00 a.m. Official Opening.

10.30 a.m. Morning Seminar
— Professional Service and Control in Community Pharmacy.

2.00 p.m. Afternoon Seminar.
— Health Education, Lifestyle and Pharmacy.

Monday, 1st May 1989

CPA Executive Committee Meeting proceedings at Corinthia Palace Hotel, Attard.

Tuesday, 2nd May 1989

CPA Executive Committee Meeting proceedings at Corinthia Palace Hotel, Attard.

8.30 p.m. Official Dinner at the Hotel Phoenicia, Floriana.
Closing of the Congress.

Wednesday, 3rd May 1989

Meetings of the CPA-COP officials with Government and University Authorities.

7.30 p.m. Lecture: Pharmacy Education-Relationship to Patient Care by Dr. J.A. Bachynsky, Dean, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Canada, at the Federation of Professional Bodies, Paceville.

Thursday, 4th May 1989

8.00 p.m. Lecture: Rational Use of Medicines by Prof. A.H. Beckett, Emeritus Professor of Pharmacy, King's College, London, at the Conference Hall, Medical School, G'Mangia.

Friday, 5th May 1989

2.00 p.m. Lecture: Stereochemistry by Prof. A.H. Beckett, at the Science Lecture Theatre, University of Malta, Msida.

Saturday, 6th May 1989

Drug Misuse in Sport. National seminar at the Assembly Hall of the University of Malta, Msida.

LECTURES

PHARMACY LAW AND ETHICS

Dr. Ivor Harrison, M.Pharm., Ph.D., F.R.Pharm.S., Director Legal and Regulatory Affairs, Medicine Research Unit, University of Wales, Cardiff, delivered a lecture entitled 'Pharmacy Law and Ethics' on the 25th November 1988.

Dr. Harrison was in Malta to advice the Government on Pharmacy legislation and to lecture Pharmacy undergraduates. He held discussions with the council of the Chamber of Pharmacists on legislation pertaining to pharmacy.

DISINFECTANTS AND THE PREVENTION OF INFECTION IN THE HOSPITAL AND OTHER ENVIRONMENTS

Dr. Sally Bloomfield of the Department of Pharmaceutics, Chelsea Department of Pharmacy, King's College, University of London, delivered a lecture entitled 'Disinfectants and the prevention of infection in the hospital and other environments' on Tuesday, 21st March 1989.

Dr. Bloomfield was in Malta at the invitation of Prof. A. Serracino Inglott to give lectures to undergraduate students.

Dr. Bloomfield's research during these last 23 years concerned various aspects of antimicrobial agents used in pharmacy and medicine.

AHOY THERE YE 'SEA-FARING' APOTHECARIES!

On Thursday, 29th December 1988, a large group of pharmacists and their guests boarded the 'Black Pearl' schooner at the Ta' Xbiex Marina to join the President and Council of the Chamber of Pharmacists in their now traditional Yuletide dinner.

The elegant surroundings of warm wood and polished brass appropriately decorated for the occasion added to the festive mood of the gathering which was made up of faces 'old and new' including a table of fresh 'graduates' and their better halves. This year each lady and gentleman again received lovely gifts donated by Mr. Reginald Fava, Vice-President.

During the dinner, the President launched the 'American Auction' and in next to no time the sum of Lm57 was collected for a beautiful print by artist Paul Carbonaro donated by Messrs. Vivian Commercial Corporation, which went to Dr. Ray Parascandolo, the Assistant Treasurer's husband. It was then raffle time and the first gift to be won by pharmacist Mrs. Pauline Grech, was a beautiful Pupa make-up set generously donated by Council member Mr. Eric Zammit. Other gifts were the generous donation of:-

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Finally, the President and Council rose to join hands and sing '...for auld lang syne!'... over a glass of champagne compliments of the Chamber...

CONTINUING EDUCATION PROGRAMME 1988 GERIATRIC PHARMACY

13th October: Physiological and Pathological Changes in the Elderly influencing Drug Response — Prof. A. Serracino Inglott, B.Pharm., D.Pharm.

20th October: Precautions required in Drug usage in the Elderly — Prof. A. Serracino Inglott, B.Pharm., D.Pharm.

28th October: Diseases in the Elderly — Dr. M. Vassallo, M.D.

3rd November: Conference — Management of the Terminally Ill Elderly Patient: Ethical Considerations — Dr. M. Vassallo, M.D., Rev. Fr. P. Pace.

17th November: Psychosocial Aspects of the Elderly — Dr. G. Debono, M.D., M.R.C.Psych.

24th November: Forum — The Care of the Elderly in the Community — Chairperson: Mrs. M.A. Sant Fournier, B.Pharm., M.Phil.

After the forum the Hon. Prof. J. Rizzo Naudi, M.D., F.R.C.P., M.P., Parliamentary Secretary for the Care of the Elderly, distributed certificates of attendance to all those pharmacists who attended a specified percentage of sessions.

The sessions were sponsored by:

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SEMINAR ON PALLIATIVE CARE

The Chamber was invited to the Seminar on Palliative Care organised by the Hospice Movement in Malta on 28th, 29th, 30th October 1988 at the Holiday Inn, Sliema.

About 200 distinguished members of the Caring Professions participated at this seminar. The Chamber was presented by Mrs. M.A. Sant Fournier, B.Pharm., M.Phil. — President; Miss M.A. Ciappara, B.Pharm. — Secretary; Miss M. Zammit Montebello, B.Pharm. — Assistant Secretary and Mr. F. Felice, Ph.C., B.Sc.

The aims of the seminar were to provide up-to-date knowledge of Palliative Care and to promote the attitudes and skills needed by a multidisciplinary team in order to care effectively for the patient with advanced cancer and the family.

The visiting speakers were led by Dr. R. Fisher, Hon. Consultant in Palliative Care, Cancer Relief (Macmillan Services), London and included Dr. R. Corcoran, Consultant in Palliative Care, The Haywood Macmillan Unit, the City Hospital, Nottingham, Mrs. J. Perron, SRN, Senior Lecturer in Nursing Services, the Dorret Institution of Higher Education, Mrs. A. Brown SRN, Macmillan Nurse Consultant, Basingstoke District Hospital and Mr. Derek Spooner, Consultant Planning Advisor to Cancer Relief.

The sessions included an Introduction to the Concept of Palliative and the Philosophy underlying Hospice Care; Definitions and Description of Pain; Principles and Methods of Pain Control by pharmaceutical medication and other methods; A Care History; The Psychological Needs of the Dying Patient and his family. The Domiciliary Care Service and the work of the Macmillan or Hospice Nurse; Day Care; The Spiritual Needs of the Dying Patient; Definition of Bereavement and its Features Risk Groups and the helping role of Counselling Aspects of Management in Palliative Care; Control of Specific Symptoms and different Methods and Relief.

CONTINUING MEDICAL EDUCATION

The Chamber of Pharmacists has long felt that pharmacists and pharmacy students should be invited to the Continuing Medical Education lectures organised by the Post Graduate Committee of the Faculty of Medicine and Surgery.

Through the intervention made by the Chamber of Pharmacists with the Chairman of Committee, the Hon. Professor J. Rizzo Naudi, this oversight has now been corrected and invitations have now been extended to include all pharmacists and pharmacy students.

NEW DRUG

Clavulanate-Potentiated Ticarcillin

Clavulanate-potentiated ticarcillin (Timentin) is a novel parenteral antibiotic which brings together the rapid bactericidal action of ticarcillin, a broad spectrum carboxy-penicillin and potassium clavulanate, a potent inhibitor of a wide range of bacterial beta-lactamases.

In Timentin, clavulanate expands the antibacterial spectrum of ticarcillin to include organisms rendered resistent to the penicillin by virtue of beta-lactamase production such as Staphylococcus aureus, Escherichia coli, Pseudomonas aeroginosa, indole positive Proteus and Bacteroides species.

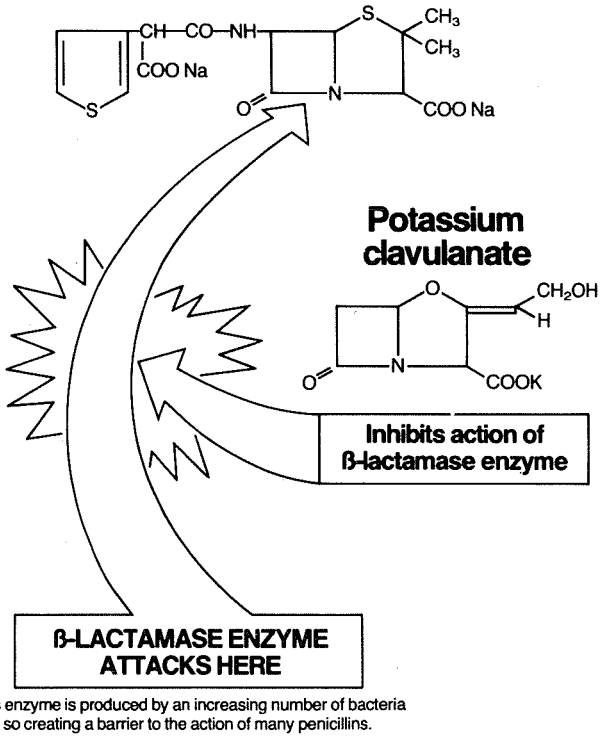
Clavulanate-potentiated ticarcillin has been extensively tested in the U.K., U.S.A., and Continental Europe. A wide range of primary conditions were treated including septicaemia, infections of the lower respiratory tract, skin and soft tissue, peritonitis osteomyelitis, septic arthritis, urinary and gastrointestinal tracts, genital and gynaecological infections, and pyrexia of unknown origin. The **in vitro** antibacterial activity has been extensively tested against a wide range of clinically relevant gram-positive and gram-negative aerobic and anaerobic bacteria.

In a study by Barry **et al**, over 10,000 bacterial isolates were tested against ticarcillin and Clavulanate-potentiated ticarcillin in serial dilution tests. The results show that clavulanate significantly increased the activity of ticarcillin against strains of E.coli, K.pneumoniae, K.oxytoca and Serratia marcescens amongst others, organisms which often present considerable therapeutic problems in patients with neutropenia and other serious underlying disease.

Clavulanate-potentiated ticarcillin compares favourably with a wide range of broad spectrum antibiotics including azlocillin, piperacillin, and gentamicin. It was found to be highly effective against aerobic septicemic isolates and was two to sixteen fold more effective than other antibiotics tested against anaerobic bacteria.

Ticarcillin in combination with an aminoglycoside is synergistic **in vitro** and **in vivo.** Clavulanate-potentiated ticarcillin extends these synergistic properties with aminoglycosides against ticarcillin-resistant strains of Pseudomonas aeroginosa, also resistant to gentamicin and tobramycin.

The Minimum Bactericidal Concentrations of



This enzyme is produced by an increasing number of bacteria so creating a barrier to the action of many penicillins.

Fig. 1 Mode of Action.

Clavulanate-potentiated ticarcillin have been shown to be the same as, or two-fold higher than the Minimum Inhibitory Concentrations against test bacteria, including beta-lactamase producing strains.

Pharmacokinetics

Results of extensive studies evaluating the pharmacokinetics of clavulanate-potentiated ticarcillin and its components demonstrate that:

— When infused intravenously, it provides serum and tissue levels of ticarcillin and clavulanate suitable to achieve activity against a wide range of beta-lactamase producing bacteria.

— The pharmacokinetic profile for clavulanate was found to parallel that of ticarcillin. Mean serum concentrations of both components were not appreciably altered when given alone or in combination.

— Urine excretion provides the major route of elimination for Clavulanate-potentiated ticarcillin.

Pharmacokinetic studies in patients with varying degrees of renal impairments have

Parameter	Ticarcillin	Clavulanate
Mean Peak Serum Conc. (g/ml)	262.78	14.33
Volume of Distribution (litres)	10.8	20.3
Protein Binding Levels	45%	9 - 20%
Mean Half-lives (min.)	60	56
Urinary Recovery (% dose recovered 0-6 hrs)	76.9	58

demonstrated that rates of excretion for both ticarcillin and clavulanate are reduced and dosage adjustment is required.

— Mean Pharmacokinetic Parameters of Ticarcillin and Clavulanate following Intravenous Infusion of Timentin 3.2g over 30 min.

Both ticarcillin and potassium clavulanate have established safety records, the first as a single antibacterial agent, the second as clavulanate-potentiated amoxycillin (Augmentin). Reproductive, mutagenic, cardiovascular and general pharmacological studies have shown that it poses no significant hazard. In addition, no interaction occurs between the two active compoents when co-administered.

Clavulanate-potentiated ticarcillin is an injectible antibiotic with a broad spectrum of activity. It is indicated for the treatment of severe infections of hospitalized patients and proven or suspected infections in patients with impaired or suppressed host defences.

The usual adult dosage is 3.2g given 6-8 hourly.

Maximum dosage is 3.2 g administered 4 hourly.

It should be given by intermittent IV infusion over a period of 30-40 min. Continuous infusion over long periods may result in sub-therapeutic concentrations.

It is contraindicated in penicillin hypersensitive patients and its use is not recommended during pregnancy. Side-effects are uncommon and typical of other injectible penicillins. Changes in liver function tests have been observed and in rare cases bleeding manifestations have been reported following high dosages of ticarcillin.

Clavulanate-potentiated Ticarcillin is a development of Beecham Research Laboratories.

CPA PRIMARY HEALTH CARE (PHC) DATA BASE

Periodically, CPA hears about pharmacists who have been involved in **non-pharmaceutical** Primary Health Care (PHC) activities in developing countries, i.e. activities which are not related to the purchase, preparation or supply of medicines from pharmacies or pharmaceutical departments. This is not surprising in view of the broad scientific and health related education and training of pharmacists.

Arising from a current study of the role of pharmacists in PHC, it has been decided that it would be valuable for CPA to compile a data base of such pharmacists and their experiences. It is intended that the data base should include activities which are not part of the traditional pharmaceutical services, e.g. we have in mind such activities of health education, the provision of general health care in rural areas, promoting good hygiene, etc. Not only will such data be of value to the current study but it will serve as an indication to the health community generally of the contributions that have been and can be made by pharmacists.

The information that is needed for the data base is as follows:

— Name of pharmacist and address of correspondence

— Qualifications and major appointments held

— PHC activities:
  Brief description of activity(ies)
  Country(ies) and date(s)

To enable CPA to compile a comprehensive data base, CPA requests all Commonwealth pharmacists who have undertaken non pharmaceutical PHC activities in developing countries, to send the above information to

The Secretary
Commonwealth Pharmaceutical Assoc.
1 Lambeth High Street
London SE1 7JN U.K.
Telephone: 01-735-9141
Fax: 01-735 7629

Bioethics

A DIALOGUE TO MAKE HEALTHCARE BEFITTING MANKIND

Mary Anne Ciappara B.Pharm.

Achievements in biological sciences and technology, particularly in biomedical engeneering, while creating new spheres of research, are presenting controversial ethical problems to health professionals and society in general.

A most significant National Dialogue on Bioethics was held between the 7th and 9th July 1988. The first session dealt with 'The various problems that the development of science and medicine raised in matters affecting life and death'. This was followed by a dialogue for health professionals on 'Life Sustaining Procedures: Ethical Considerations'. The National Dialogue was brought to an end by the National Seminar on "Bioethics — The Case for a Health Ethics Council" at the University of Malta.

The Prime Minister, Dr. E. Fenech Adami, in his opening address, put forward a proposal which the Government is considering to present to the United Nations, so that an International Law on Scientific Research will be drawn up, which will regard research as a common Heritage of Mankind.

For this Dialogue, Prof. Laurence J. O'Conenll, Associate Professor at St. Louis University, Missouri, in Theology and Bioethics, and Rev. Fr. Charles Vella, who teaches Ethics and coordinates the Ethics committee at the Instituto San Raffaele in Milan, were joined by experts from the legal, medical, social and moral fields, to examine the problems we are facing in our country in the field of Bioethics.

Among the various issues discussed were artificial insemmination, *in vitro* fertilisation, genetic engeneering, donor embryo transfer and organ transplantation. Other issues were terminally ill patients being kept alive on respirators, patients on renal dialysis, clinical research and drug therapy.

The objectives, methodology and functions of an ethics committee were also discussed. The functions of an ethics committee is three pronged. On one hand, it is a consultative and advisory body providing guidelines and advice and mediating, if necessary, between doctors, health administrators, patients and their families on the other hand, it will evaluate scientific research and be assigned a formative function, acting as a catalyst for educational programmes at the University and for Continuing Education for all those involved in Health Care.

This first dialogue has made us aware of the various ethical issues in medicine and has laid the foundation for a health ethics committee. The time is now ripe for the setting up of this ethics committee in Malta and for a follow up of this dialogue.

The president and the secretary of the Chamber of Pharmacists attended all proceedings and participated in the discussion during the National Seminar. They had the opportunity to meet Fr. Vella and Prof. O'Connell. Fr. C. Vella was interviewed during a subsequent visit to Malta (See page 14).

THE PHARMACIST AND BIOETHICS

Communciation by President, Mrs. M.A. Sant Fournier, B.Pharm., M.Phil.. at Discussion on 'Ethical Issues in Medicine' during the National Seminar, 'Bioethics: The Case for a Health Ethics Council'. Saturday, 9th July 1988 at the University of Malta.

Honourable Sirs, Mr. Chairman,
Ladies and Gentlemen,

Firstly, I wish to thank the Honourable Minister for Social Policy for inviting the Chamber of Pharmacists to participate in this National Dialogue on Bioethics.

Secondly, may I point out that ethical issues concern an important professional member of the Healthcare Team — that is the pharmacist, the dispenser of medicines to patients and colleagues and of ethical healthcare counsel to the patient and his family — for surely life-sustaining is also concerned with administration of medicines.

In the U.S., Clinical Pharmacy (or Ward Pharmacy there is some controversy regarding the name) has become a discipline in its own right and is being given growing importance in European countries, including Great Britain.

So, granted that much needed progress in hospital pharmacy locally will become a reality in the not too distant future, Maltese Pharmacists will be faced with still more 'anguishing' ethical issues together with their medical colleagues in the healthcare team — I am thinking of cessation of therapy, TPN, hydration, chemotherapy and also of research such as clinical trials of pharmaceuticals, traditionally produced or through biotechnology.

But this ethical aspect can also be extrapolated to Community Pharmacy Practice which is becoming more patient-oriented and is faced with ethical issues as supply of I.U.C.D.'s, Abuse of Drugs, Misuse of Medicines, irrational prescribing, patient's and family's right to know and confidentiality (to name but a few).

In humanizing hospitals and general practice. the pharmacist cooperates with his medical colleagues, especially in informing the patient on particular therapy thus improving compliance. The crux is inter-professional relationships and communication.

Re: ethics in curricula — to which Dr. Aquilina, Rev. Pace yesterday and Prof. Muscat today — have referred I have read in the March 1988 issue of Sanare Infirmos, the HSR excellent journal, that EEC countries will be including Medical Bioethics in their curricula — and propose their inclusion in Pharmacy Courses too. The pharmacy profession in Malta has long been governed by an ethical code and the inclusion of Ethics in the local Pharmacy course curriculum is warranted.

INTERVIEW

Rev. Charles G. Vella

Mary Anne Ciappara, B.Pharm. and Mary Ann Sant Fournier, B.Pharm., M.Phil.

"THE BASIC PRINCIPLE IS THE RESPECT FOR THE HUMAN PERSON AS AN 'ESSERE UNICO, IRREPETIBILE' WHO HAS THE RIGHT OF CHOICE".

Instituto Scientifico H San Raffaele

Q. How did you get involved in Bioethics?

A. I was always interested in what we used to call the moral-medical problems because of my involvement in counselling with the Cana Movement. My interest goes way back to the first centre which the Cana Movement opened at the Blue Sisters Maternity Home, St. Julians in 1959. This was a centre for counselling and birth regulation and together with a group of doctors I used to meet regularly to discuss current moral-medical problems affecting marriage. But it is only in recent years that Bioethics as a discipline came into being. My interest goes back recently in 1985 when I started preparing to organise a congress in Milan on Bioethics and ethics committees. At the time I was director of the Centro Internationale Studio Famiglia (CISF) and we thought of branching into this whole new field of bioethics. So I invited various experts from Europe, the United States and Canada to come for this congress. This was the first meeting of its kind in Europe and in Italy on an international scale. The meeting was held in May 1986 in Milan. Since then I went to work at the Istituto Scientifico Ospedale San Raffaele and now I am fully involved in Bioethics.

Q. We have read in the pamphlet on the Istituto San Raffaele "Un polo universitario di medicina e scienze umane" — this seems to be the prime characteristic of San Raffaele. Could you please explain?

A. The founder of the Istituto Scientifico San Raffaele, Prof. Don Luigi Maria Verze, when he founded the hospital in 1972 wanted not just to introduce a new hospital but also to bring into medicine 'scienze umane' (medical humanities). His philosophy is that every doctor needs grounding in humanities. San Raffaele is a teaching hospital of the Università degli Studi di Milano and very often students come to us with a good scientific background but no humanistic studies and it is difficult to talk to them about patient-doctor relationship. So this is the first centre of its kind in Italy and in many countries where you have — 'polo di medicine e scienza umane' — the two linked together. Since 1981, medical humanities have been part of the medical curriculum, and of course when we say medical humanities we also include Bioethics. We are unique in as far as six years ago, we established in Verona and now in the hospital grounds in Milano, what we call

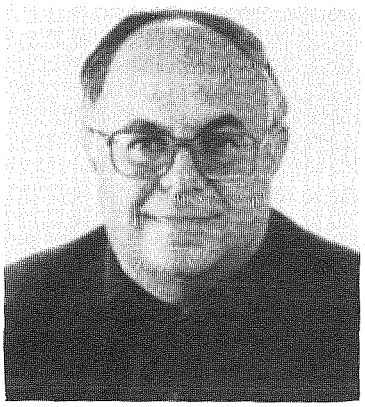
a "liceo classico con indirizzo biologico sanitario", that is we take young students after they finish the scuole medie and start teaching them the humanities with a specialised orientation to medicine. It isn't that all of them are going to be doctors, some might become hospital administrators, nurses, etc. It is what we call 'vivaio' or 'seminario'. Just as dioceses have to have future priests, we have to have future doctors, etc. for our hospital.

Q. Your article 'Della frammentazione della persona alla comprensione della sua unicità irrepetibile' in the March '88 issue of 'Sanare Infirmos' you mentioned that in order that the health care professionals have a great sensibility towards patients as human beings they need a continuous formation in humanities. How is this being done at San Raffaele?

A. First of all I think doctors, nurses, pharmacists or anyone involved in this work need to have the right motivation as a starting point. At San Raffaele this is based on our philosophy, what we call the principles of San Raffaele — guidelines for all those who work in the hospital. Continuing education is very important otherwise people do not grow and it is easy for many people, to remain like the Japanese plants 'Bonzai', very small because they do not have any roots. If you do not update, you do not grow, you remain 'Bonzai'. So it is very important to have an ongoing education. We have our 'Scuola di Medicina e Scienze Umane' which does regular courses. We have a course that takes place every Saturday morning and various seminars in which we have prominent people from abroad like Fr. Manuel Cuyos of Barcellona, Prof. Jean Francois Malherbe of the University of Leuven and several others. We have a very good response not only from within the hospital but also from outside. We have priests, social workers, nurses, pharmacists and doctors attending because there is a big demand and interest in these subjects.

Q. What do you mean by 'umanizare'?

A. 'Umanizare' is part of our philosophy at San Raffaele. It is very easy today that a big hospital will loose its sense of humanity, will only look at technology and not at the person. Very often advanced technology itself can be a barrier between the doctor and the patient. So we need to humanise 'medicine'. When we say 'humanities' we mean the interpersonal relationships between doctors, nurses and the patients and their families and today there is a greater trend not only towards Bioethics but also for humanisation of the hospitals. In San Raffaele we have what we call the "gruppo promotore per l'umanizazione dell'ospedale" which includes a group of people and our job is first of all to educate the staff itself of the hospital to be conscious and aware of their 'saper essere', of their being persons first, because you cannot humanise other persons if you do not know yourself; afterwards, we give them an input of 'sapere', knowledge, regarding humanisation and third the 'saper fare', the know how, what we call the clinical encounter between the patient and doctor, nurse, etc. Today the idea does not only exist at San Raffaele but in many other centres, for example, the religious congregation called 'Fate Bene Fratelli'. Their Prior General, Fratel Marcese has been expanding this thought in their 200 hospitals throughout the world. The Pope at the Vatican last November also spoke precisely on 'Umanizare la medicina'.



Charles G. Vella

From Cana to San Raffaele

In 1956, Rev. Charles G. Vella, after founding the Cana Movement introduced marriage and family counselling service in Malta. As a result of this work, in 1975 he went to Italy to become the first director of the 'Centro Internazionale Studi Famiglia" (CISF). As director of CISF he organised in 1986 the first International Symposium on Bioethics and Ethics Committee on the occasion of the 1st European Day on Bioethics in MILANO MEDICINA. This experience has led him to the Istituto Scientifico San Raffaele, Polo Didattico di di Medicina e Scienza Umane" where he is responsible for Public Relations and Publications, a member of the Ethics Committee and a lecturer in Ethics. He is a member of the European Association of Ethics Centres of the International Foundation "Hippocrate", Luxembourg, and the coordinator of the Italian "Committee for Ethics in Medicine and Ethics Committees". He is a member of many international organisations and is consultant to the Minister for Social Policy.

Q. In this 'saper fare' do you mean that you put them in a clinical situation and teach them interpersonal skills?

A. 'Saper fare' is the know how, where we teach them the skills, true case studies to discuss and role playing. There are many ways on how to approach it, especially the ministry of listening. For me listening is the eighth sacrament and many patients want to be listened to. We tried to educate the young doctors in particular to spare some time (and I must say they are very generous) so that they listen to patients. This moment a young assistant comes to mind, in my hospital, who has to take about 80 days of leave which he has not taken; so they are dedicated people, they are motivated! They have a philo-

sophy! They do not have private practice either, and most of them are full time at the hospital and I am edified by their example when I see what we call 'primari' consultants going to the hospital at 7.30 a.m. doing their case meeting at 7.45 a.m. every day with these doctors and remaining there till 8.00 p.m. So to listen you have to have time and to be there and be on the spot.

Q. How can this concept be applied to the pharmacist?

A. What I have said also applies to the relationship of pharmacist/client. Of course here it is more difficult because sometimes there are many people in a pharmacy. I have seen this in Malta; they want to buy anything and have various needs and so it is very difficult to have a private conversation. But in the old times the pharmacist was a key person in the village to whom the people went not only for their 'riċetta' but very often was one of the support people in the village. Just like the parish priest was the person they referred to for many needs, so was also the local pharmacist. Now unfortunately, there are so many demends in a pharmacy that it is very difficult I suppose for the patient to be listened to.

Q. The Chamber of Pharmacists is putting a great deal of emphasis on communication skills, and in doing so, we are following the examples of our colleagues in U.K., Europe and America. They are putting psychosocial pharmacy as part of the curriculum, not only as a subject to be taught but probably as you do in San Raffaele, as an integral part of the way one works. San Raffaele sounds something unique, special. Is it unique?

A. Well, first of all I want to add something of what was said before, because I have had a close association for three years running, when I went for the convention on Drug Abuse in Atlanta in the U.S. and Washington for the meeting of the White House which Mrs. Reagan organised. I met there a parent body as yours and they were called 'Pharmacists Against Drug Abuse' and they were very well organised. I met some of them and they have even been giving out cards where you have a window which tells you the signs to look for in drug addiction in your children. They give these and they explain them to their clients. We've discussed even the possibility of doing something like this with the Pharmacists' Union in Milan. Now pharmacists in Italy are very much involved in the question of drug abuse and for this communication is indispensable because you are not going to give out just information or a leaflt or a sheet but you need to take time perhaps you need to see these people after closing hours or at special times to have a chat with them because very often the pharmacist is the very first person these people are in contact with.

For your second remark "is San Raffaele unique?" I say no, it may be different to many other state hospitals. We are a private foundation with over 900 beds but all other beds are 'concenzionati' i.e. part of national health service. In Italy we have people who come from some of the richest families. I would say the top 5, to the gypsies! They come because they can find there certain technology which other hospitals do not have, be they public or private. But as the President, Don Luigi Maria Verze said to our Prime Minister Dr. E. Fenech Adami when they met here in Malta, "we cater not for the rich nor for the poor, we cater for the sick person because when the person is sick he is neither rich nor poor" i.e. what you can make available to those who pay should also be available to those who cannot pay, on an equal basis. In that perhaps we are unique!

Q. You have mentioned distribution of cards by pharmacists in America and Italy. We have started doing that in Malta. Caritas has prepared a series of leaflets on drugs of abuse which we are distributing to those pharmacists who are interested. How do you view pharmacies as distribution points for these leaflets?

A. The pharmacy is an excellent information centre but it all depends on how much trust the pharmacist builds in the community. If he reduces himself to a salesman, then there can be no relationship but a smile, and a smile does not cost anything, a word, a gentle word, a question put indirectly without being curious, can help people to open up to start talking and express needs which perhaps they are afraid even to express. The leaflet is an instrument for building this bridge, just an instrument, you are not going to solve anything, maybe the person puts it in his bag and would not even read it, but he has talked to you and that is important, talking and listening to you.

Q. What do you think of this Maltese saying which was told to me by a Maltese doctor when we were discussing the role of the two professions. As you know, the roles of doctor and pharmacist sometimes overlap. I was using the word 'patient' though I noticed, you use the word 'client' . . . we try to be 'patient oriented'. The gentleman said "tidħolx bejn il-basla w qoxritha. Il-pazjent huwa tat-tabib u ma hemmx post għat-tielet persuna".

A. Well first of all I was using the term client in the sense of psychotherapy. Karl Rogers talks of the person centred therapy or the client centred therapy. There is a moment when a person can become a client and there is a moment when the person can become a patient. Not every person that comes into the pharmacy is a patient because it depends on what he demands. There are 15,000-20,000 diabetics in Malta, some of them may be in a state of being a patient. They may not have time to grasp how to use the insulin and may need an explanation from you. They may not even have knowledge about diet, it is a question of empathy, it is not a question of anyone having a monopoly of one patient. It is the person, if we respect the person, who decides on whom to and where he or she goes. If they find the pharmacist 'sympathetic' and have confidence in him or her then they go to him. In many things you can give advice and guidance without usurping the doctor's role. This is were the policy of this Government is good in studying the scheme of giving the patient the right to have his own doctor and his own pharmacist, from where he obtains his medicine and

health care. So the basic principle is the respect for the human person as an 'essere unico, irrepetibile' who has the right of choice.

Q. In the leaflet about your book which you have written together with other authors, "Dalla Bioetica ai commitati etici" reference is made to 'la drammatica solitudini dei medici'. Could this solitude be self inflicted? . . . there can be lack of communication between healthcare professionals and between themselves; through communication they could lighten their burden!

A. I think this principle counts for everyone, if a person does not remain on an island then he is ready to communicate. It is what I call in Italian "gettare ponti", build bridges to others. That phrase in the book the 'isolamento' — very often the doctor in the community can easily work alone that is why today in medicine many doctors work in a group. One of the aims of the ethics committee is precisely to have this dialogue, chance of listening and discussing, agreeing and disagreeing. There can be solitude in a doctor as there can be solitude in a priest if he is not within a community.

Q. Is it not better to have a national committee and not a hospital based ethics committee, so that health professionals in the community will be involved?

A. This is not going to solve this problem but I think this is why when we held the meeting in Malta on Bioethics at St. Luke's, I had a feeling and likewise Prof. Lawrence O'Connell that this was an occasion when people did not have questions to ask directly on what they heard but they wanted to stand up and speak about their needs, their problems and their experiences and perhaps I hope that the medical school, the Doctors' Union and pharmacists like you will create more moments of communication and dialogue like this. I felt that many people were standing up not to ask questions on the subject but where making their own observations, questions and experiences which is excellent but at the same time one felt that there was a poverty of dialogue among the medical profession and the absence of a whole generation. A whole generation was not there. It is good that the young will listen to their elders and the elders to their young, so you get interaction in the medical profession and in the community. This applies to pharmacists too. Yon don't want to have an ongoing education for young pharmacists, but you want it for all generations so that there is interaction and team work.

Q. The Prime Minister speaking at the seminar on Bioethics referred to genetic engineering and biotechnological production of pharmaceutics, etc., and advocated the placing at the disposal of developing countries, the research findings of Industry as an institutional resource. Now Don Verze says "Funzioni del ethica non e' tarpare le ali alle scienze, ma affilarle per un volo più veloce". In what way does ethics not hinder research?

A. First of all ethics definitely should not hinder research. I think ethics when seen in a true way helps research and the researcher, because the researcher is in the lab doing experiments, e.g. on test tube babies, will have many problems in his conscience. Jacques Testart of Paris in his book wrote, explaining why he gave up research (he was one of the first to do this sort of research) when he examined the ethical value, he saw that the first value was not science but the sanctity of life and the human person and when he stopped doing experiments like Dott. Campagnoli of Torino, he was not giving up something but he was giving nature its right. Because the baby should not be conceived in a lab but in the mother's womb. Now of course one can help a mother's womb to conceive. So you are giving the right to nature. The second point on genetic manipulation, I think, the Prime Minister was pronouncing a very important speech on that occasion, and only this week in Russia, the Russian Government is doing something similar to what we have done in Malta. I am in touch with the Commission on Ethics of the Council of Europe, the Director is Dr. E. Hondious, who will be coming shortly to Malta to discuss genetic manipulation and I fully endorse the Prime Minister's proposal to put this on the U.N. level.

The third point is what Don Verze said. We should not be afraid of science, or laboratory experiments. The laboratory is not 'the inferno'. Sometimes one needs to trim the wings, so that science can go smoother. Dr. White of Cleveland, Ohio, when he met the Pope three years ago, said that he was renouncing his experiments on the brain of apes and monkeys because he did not know where his experiments where going to lead him to. We do not know what is happening in the laboratories throughout the world. We don't know what the multinationals are doing and experimenting in. At the Council of Europe when I represented the Ministry for Social Policy, all were definitely concerned that one needs an ethical consideration regarding genetic manipulation.

Q. A final comment from you regarding the future of ethics in health care in Malta with special reference to the community pharmacist.

A. Well I think it is a very good sign of the times that a debate and dialogue has opened up on ethics which is also involving the pharmacist. I think the Government has taken the lead in this and the Church also. It is a common effort which concerns every one without any barriers, that is man, and man is of interest to us all. When we are talking about ethics we are talking about ourselves, when we are talking about ethics committees we are talking of a service which one day will help us and I hope that one day your Chamber will have the chance to expand on this topic, that you will also be represented on the National council and that you will continue very much on this line, on ongoing education to pharmacists especially the young ones starting from when they are still students at the university — catch them young so that they will grow and no one in Malta will remain 'bonzai', because the future of Malta like the rest of the world will depend very much on culture and education.

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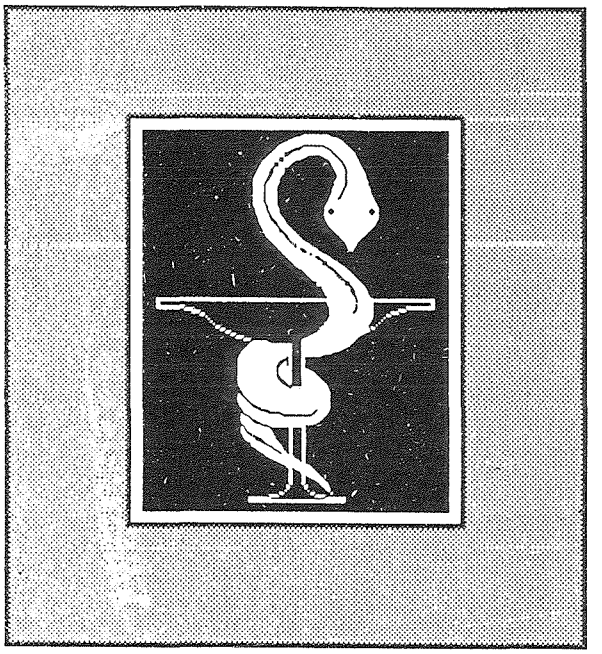

CHAMBER OF PHARMACISTS

MALTA

DISTRIBUTION OF NATIONAL HEALTH SERVICE MEDICINES

APRIL 1989

The aim of this report is to propose the necessary changes to the current system of distribution of Free Medicines. A brief summary of the current system is first given followed by a discussion of the possible alternatives. The guidelines in mind are the policy of the Chamber of Pharmacists and the stated government policy of 'reducing waste' and the distribution of essential medicines free of charge.

Finally the Chamber's recommendations as to the best method of implementation will be provided.

This report has been presented to the authorities concerned and the Chamber is holding discussions with the Free Drugs Scheme Working Committee which has been set up recently to study and give proposals for the setting up of the scheme.

It was compiled by Mrs. M. Brincat B.Pharm.

NOTE: The term 'pink card holders' used in the text includes the blue card holders (diabetics) and green card holders.

Contents

1 — The Current System

1.1 *Group I Patients*: (Yellow Card Holders)

Patients who suffer from a condition which falls under the third schedule of the NI Act. This schedule refers to a series of diseases and conditions in respect of which free medicines are provided irrespective of financial position (e.g. congestive heart failure, hypertension, schizophrenia). Mostly validity is for one year.

No data is available which reflects the actual number of patients using this service.[1]

Table 1 shows the number of applications approved each month in 1984.

1.2 *Group II Patients*:

These patients benefit under the Medical Aids grant of the NI Act. Entitlement is based on a means test. The assessment is based on total household income, however each member must have his/her control card.

Since 1978 renewal every four weeks has been necessary except for people over 60 years — renewal every six months being required.

Data on the actual number of patients benefitting from this grant is not available. The only figures available indicate the number of eligible applicants which totalled 15,087 in 1984.[2]

Table 1

Number of Schedule III Applications Approved Malta: 1984

Month	*Number of Schedule III Applications Approved*
January	1,053
February	1,234
March	1,112
April	885
May	1,093
June	1,097
July	1,021
August	1,124
September	1,074
October	1,115
November	1,370
December	885
TOTAL	13,063

1.3 *The Formulary*[3]

The formulary consists of a list of those drug preparations available for use within the Government Pharmaceutical Service.

There are:

A. General Practitioner list.

B. Open Drugs list — may be prescribed by any medical practitioner working in hospital services. It includes a broader group of pharmaceutical preparations than the G.P. list.

C. Consultant Drugs list — only prescribed by consultants.

D. Designated Drugs list — may only be prescribed by consultants in the field related to the use of the drug.

Non-formulary drugs may only be prescribed after approval by the Drug and Therapeutics Committee.

1.4 *Methods of Distribution*

a. *Direct System*

This is the term referring to those patients

who collect their medicines from the hospital. Too many people make use of the service. In January 1984, 94% af patients using this system were[4] follow ups while only 6% were new cases.

b. *Postal System*

This refers to the collection of packages prepared at St. Luke's Hospital and collected by the patient or his representative from the 'berga'. Of the patients making use of this system 69%[5] were geriatric patients and most of them had their medication collected for them. About a fourth also utilised the direct system because of urgency on the signatures required.

2 — Deficiences of the Current System

The current system has a number of shortcomings which can be grouped under
— waste
— lack of good quality drugs
— complete lack of professional service

2.1 *Waste*

It is a common occurence for people to hoard medicines. Cases are known of people who go to pharmacies to exchange hospital drugs. Also, several instances are known of people who have been repeatedly supplied with a drug therapy, months after the treatment should have finished.

Money is spent on repacking items, some of which would be much cheaper if distributed in an original small pack, as well as of better therapeutic effectiveness when it reaches the patient (cf. Chamber Memorandum dated 1987).

2.2 *Quality of Drugs*

The Chamber has already made detailed comments about this topic in its memorandum. The examples quoted are so serious that a revision of purchasing policy for Government drugs is an immediate necessity. Clearly the requirement of a 'free sale' certificate is in no way a guarantee of quality as amply documented. In addition special consideration must be given to those drugs which present therapeutic equivalency problems

The participation in the W.H.O. certification scheme is a much better safeguard, and in our opinion this is a step forward.

The articles in Appendix II throw more light on the problems in drug purchasing

2.3 *Lack of Professional Service*

There is a complete lack of professional service. Society's Drug Expert, the pharmacist, is not available for patient counselling which is necessary
— to improve patients' compliance
— to advice on drug interactions and avoid drug related diseases
— and to monitor therapy.

Patient Compliance: Non-compliance can be defined as a situation where failure to comply is sufficient to interfere appreciably with attaining the goals of therapy.[6]

Patient compliance is an indirect assessment of the counselling activities offered by the system. The poorness of the current postal system is illustrated by the result (Table 2)[7] from a survey carried out on 300 patients who make use of this system.

Table 2

Survey carried out on patients who make use of postal system.

Sample No. 300

Complaint 59%	Non Complaint 41%

The handwritten labels and overall poor packages also contribute towards non-compliance.

The lack of professional service is also reflected in the kind of packaging used for the drugs. Several preparations deteriorate very rapidly unless properly stored especially in our climate.

The poorness of the service is also reflected in the time spent at the St. Luke's Hospital Pharmacy by patients who have to collect their drugs from the hospital.

Furthermore, currently, most of the postal packages are being prepared by completely unqualified staff resulting in frequent errors

3 — Alternative Distribution

Use of Community Pharmacies

In view of the above shortcomings it is imperative to make changes to the system. The first change that is in the process of being implemented is the dispensing of medicines to outpatients from a specially set up outpatients pharmacy at St. Luke's Hospital.

The postal system should be eliminated. The best alternative method of distribution which will ensure a professional service for the patient is the use of community (retail) pharmacies as

distribution points, the packaging of medicines at the hospital being done away with completely.

3.1 *Methods*

There are various ways of implementing this proposal. These will be discussed under two headings:

1. The 'Cupboard' system
2. Proprietary system or Free Choice system.

3.1a. *The Cupboard System* (D.H. Preparations)

This has been so called because it means the creation of a separate section of medicines in community pharmacies — the D.H. medicines.

These can be directly supplied by the hospital to the pharmacies, or ordered from the importer.

Hospital Supply — involves the organisation by government of a

(i) distribution system

(ii) accounting system

Normal Supply (or Tender System) — The usual distribution routes are used. Government will issue tenders for a particular drug, e.g. ampicillin and all ampicillin to be dispensed on the Government's Health Scheme will be of this particular brand. This has the advantage of having a standard tender price for the particular drug which will be the charge then reimbursed to the pharmacist.

3.1b. *The Free Choice System*

This term is being used to refer to a system where there is complete freedom of choice of trademarks. This means there will be no D.H. drugs at the pharmacies.

This system eliminates the problem of quality which to date seems to be part of generic drugs purchased by the hospital. In addition normal sources of medicines are retained. Also normal market prices will be retained for medicines dispensed.

4 — Finances

4.1 *Payment*

Payment must include the accepted markup on the cost price of the drugs together with a professional fee on every item dispensed. The latter will cover the paper work involved in dispensing together with the professional advice and patient monitoring by the pharmacist.

There are various ways in which this can be done:

1. directly by Government
2. through a finance bank
3. by the patient who is then refunded.

4.1a. *Directly by Government*

The pharmacist sends the bills to the government who will eventually pay them.

Any bureaucratic delay in payment will put a significant strain on pharmacy finances. For this reason, we are not in favour of this idea.

4.1b. *Finance Bank*

The government sets up a special fund for payment of pharmaceutical services. The pharmacist then sends all bills to the bank for settlement.

This would seem to be faster than having the civil service handling payment.

4.1c. *Payment by Patient*

The patient foots the bill. Expenses will then be refunded by tax deduction or in the form of an allowance to the individual.

This method has the advantage of not needing a new set up. The original payment by the patient is only a temporary expense which it is hoped will have the effect of discouraging waste.

4.2 *Costings*

It is impossible to draw up an estimate of the actual total cost of the system. In 1984 total drug imports amounted to more than Lm4.2 million[8]. It has been estimated that Government consumed about one third of these imports[11] i.e. more than Lm1.4 million. However if the list of Government health service medicines is based on a list of essential drugs and a system of payment and free distribution is introduced as we suggested here, then the cost can be contained. Furthermore it should be possible to ensure that only good quality medicines are used.

The poor remuneration of the pharmacists involved must be kept in mind since the success of the scheme depends largely on them. Also the pharmacist's tremendous importance in the success of therapy must not be forgotten.

5 — Recommendations and Implementation

1. The number of people making use of the current free medicine service is such that it

can readily be handled by the community pharmacies.

2. There should be freedom of choice of pharmacy by the patients and also pharmacies should be free to decide whether to participate or not.
3. A compromise of the two systems discussed under alternative distribution should be adopted. This is the definition of a list of essential medicines which will be available on the Government Health Scheme, the usual supply channels for pharmacies being used.
4. This list of essential medicines will be the core of the National Formulary and will replace the current G.P. list, and in whole or in part the open list of drugs. The categories of Consultant Drugs and Designated Drugs currently in the formulary should be retained. Also the possibility of prescribing non-formulary drugs after approval by the Drugs and Therapeutic Committee should be retained.
5. The W.H.O. definition of essential medicines is *those drugs which are of the utmost importance and are basic, indispensable and necessary for the health needs of the population.*[10] The current WHO list cannot be transplanted to Malta because, as the WHO itself states, the differences between the countries make it impossible to draw up a list of uniform, general applicability and acceptability. The best current set up to take care of drawing up the essential medicine list is the Drugs and Therapeutics Committee in consultation with the Chamber.
6. The current category of pink form holders should be revised We are of the opinion that to reduce waste it is best to retain eligibility for completely free medication only for special categories of people.
7. The list of diseases for which medicines are currently distributed free irrespective of income level should be retained. Some of the medicines for these diseases will not be included in the essential drug list. However, financial help should still be provided, though we once again recommend that only special categories of people should be entitled to total free medication.
8. It must be ensured that only effective medication reaches the patient. It is of little use to provide free medication and then deliver therapeutically ineffective or partly effective medication.
9. The choice of make (trademarks) should be left up to the Health practitioners.
10. Diversion of pink form holders to community pharmacies should be the first step. Those follow up patients making use of the direct system should be diverted to pharmacies after the intention of having specialists at polyclinics to follow them up has been implemented.[11]
11. Reimbursement for medicines dispensed. As already stated, it is important that financial strain is not thrust on pharmacies. The patient should pay for the medicines he collects and then he is reimbursed for his expense in whole or in part by the government, either by tax deduction or direct payment.
12. Quality control facilities must be improved. They must be at least as good as those of the local industry the products of which are checked by the government as part of the WHO certification scheme.

6 — Appendix I

6.1 *Foreign Experience*

Some International Experiences with National Health Service Drugs.

A common factor in all National Health Insurance providing drugs is the ever increasing expense of the system. It is noticeable that in most systems there is some kind of payment by the patient. Often a list of drugs which are not included in the scheme also exists. The examples provided here are:

a. The Swedish System
b. The Italian System
c. The British System

6.1a *The Swedish System*[12]

The national insurance system provides injury, disablement and sickness benefits, invalidity and retirement pensions etc. It also provides an allowance covering a part of the doctor's and dentist's bills as well as medicine. The patient obtaining a medicine on prescription pay up to SEK 20 and half of the exceeding amount to SEK 50. Free medicines are provided for some chronic and severe diseases. Finally, high medical care and medicine costs are covered through a high cost protection provision. Oral contraceptives are also covered by the scheme, but not prophylactic use of drugs. Recently, antitussives and expectorants have been exempted from the drug benefit scheme. This restriction might be seen as a first step on the

way to a negative list, where analgesics are thought to be the next group to be removed from reimbursement. Today patients pay 18% of the costs of a prescription drug on average. Medical care drugs which are not included are tax-financed to more than 90%. The costs have expanded at a faster rate than the GNP and account today for 10% (against 3% in 1960). The total drug costs amount to 8% of the medical care costs.

6.1b *The Italian System*[13]

The 'ticket' is the small detachable part of the outer packaging of patent medicines which carries the 'tariff' to be paid by the patient to the pharmacist — the balance of the cost of the medicine is then reimbursed by the Government to the pharmacist.

This 'ticket' which in 1984 stood at 150 Italian lire has been increased to 250 Italian lire for every 1000 lire of the cost of the medicine dispensed. Also, each prescription cannot refer to medicines the total cost of which exceeds 39 thousand lire. Moreover, the dispensing or professional fee per prescription has increased from 1300 to 2000 lire as at 1986). The exemptions from payment are as follows:

Persons per household	Income (not more than)
1	5 million lire
2	8 million and thousand lire
3	10 million and 800 thousand lire
4	12 million and 900 thousand lire

It may be interesting to note that each taxable Italian citizen pays at source or on income an average of 648 thousand lire (1984 figures) to finance the national health system of the country. The overall national health care expense (including medical assistance, hospitals, pharmaceuticals, prevention, public health) amounted to 37 billion lire.

Shortcomings of the Italian System

The difficulty with the above system lies in that although the balance should be reimbursed to the pharmacist within thirty days in reality there is a great delay in the effective payments this being of great financial burden on the pharmacists. Indeed, not too long ago and on several other occasions the Associatin of Italian Pharmacists has had to resort to a call for strikes in order to bring pressure to bear on the authorities for payment to be effected.

Ic. *The British System*[12]

There has been a change in the community pharmacist's function so far as dispensing is concerned. The way in which medicines are now compounded has reduced the calls on the pharmacist's manipulative skills, while the change in the nature of drugs has increased the potential demand on the pharmacist's knowledge.

The future

We claim no greater prescient powers (than others) but, confining ourselves to the next twenty years or so, we would venture the following predictions:

a. The discovery and development of new drugs will continue, some of which will be more complex and, unless used with the appropriate advice, potentially more toxic than their predecessors. New delivery systems will continue to be introduced, as well as further developments of existing systems. There will be an increasing need to match the individual medicament to the individual patient.
b. The cost of treatment will continue to rise. Successive governments will continue to look for ways of reducing expenditure, including the transfer of treatment, wherever possible, from hospitals into the community. As a result general practitioners and community pharmacists will handle potentially more complex medicinal treatment.
c. The proportion of the elderly in the population will increase. The elderly require both greater and more specialised attention.
d. The use of information processing facilities, such as computers, and of improved electronic means of communication within the health services will greatly increase.
e. Exploitation of the potential of the new treatments will lead to increasing cooperation between the professions engaged in health care.

The giving of advice and treatment to members of the public in respect of minor ailments was, prior to the introduction of the NHS, a major part of the pharmacist's role.

We believe that the service provided by the pharmacist is one that could be more extensively used and we therefore welcome the steps taken by the National Pharmaceutical Association

to draw people's attention to it. We consider it important that the pharmacist should be properly educated and trained to perform this role which includes the ability to assess when an inquirer should be recommended to seek medical advice. It will be for the public to decide the extent to which they wish to make use of the pharmacist's services.

Responding to special needs

The final stage of dispensing is the handling of the medicine to the patient. It is important that advice should be available to those who would benefit from it.

One such group is the elderly who are due to form an increasing proportion of the population. They consume far more drugs than the population at large. It has been observed that there was a much higher prescription rate among the elderly (particularly women) but that this was not matched by a higher consultation rate or increased purchases of medicines over the counter. Age concern have reminded us of the substantial proportion of the elderly who live alone.

There is thus a strong case, in the interest both of ensuring that medicines are properly used to the benefit of the patient and of reducing NHS costs, for the pharmacist to be able to provide such counselling services to the aged. A study carried out for the Royal Commission on the National Health Service showed that, in two parts of the country, 69 per cent and 80 per cent respectively, of the elderly used one particular pharmacy. We think there is scope, therefore, for encouraging older people to register with a single pharmacy in which medication records would be kept and from which they could expect to receive special advice and assistance in handling their medicines. In individual cases, and within the rules of professional conduct, it would be desirable for the pharmacist to cooperate with members of other professions involved in the provision of primary care.

As a generalisation it can be said that anyone who is chronically sick or mentally handicapped, and who has to rely on a continuous drug regime, should be a candidate for additional support and help from the pharmacist. In most cases it will be the individuals themselves to whom such help should be given, but in some cases it will be the people looking after them. This is particularly true of the mentally ill. Drugs now play a much bigger role in psychiatric treatment but they require careful handling by patients, some of whom may find this difficult without help. The transfer of patients into social care within the community means that they could be deprived of the support that was available to them in a hospital. Many of these patients require continuous medication.

Commercial context

The pharmacy profession is not alone in engaging in commercial activities. Members of all professions do so. Any professional in private practice is also a businessman. What distinguishes community pharmacy from other professions is the divorce that exists between the professional service given by its members and the way they are remunerated. Advice brings no return: the sale of a medicine does. A serious criticism of the way in which the community pharmacist is at present remunerated is that it acts counter to, rather than in support of, the exercise of a professional role. This criticism, we would stress, is a reflection on the system and not on the individual pharmacist. It is the system that needs to be changed.

Remuneration

The ways in which the NHS services provided by a community pharmacy are paid for act counter to, rather than in support of, the exercise by pharmacists of their professional role.

Professional activities which should be specifically remunerated might include:

a. Work done in collaboration with doctors, either in individual practices or at health centres, to improve the effectiveness and reduce the cost of prescribing. This would also cover work done as a member of a drug and therapeutics committee.
b. Advice to patients on response to symptoms, which may or may not then lead to the sale of a medicine. It would be preferable to make a standard payment in respect of this work. (It would hardly be sensible to charge the individual for a consultation with a pharmacist when he could visit his doctor free.) There is a variety of ways in which it would be possible to define the work for which payment is to be made and to monitor that it has been done. These include specifying the facilities that have to be provided to qualify for various levels of payment, and the keeping of simple records. We consider it quite wrong that payment for this important work should be hid-

den in a general sum, the amount of which depends on the quite irrelevant consideration of the number of NHS prescriptions dispensed.

c. Services provided to individual patients on long-term or complicated medication. These might include the elderly, the mentally handicapped and the mentally ill. One possibility would be for payment to take the form of a capitation fee for patients opting to register at a single pharmacy.
d. Domiciliary activities and attendance at clinics.
e. The supply of an appropriate range of pharmaceutical services to NHS and other publicly owned residential establishments.
f. Health education.

Appendix II

6.2 *Quality of Drugs*

6.2a *Drug Adulteration and Dumping* [15]

During the Commonwealth Pharmaceutical Association Conference held in Nairobi in March 1987, Sam Agboifo, the representative from Nigeria touched on a very sore point which made all delegates stop and think.

It appears that in his country it is very common practice that drugs arrive at patients in an identically packed but adulterated form. He showed us two identical packs of Ambaxin and asked everyone to try and identify any differences between them. This was impossible to do since they were absolutely identical with the expiry date, batch no., designation etc. on both. In actual fact one was the genuine drug, the other had its capsules filled with talc! This seems to be rampant practice in Nigeria with, naturally, the fake drug selling at a cheaper price and the public complaining about the price of the actual drug. He did mention the suspicions of his Association as to which countries are responsible for such an unprofessional and criminal practice. These countries seem to be luckily quite far off from our Island. But can we be absolutely sure that no such adulterated drugs are touching our shores? We have had in Malta instances of pirate importation at cheaper prices.

Sam Agboifo explained that if his country was plagued with this problem of drug adulteration one had to try and imagine the magnitude of the drug dumping problem in his country. If completely 'faked' drugs were available freely, was it so difficult to have medicinals with faked dates? And what about generics? Was it so difficult to have generics which have been discarded by other countries for being sub-standard or expired?

What about the quality control measures taken in Malta?

The examples reported in the Chamber's memorandum make us doubtful as to the sufficiency of import controls.

6.2b *Equivalence of Generic Topical Glucocorticoids*

Trade name glucocorticoid formulations, triamcinolone acetonide, fluocinolone acetonide, and betamethasone valerate were compared with the irgeneric equivalents because of increasing substitutions of generic formulations for trade name formulations. The vasoconstrictor assay was the method used for these comparisons. Large differences were found between generic and trade name formulations containing the same steroid in the same concentration in both cream and ointment vehicles. If generic substitutions are to be used for trade name formulations, the physician must be aware that significant differences in therapeutic effectiveness may be expected[16].

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AIDS PREVENTION – A Role for Community Pharmacists

Mary Louise Valentino, Pharmacy Student

'Problems associated with Drug Abuse' clearly fall within the advisory role, which pharmacists should recognize as their present and future area of special responsibility[1]. AIDS is now a pandemic disease and is spreading at an alarming rate among IV drug abusers in many European countries and in the U.S.A. The sharing of syringes and needles contribute significantly to its spread but this may be limited if community pharmacists supply syringes and needles to drug abusers.

Aims

A survey was carried out in community pharmacies as part of the dissertation for the B.Pharm. degree entitled "The Role of the Pharmacist in Drug Abuse Prevention".

A section of the survey concerned the supply of disposable syringes to drug abusers and in what way pharmacists can contribute to prevent drug abuse and the spreading of AIDS.

Method

The survey was carried out on 138 Maltese Community Pharmacies. A questionnaire to analyse the community pharmacists' view on the problem was handed personally to each pharmacist. 61% of the pharmacists filled and returned the questionnaire.

Results and Discussion

Evidence exist that needle sharing is a route for transmission of AIDS virus among I-V drug abusers and that needle scarcity promotes needle-sharing behaviour.

The use of syringes creates debate among pharmacists. Table 1 shows the number and percentage of clients buying syringes from pharmacies. Relatively, there are only 11% who have no young people visiting their pharmacies for syringes compared with the 60% who have.

Table 2 indicates the views of pharmacists about supplying syringes to drug addicts.

The majority of pharmacists (76%) have responded positively as to whether syringes should be supplied to drug addicts to prevent the spreading of AIDS and Hepatitis B viruses.

Table 1: the % of clients buying syringes from pharmacies.

Patients	No.	%
diabetic patients	40	43.5
many young people suspected as drug addicts	23	25.0
only a few young people	33	35.8
no young people	10	10.9

Table 2: The view of pharmacists on supplying syringes to drug addicts.

Statement	No.	%
Do not agree	15	16.3
agree	70	76.0
give, not to cause trouble	1	1.0
makes no difference	6	6.5

These pharmacists understand that not giving syrings will not hinder abusers from using the drugs.

Conclusion

Pharmacists have a role to play in minimising the risk of AIDS in drug abusers by providing syringes/needles and arrange for the safe disposal of used equipment. However built into this role, must be an effort to educate those people on the transmission on AIDS in addition to helping them give up drugs altogether. Dr. M. Sciberras in the October issue of "The Pharmacist" stated that no IV drug abusers attending the Detoxification Centre at St. Luke's Hospital or Caritas Rehabilitation Centre have been reported to be HIV sero-positive but measures must be taken beforehand for its prevention.

76% of the pharmacists agree to give syringes to drug addicts. It would be interesting to see how many would volunteer to take part in a needle exchange scheme.

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Total Cholesterol Levels in the Maltese sausage

Josef N. Grech, B. Pharm.

Abstract

An interesting, but relatively unexplored field in the assesment of the Maltese diet, is the evaluation of the nutritional status of certain traditional dishes and delicacies which, if not endemic to our islands, may only be found in the vicinity of the Mediterranean region. Amongst the more important constituents of such foods, one will most certainly dwell on the cholesterol content of these dishes, this being the most abundant sterol in the body and definitely one with the greatest health implications.

With this perspective in mind a study was undertaken to investigate the total cholesterol levels of the Maltese sausage. Using a semi-enzymatic analytical procedure, the total cholesterol concentration of a particular sample was measured, and the value found to be approximately 1mg per gm. This value could have serious consequences on atherosclerotic patients.

Introduction

The Maltese sausage is a common delicacy on the Maltese Islands and is very often an added entry to most local traditional dishes. It is made up primarily of pork offals enclosed in a gut membrane, either raw or smoked, but the exact constitution and relative abundance of the various pork portions depend very much on the tastes of the sausage maker. As these sausages are traditionally made by hand, there is no standard recipe, and as a result, great variations may exist from one sample to another. Consequently, it was not the aim of the experiment to obtain an absolute value for the total cholesterol content of the Maltese sausages, but nevertheless, to obtain a value which is indicative of the cholesterol content present. Furthermore, the use of the Test conbinations as generously supplied by Boehringer Mannheim GMBH provided an opportunity of evaluating this method of analysis.

Principle and Methodology

Measurement of the cholesterol concentrations was based on the formation of a light absorbing dye in the visible region of the spectrum.

Any cholesterol esters present were first hydrolysed to free cholesterol and fatty acids (Fig. 1). In the presence of oxygen and cholesterol oxirase, the free cholesterol was then converted to — cholestone and finally in a reaction catalysed by catalase, the hydrogen peroxide produced in the latter reaction, oxidised methanol to formaldehyde which subsequently reacted with ammonium ions and acetylacetone to form a yellow lutidine-dye. The concentrations of the lutidine-dye (3, 5-diacetyl —1, 4-dihydrolutidine) formed was measured by the increase of absorbance in the visible range at 405 nm and as this concentration was stoichiometric with the amount of cholesterol, it gave a direct indication of the original cholesterol concentration present.

The analytical procedure was divided into four main operations, namely

1. The standardisation of the spectrophotometer in use as specified by the B.P.
2. The preparation of the test solutions.
3. The treatment of the Maltese sausage prior to assay.
4. The assay and spectrophotometric measurement of the increase in absorbance in the visible range at 405 nm.

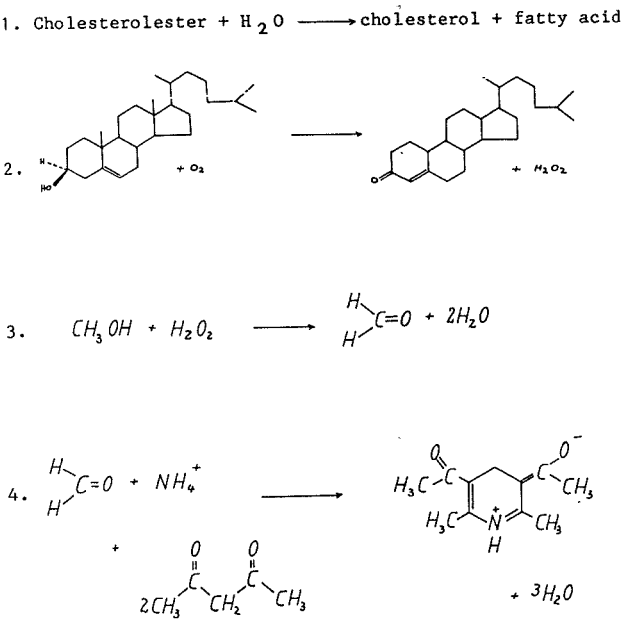

Fig. 1 Hydrolysis of any cholesterol ester present

The British Pharmacopoeia 1980 stipulates various requirements. But only two specifications were considered namely the control of absorbance and the limit of stray light.

In order to achieve the stated stability the test reagents were stored in a refrigerator at +2°C to +8°C prior to use. Furthermore, freshly redistilled water from a glass distilling apparatus was used for dissolving auxilliary reagents. Amongst the test solutions prepared, a cholesterol standard solution was made to give a final standard cholesterol solution of 0.25mg/ml concentration.

However, prior to assay, the sausage sample had to be subjected to a chemical treatment in order to facilitate the extraction of cholesterol present. This involved an initial exposure of a well broken down sample to a volume of 1 Molar methanolic solution of potassium hydroxide in the presence of a quantity of clean sea sand. This sand was previously ashed in an oven to free it from any organic material present. The flask and contents were then heated to 160°C in a waterbath placed on an electric hotplate and refluxed for 25 minutes while stirring with a magnetic stirrer. Repeated reflux and washing with specific volumes of isopropanol resulted in a cholesterol containing supernatant which on filtering gave a clear solution and which could subsequently be assayed.

Each assay run required the addition of further reagents and an incubation period of 1 hour at 37-40°C. This applied to both samples, standard, as well as sample and standard blank solutions respectively. The absorbance at 405nm was monitored using a double-beam spectrophotometer, and by means of a mathematical equation, the cholesterol concentration was determined as a function of the mean value of absorbance. Statistical considerations gave a final value of the cholesterol content per gram of sausage as being equal to 1.315 + 0.579 mg.

Discussion

Although this semi-enzymatic estimation does have its drawbacks, when compared to a fully-enzymatic estimation, it provides, together with the latter, a number of major advantages, namely a high degree of specificity, the absence of the need to deproteinise the sample, and the absence of drug induced interactions.

On the other hand, the major disadvantage of this method are the time consuming hydrolysis which is liable to interference and the tedious but indispensable removal of the reducing substance formed in the course of alkaline hydrolysis. This introduces a wide range of error. In view of this, a fully enzymatic method for the determination of total cholesterol content is suggested in which the conversion of cholesterol is also enzymatic (using cholesterol oxidase) and which occurs under mild and convenient conditions. The accuracy and precision of a fully enzymatic method are thus highly satisfactory and recommended. Furthermore, such a procedure would also offer the opportunity for a differential analysis of the free and esterified cholesterol content in a given sample. This may be achieved by the separate but successive addition of cholesterol oxidase and cholesterol to any assay mixture.

Conclusion

The estimation of cholesterol is of paramount importance both in the food industry, as well as in clinical diagnosis, hypercholesterolaemia being the major risk factor for atherosclerosis and related disorders.

Keeping in mind the methodology involved and the associated range of error one may conclude that the total cholesterol content in this particular sample of Maltese sausage is approximately of 1 mg per gram of sausage. This value has to be seen in the light of the observation that a reasonable 'bite' of sausage by an adult would comprise from 4 to 7 grams of sausage content. One has therefore to evaluate the amounts of total cholesterol taken into the gut on continuous ingestion of this favourite delicacy, especially when the adult eating the sausage may unknowingly be an artherosclerotic subject.

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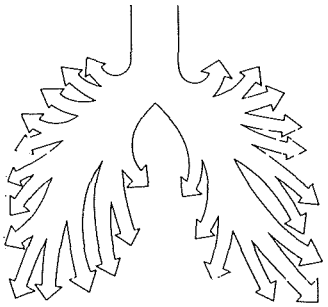

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The Pharmacist Clemente Mifsud Bonnici and his views of the Plague of 1813

Paul Cassar M.D., Ph.C., D.P.M., F.R.Hist.S. (Lond.), D.Litt. (Hon. Causa)

Plague has been no stranger to the Maltese Islands since at least the 13th century. In fact it visited us no less than sixteen times from 1270 to 1945 — the last epidemic on record.

The most severe outbreak — in terms of mortality — was that of 1675-6 with 8569 to 11,300 deaths. The second largest was that of 1813 with 4,676 fatalities[1].

An unpublished account of the 1813 plague comes from the pen of the pharmacist Clemente Mifsud Bonnici who lived through it.

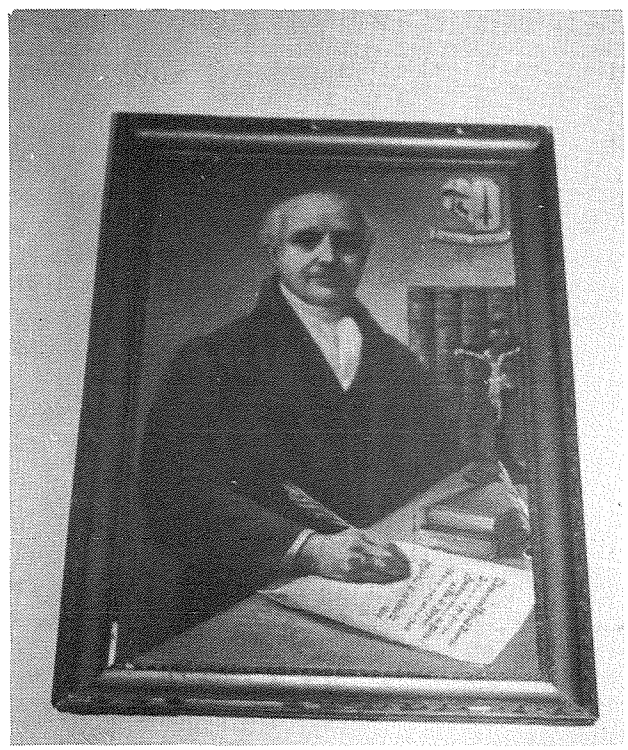
Biographical Outline

We know very little about Clemente Mifsud Bonnici. He appears in public life during the rising of the Maltese in the countryside against the French forces that occupied the Maltese Islands between 1798 and 1800. He was one of the three delegates sent by the provisional Maltese government of Mdina with a letter to the King of Naples asking him to send to Malta "a superior official to hold in check the inhabitants of the countryside".

Having completed this mission he was active at Zejtun where he was attached to the provisional hospital in that area, probably the so called "General Hospital", set up in the "Old Church of St. Gregory". He contributed four hundred **scudi** to this venture and undertook the treatment of the sick in this hospital. He claimed to have "cured them all" after discovering the cause of the "pestiferous illness" that prevailed in those days. He has, however, left us completely in the dark as to the nature of his aetiological discovery and as to the kind of treatment which he employed. His contemporaries referred to the illness as "tertian fever" (malaria?), "influenza" and "typhus" but as no description of the clinical picture has come down to us, it is not possible to identify the disease[2].

Apart from engaging in these medical activities, he also joined the National Battalion as a combatant and took part in the fighting "on various occasions advancing towards the enemy lines and exposing himself to the cannonades and fusilades of the enemy while leading his men".

On the cessation of hostilities he asked government, on July 1801, to be granted some form of employment. His request was only partially met when he was assigned "provisional work" with the Master Mason Antonio Cachia; but we do not know what kind of occupation it was[3].



Clemente Mifsud Bonnici

We then lose trace of him.

He styled himself **aromatario e dilettante di medicina** (a pharmacist and an amateur of medicine)[4] but an inscription in a portrait of him[5] describes him as **Dottore in Medicina.** There are divergencies also between this inscription and the documentary evidence regarding the dates of his birth and death. The portrait bears the words **nato nell'anno 1740** and **morto il 18 Ottobre 1830**; but the **Liber mortuorum** of the Parish Church of St. George of Qormi records his death as occuring on the 28th February 1836 in his ninetyninth year of age which would indicate that he was born sometime during 1737.

He was the son of Joseph Mifsud and Olympia Bonnici and, at the time of his demise, was the

widower of Maria Teresa Falzon[6]. He died at Qormi and was buried in the Parish Church of St. George[7].

Criticism of the medical profession

Clemente begins his manuscript with a bitter criticism of the medical practitioners of his days who, in his words, "either did not want — or else neglected — to treat an illness which is easy to cure because we know what causes it; but which, if neglected especially if it is contagious, extends its roots, spreads and augments the poison which is derived from a daily and extensive mortality. In such a case doctors deserve the title of murderers".

Further on he states that though "the doctor is not responsible (for the origin of the illness) nor is he expected to work miracles, he is still blameworthy on account of crass negligence. In fact had the doctors recognised that the cause of the malady was putrefaction many patients would have been cured and saved from the very beginning (of the outbreak) without so much commotion, without the great expenses incured and without so many sad and dismal consequences".
es".

He accuses the medical establishment "for failing to adopt the measures provided by medical art and, worse still, for abandoning the sick or treating them from a distance of fifteen paces from where (the practitioner) could not see and observe the signs of the patient's illness. Thus forsaking the sick to perish like animals without any succour was certainly a most cruel deed".

"How much trouble," he asks, "anxiety, expense, suffering, destruction by burning of clothes and furniture would have been spared if Maltese doctors were more adept and humane in diagnosing the illness, in seeking the best way of treating it, in not mistaking one malady for another and in refraining from labelling all ailments as plague? How can they be acquitted of their responsibility in their lack of care for the sick and from paying the debt that they owe to Divine Justice for their guilt?"

He condemned the conditions that prevailed at the **baracche** (wooden huts) to which the sick and their contacts were conveyed "under the escort of so many guards armed with swords, pistols and every kind of weapon... and then exposed to the heat of the sun and the bad air polluted with the transpiration from dead bodies: and making them lie on a thin layer of straw on the bare ground... To describe in detail all that occurred in these **baracche** will fill a large volume".

He rebukes the sanitary authorities for isolating the sick and for restricting the freedom of movement of healthy people. He draws a comparison with the actions taken by the countries of the Levant to deal with the control of plague. "No doctors are required", he states "no precautions are taken, no expense is incurred, no separation (of the sick from the healthy) is resorted to... and yet experience has shown that in a very short time the plague, or to be more exact, the concentration of the contagion, comes to an end". And he further comments: "It is surprising that in the Levant not only no (sanitary) precautions are taken but the healthy continue to communicate and trade openly with the plague stricken and to make use of their clothes and linens".

Speculations regarding the cause of the malady

From the very beginning of the malady, Clemente was convinced that its cause was the "bad and putrid grain consumed by low class people and the poor". He argues that "putrid" food produces a "putrid" illness which if not treated, or which is inadequately managed, causes not only the death of the patient but also affects those exposed to the "heat" that exhales from the patient; in this manner the illness spreads resulting in a great disaster. He supports his thesis regarding the cause of the malady by calling to his aid the "evidence of authoritative physicians from Hippocrates onwards who affirm that bad bread always produces epidemics of putrid illnesses and, sometimes, even the plague".

He condemned the importation of grain from Alexandria (Egypt) where the grain could be spoiled by exposure to the "pestiferous lakes of the Nile". The consumption of bread made of putrid grain underwent fermentation, decomposition and putridity once it reached the stomach; this process produced such symptoms as headache, vertigo, delirium, bleedings in the skin and tumours and even worms which, feeding on the putrid material, sicken inside the intestines and kill their hosts". According to Clemente the highest mortality occurred among the low classes who, because of their poverty, had no choice and were constrained to eat bad bread that "was only fit for dogs and that, owing to its offensive smell would upset the stomach of an ostrich".

In opposition to the "contagious" theory of the malady upheld by the medical establishment he advanced the following two arguments. First, he claimed that during the French blockade of Malta (1798-1800), while he was with the Maltese insurgents in the countryside, he had treated a malady which carried off thousands of persons with manifestations similar to those of the 1813 epidemic. He decried the fact that no doctor would perform post mortems in an attempt to unravel the aetiology of the disease that ravaged the countryside during the blockade; and, therefore, not knowing the cause of the illness no remedial measures could be taken to fight it. "The heat", he states, "emanating from the patients infected others and the epidemic spread to such an extent that in one village alone there was a mortality of 15 to 20 persons a day. I mustered all my courage, asked and obtained permission to treat the sick and also to carry out necropsies which in fact I did. By the grace of God I thus succeeded in discovering the cause of the malady which was none other than one of "putridity caused by the consumption of bad bread". He, thereupon, applied the remedies suggested by his experience and by the help of the Almighty succeeded not only in curing the remaining patients without the loss of any of them but also in preventing attacks (in others)".

His second argument refers to the 1813 outbreak. "That the current illness", he observes, "is of an epidemic nature and not plague is proved by the fact that the military personnel remained exempt from the illness except for a few soldiers who had sold their wholesome bread and bought and consumed the (cheaper bad) bread of the poor. Apart from all this none of the thousands of seamen in our harbours who eat biscuits (and not bad bread), suffered the minimal ailment".

The end of the malady

Clemente ends his manuscript on a note of hope and almost euphoria for in the midst of so much suffering he discerns not only the intervention of the punishing hand of the Almighty for man's depravity but also His Divine Clemency through the appointment of a new Governor or Malta by His Britannic Majesty. The manuscript does not name him but the reference is to Sir Thomas Maitland who arrived in Malta in October 1813 and under whose administration Malta began, "step by step to experience such relief that in the very brief period of two months, if not less, Valletta, Floriana, The Three Cities and seventeen villages became free of contagion". Such an improvement was attributed by Clemente to Maitland's "paternal care, under the guidance of our Divine Mother, for the relief of the indigent, for his stern instructions to the doctors as to how to deal with the malady... and to his personal surveillance over the moral and material conduct of all classes of the Maltese population".

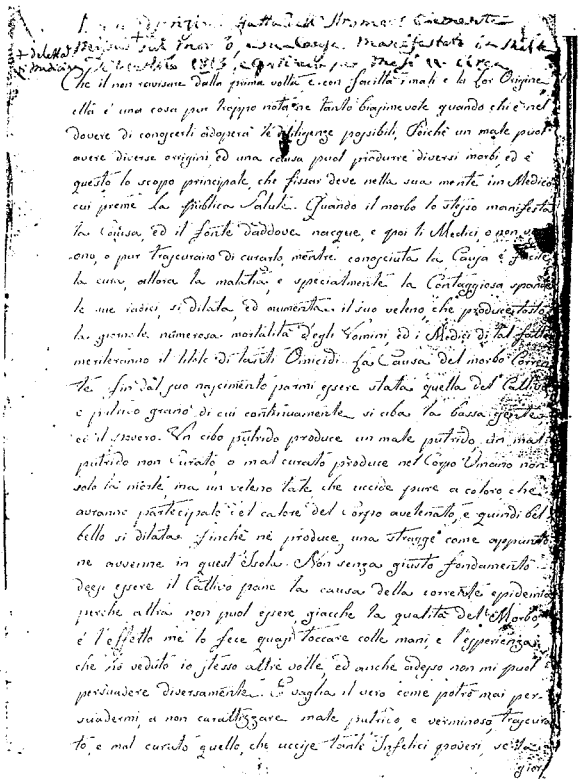
In his final paragraph he erupts in a flourish of praise for the new Governor: "This man will be our comfort and our peace; under his aegis we shall be happy and contented. He shall be our guide, our leader and our father; and after God and our Sacred Christian Religion he shall be the culmination of our consolations. Let us praise God, therefore, for sending us this man. Long live His Britannic Majesty who appointed him! Long live our Governor. May God preserve him for ever to the shame of the malefactors who OPPRESS US!"

Clemente penned these last words in the ninth month of the outbreak i.e. January 1814 Plague, however, although on the decline had not yet ceased. In February it invaded Xagħra, Gozo, and until the beginning of March it still raged at Qormi. Free pratique for Malta and Gozo was ultilmately proclaimed on the 8th September 1814.

Discussion

Clemente Mifsud Bonnici raised a number of questions which he leaves unanswered. What provoked his hostile attack on the Maltese medical and sanitary establishment? Did it stem purely from a divergence of medical views about the aetiology and pathogenesis of the epidemic as held by Clemente in contrast to the orthodox one sustained by his medical contemporaries? Was it motivated by humane sentiments of sympathy for the sufferings of the sick, or was the spirit of dissent the outcome of some personal issue?

Was his manuscript ever published? I have found no evidence that it was. So why was it written at all? Or if he meant to publish it, what kept him from doing so? Did hand-written copies of it come to the knowledge of the medical profession or of the government? Did it provoke the wagging finger of official disapproval? Or some form of penalty as envisged by government for those who spread mislead-



The first folio of the manuscript by Clemente Mifsud Bonnici in which he describes the events of the plague of 1813 as seen by him (Ms. 1318 National Malta Library).

ing notions as to the nature and causation of the plague?[8].

On the whole the manuscript gives the impression that much is left untold but in the last paragraph there are hints — though very vague ones — which seem to show that Clemente had an axe to grind not only with his medical contemporaries but also with the government administration. How else, one may ask, can we interpret his relief at the appointment and arrival of a new British governor under whose "paternal care" the plague began to recede and the future started to look bright "to the shame of the malefactors who OPPRESS us" (the capital letters are his). This is the only part of the manuscript where Clemente uses the plural "us" instead of the first person singular "I". Does "us" mean the "people"? If so, is this not an indication of some politico-medical animosity at the root of his attacks against the medical profession and the government administration?

However that may be, there is a final irony to this controversy i.e. that at the end of it all, both sides were wrong as their speculative aetiological concepts were very far from the scientific truth regarding the causation and the path of transmission of plague.

The causes of plague and its chain of transmission

The aetiology and chain of spread of plague were discovered in 1894 when it was established that the disease was caused by a bacillus and that the infection in man was associated with a plague epizootic among rats; while it was only in 1897 that it was shown that the rat flea (and sometimes the human flea **Pulex irritans**) were the intermediaries between rodents and man[9].

The rats implicated are the jet black **Rattus rattus** and the brown-grey sewer rat **Rattus norvegicus** which become infected by the bacillus **Yersinia pestis** (formerly called **Pasteurella**

pestis). The microbe passes from one rat to another by the rat flea **Xenopsylla cheopis.** When feeding on an infected rat, the flea ingests the bacillus and then, feeding on a healthy rat, injects the bacillus in the blood stream of the latter. An epizootic among rats thus occurs. When the plague-stricken rats die, the flea harbouring the **Yersinia pestis** in its stomach, turns on human beings as its new hosts and injects them with the bacillus.

In human beings the bacillus may travel via the lymphatics to reach the lymph nodes in the armpits, neck and groins. The nodes become inflamed and swollen forming an abscess called bubo — hence the name of bubonic plague; or else it may invade the blood stream producing bleedings of small blood vessels on the skin manifested as black or blue blotches or patches. This is the septicaemic form of plague.

Patients with either bubonic or septicaemic plague may develop pulmonary lesions if the bacillus lodges in the lungs causing a rapidly fatal pneumonia (pneumonic plague). This is the most infectious type of plague as it spreads from man to man directly by means of droplets from the coughing and sneezing of the patient[10].

Nothing of this was known to Clemente and to the medical profession in 1813. Interestingly enough, however, some medical observers, including Avicenna or Ibn Sina (980-1037 A.D.), had noted that a massive mortality among rats heralded an outbreak of plague among humans; while another commentator of the 15th century stated that plague was brought about by fleas and vermin[11]. Centuries later, during the 1813 plague of Malta, some medical practitioners observed that people living in cellars and ground floors of houses were more often attacked than those who occupied the upper floors so that the plague became known as the disease that "seldom went upstairs". The real significance of this observation, however, eluded them i.e. that the plague-carrying rats with their fleas were more likely to inhabit cellars and ground floors than the higher parts of the house[12]. Thus from the 10th to the 19th centuries there was a failure to perceive the link between the rat and its flea and an outbreak of plague among humans.

At the time that Clemente was penning his manuscript there were two main theories concerning the aetiology and dissemination of plague: (a) the contagion theory which held that the disease was spread by contact with plague-stricken persons or with their clothing or other personal effects; this was the general medical thinking in Malta; and (b) the miasma theory which attributed plague to pollution of the air by foul odours and decaying matter.

Clemente dissented from both these views and attributed the cause of the plague to "the bad and putrid grain consumed by low class people and the poor".

As we have seen, subsequent medical progress discredited not only the long-held theories of the orthodox medical establishment but also the over-confident claims of Clemente so that both exponents were proved wrong. We must not, however, judge their failures, in the first decade of the 19th century, by the hindsight of the achievements registered in the last decade of the same century when the role of the microbe, the rat and the flea in the causation and transmission of plague became known. Thus while Clemente's manuscript falls completely short from the scientific angle, it is not without merit. It is in fact a vivid evocation of the psychological impact and of the feelings of frustration and despair experienced by a helpless community threatened by a formidable but unseen enemy that lurked everywhere and relentlessly struck at life and disrupted the social and economic organization of the Maltese Islands. Another value of the manuscript is that while it shows that its author was mistaken scientifically, it gives him stature for his boldness in breaking away from the orthodox — and equally false — thinking and convictions of his medical and administrative contemporaries.

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(7) I am indebted to Mgr. Annetto Depasquale, Vicar General, and to Canon Carm. Aquilina, Archpriest of St. George's Parish Church, Qormi, for a copy of the Death Certificate.
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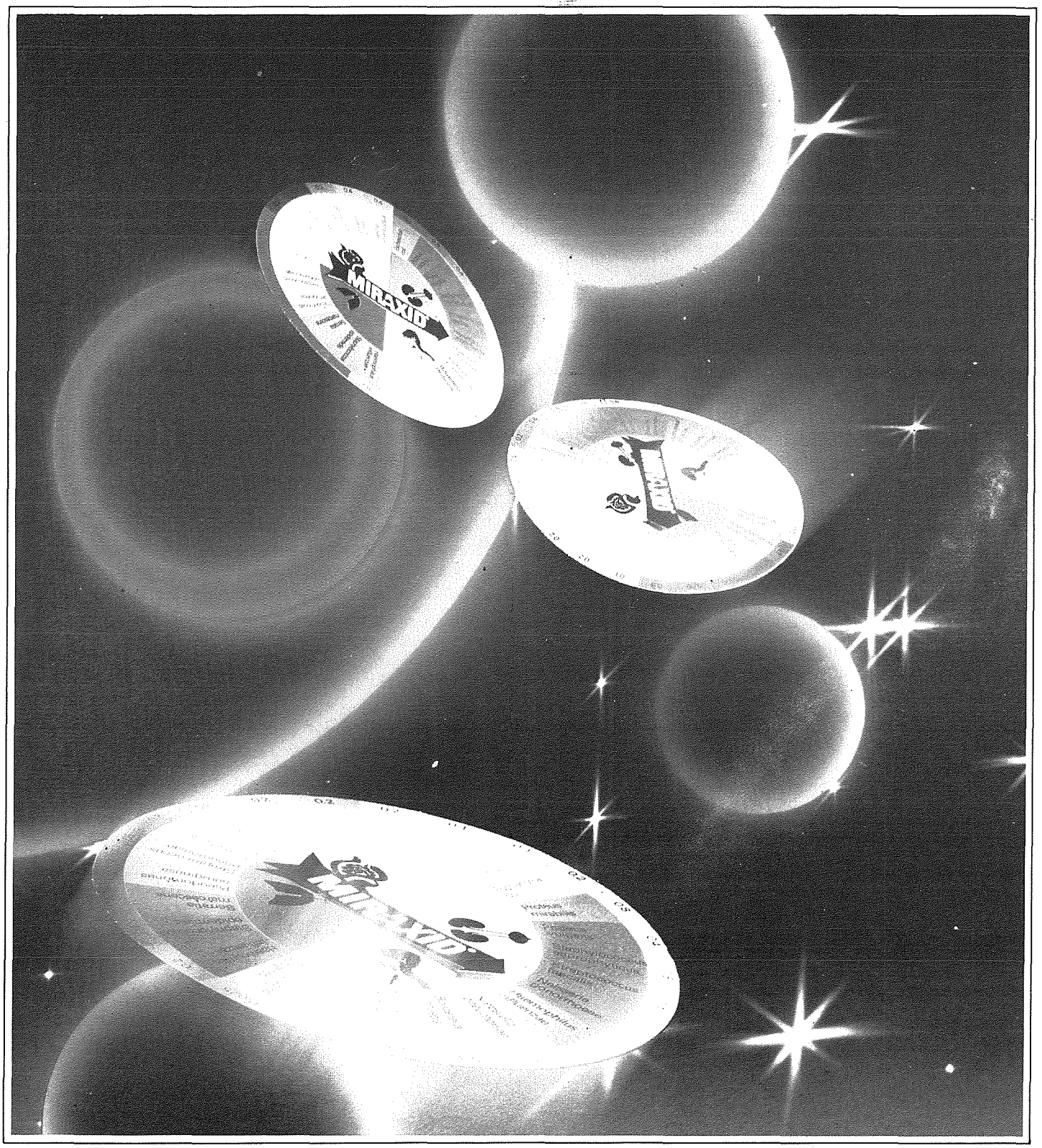

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Clinically Important Drug Interactions

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A Morass of Irrelevant Information

Much attention has been focused on adverse drug interactions during the last 15 years or so, and as a result many drug-drug interactions are now predictable and many of the unwanted consequences of using drug combinatious can be avoided by simply adjusting the dosage of one or more of the interactants. As a result of this, there has been a considerable improvement in the safety and efficacy of therapy with drug combinations.

Unfortunately, however, because much has been written and published with a lack of clinical perspective, the literature has become clogged with a sticky and inpenetratble morass of irrelevant information much of which has been generated in animal studies or in single-dose pharmacokinetic studies in healthy subjects usually drawn from a young adult age group. Such studies can be of predictive value, but only if they mimic the clinical situation and if they relate to drug combinations and dosage regimes that are normally used in sick patients. Likewise a large number of uncorroborated or anecdotal observations on individual patients have appeared. These are useful if they stimulate other clinicians to report similar experiences in their own patients. However, if other reports are not forthcoming then the original report should be regarded as idiosyncratic and be accepted with some reservation as to its generality.

Currently much information is appearing in the literature usually from pharmaceutical research sources on drug-interactions **in vitro**; these can be useful and may indeed indicate possible mechanisms by which drugs or formulation components interact; they may indeed act as an 'early-warning' system and prevent interactions occurring in the clinic. **Per se**, however, they are of limited value unless confirmed **in vivo**, preferably in man.

There is a need therefore to focus attention on those drug-drug interactions which really do influence the efficacy or safety of human drug therapy in all age groups, especially the elderly or very old patients. Fortunately only a relatively small number of drugs enter into those interactions which present clinical importance or life-threatening clinical emergencies. The drugs in these two categories include: anti-arrhythmic agents (especially quinidine), anti-coagulants (especially warfarin), anticonvulsants (notably phenytoin), beta-blockers,H -receptor blockers (especially warfarin), anticonvulsants (notably (mainly digoxin), lithium salts, oral contraceptives, hypoglycaemics, psychotropics (antidepressants and neuroleptics), theophylline, and the immunosuppressants (notably cyclosporin).

It may be noted from this list that most of the drugs involved in clinically relevant interactions are those on which patients are carefully stabilised for relatively long periods. It may also be deduced that many of these patients will be in the older age bracket. Past-experience has clearly shown that it is these drug-stabilised patients who are at special risk of any changes in therapy or environment which will influence the potency or availability of their normal medication. It should also be clearly understood that removal of a drug from a stabilised regimen of treatment may also initiate a serious interaction sequel.

It is not possible within the space allocated to this presentation to discuss all the clinically relevant interactions that occur with the list of drugs that has been detailed. Instead it is intended to concentrate on interactions involving four of the groups of drugs that have been mentioned: the anticoagulants, H -receptor blockers, oral contraceptives, and the immunosuppressants. These will serve to illustrate the types of problems that can occur and how these may be prevented or managed in the clinical situation. Information on the other drugs and their interactions is listed in The Griffin, D'Arcy and Speirs 'Manual of Adverse Drug Interactions'.

Anticoagulants

Warfarin interactions may take place at virtually all stages of its pharmacokinetic progress through the body including absorption, distribution, and metabolism, as well as at the receptor site (the pharmacodynamic phase). In addition, since the main action of the anticoagulants is an inhibition of the vitamin K-induced sythesis of blood clotting factors, it follows that any other drugs (e.g. oral contraceptives) affecting these clotting factors will modify the overall response to warfarin as well. The result of these interactions (see Table 1) may be to potentiate the therapeutic response to warfarin (a drug with a narrow therapeutic 'window') which may lead to uncontrollable haemorrhage. A comparatively mild symptom of moderate overdosage of warfarin can be excessive bruising which should alert the clinician that something is starting to go wrong with the patient's anticoagulation status. Alternatively, the efficacy of warfarin may be decreased (Table 1) and a thromboembolic condition may develop or worsen. It should be noted from the drugs listed in the table that the non-steroidal anti-inflammatory agents are well represented among treatments that are capable of potentiating the anticoagulant effects of warfarin, while enzyme inducers will antagonise the therapeutic action of the anticoagulant. Many of these drugs are commonly used in the elderly patient and it may well be this age group that is likely to suffer the greatest hazard from such interactions.

Table 1 Drug interactions involving anticoagulants

Mechanisms	Effect	Examples
Inhibiton of vitamin K absorption from gastrointestinal tract	Potentiation of oral anticoagulant	Cholestyramine, liquid paraffin
Inhibition of vitamin K synthesis by gut flora	Potentiation of oral anticoagulant	Aminoglycoside antibiotics cephalosporins, penicillins, sulphonamides, tetracyclines
Alteration of absorption of coumarin anticoagulants from gastrointestinal tract	Reduces the efficacy of oral anticoagulants	Antacids
Displacement of coumarin from plasma-binding sites	Potentiation of oral anticoagulant	Non-steroidal anti-inflammatory agents, e.g. aspirin, indomethacin, ketoprofen, naproxen, phenylbutazone, sulphonylureas, e.g. chlorpropamide, metachlorpropamide, tolbutamide
Enzyme induction reducing coumarin plasma half-life	Reduces the efficacy of oral anticoagulant	Barbiturates, glutethimide, griseofulvin, meprobamate, phenytoin, tybamate
Inhibition of the metabolic breakdown of coumarin	Potentiation of oral anti-coagulant	Tricyclic antidepressants, xanthine oxidase inhibitors, e.g. allopurinol
Interacting drug increases the synthesis of blood-clotting factors	Reduces the efficacy of oral anticoagulant	Oral contraceptives, xanthines e.g. choline theophyllinate (Choledyl), theophylline containing medicines (Franol)
Interacting drug reduces the synthesis or increases the catabolism of blood-clotting factors	Potentiation of oral anti-coagulant	Anabolic steroids, cholestyramine, propylthiouracil, quinidine, quinine, thiouracil, thyroxine
Potentiation of inherent fibrinolytic activity	Potentiation of oral anti-coagulant	Biguanides, e.g. metformin
Multiple mechanism of interaction	Variable	Clofibrate, dichloralphenazone

H -receptor blockers

The histamine H -receptor blocker, cimetidine, has well established clinical use mainly in the treatment of peptic ulcer disease. This clinical use has also clearly indicated the extent to which cimetidine may participate in drug interactions. Early work by clinical investigators showed that cimetidine potentiated the anticoagulant effects of warfarin and suggested that it did so by inhibiting hepatic microsomal enzyme oxidase activity. It was also predicted from this that cimetidine might also interact with other drugs that were metabolised by liver microsomal enzymes.

That this prediction was justified has been well shown by subsequent reports in the literature and it is now certain that cimetidine has the potential to interact with a wide range of drugs including some benzodiazepines (diazepam, chlordiazepoxide, prazepam, nitrazepam, alprazolam), carbamazepine (conflicting reports), chlormethiazole, morphine (conflicting reports), metronidazole, phenytoin, theophylline, flecainide, and digitoxin/quinidine (a double interaction) due to inhibition of liver enzymes. It has also become evident that cimetidine will potentiate the actions of the beta-blockers propranolol, labetalol, and metoprolol, but not atenolol, by mechanisms that may be related to reduced liver blood flow. Cimetidine is also reported to inhibit the tubular secretion of both procainamide and n-acetylprocainamide in man and this interaction may necessitate dosage adjustments of procainamide in patients being treated concomitantly with both drugs. The more commonly reported interactions involving cimetidine are summarised in Table 2.

The literature on interactions involving cimetidine has become almost voluminous and to save space in this present context the reader is referred to primary reference sources that are cited in the following reviews: Bauman and Kimelbatt (1982), Sorkin and Darvey (1983), Griffin, D'Arcy and Speirs (1988), and Penston and Wormsley (1986).

In view of the conflicting therapeutic indications for cimetidine and the anticoagulants, it is not altogether surprising that, apart from the early studies on the cimetidine-warfarin interaction, there have been relatively few cases of prolongation of prothrombin time by cimetidine in patients taking warfarin. Indeed of 9907 patients identified in an American, post-marketing, outpatients surveillance programme as receiving cimetidine, only nine cases of haematological problems were reported. Of these only a single case was considered to be related to a cimetidine-anticoagulant (Gifford **et al.**, 1980). Furthermore, evaluation of a world-wide spontaneous reporting system indicated that 0.4 per 100,000 patients, who had previously been stabilised with oral anticoagulants, required re-titration after the start of cimetidine therapy (Davis **et al.**, 1980). It is therefore of interest that Kerley and Ali (1982) have reported that this type of interaction was responsible for the development of a huge retroperitoneal haematoma which was life-threatening to their 19-year-old patient.

Ranitidine is thought not to have an inhibitory effect on hepatic microsomal enzymes and would therefore not enter into interactions with

Table 2 Drug interactions involving cimetidine

By inhibiting hepatic microsomal enzyme oxidase activity, cimetidine potentiates the activity of the following drugs:
Anticoagulants, e.g. warfarin
Benzodiazepines, e.g. chlordiazepoxide, diazepam, prazepam but not lorazepam or oxazepam.
Carbamazepine (neurological toxic symptoms)
Chlormethiazole (significant increase in sedation)
Digitoxin/quinidine combination (resulting in cardiotoxicity)
Morphine (a potentially lethal interaction)
Phenytoin (rash or signs of intoxication)
Theophylline (half-life increased, potential toxicity)
By reducing hepatic blood flow (?), cimetidine potentiates the activity of the following drugs:
B-blockers, e.g. propranolol, metoprolol, labetalol, but not atenolol
The activity of cimetidine is reduced by the following drugs:
Antacids (reduced bioavailability with Al/MgOH containing preparations)
Metoclopramide (bioavailability of cimetidine reduced by 20-30%)
Propantheline (bioavailability of cimetidine reduced by 22%)

warfarin or other drugs that are metabolised by the liver. However, ranitidine may enter into interactions by mechanisms other than enzyme inhibition since, like cimetidine, it reduces blood flow in the liver, and could impair the hepatic elimination of a small number of drugs like propranolol or lignocaine which are highly extracted by the liver and whose systemic clearance is highly dependent upon liver blood flow. Exploratory studies in healthy subjects have, however, been controversial and conflicting in their results.

Oral contraceptives

Interactions involving the combined type (oestrogen plus progestogen) oral contraceptives are often ususpected and even unestablished. The sequel, an unplanned pregnancy, is often mistakenly blamed by the consulting physician on to poor subject compliance with medication instructions. Evidence has started to accumulate that neither the patient nor the "pill" is at fault in some contraceptive failures. It may be because the patient is taking other medicines and these may be preventing the pill from suppressing ovulation.

Most drug interactions reducing or negating contraceptive activity are due to concomitant use of drugs having microsomal-enzyme inducing activity (e.g. some antibiotics, especially rifampicin, and anticonvulsants, including phenytoin, phenobarbitone and primidone. Other antibiotics (e.g. tetracycline) may also interact by interruption of the enterohepatic circulation of contraceptive steroids.

Less well appreciated, oral contraceptive steroids may themselves modify the metabolism and pharmacological activity of various other drugs (e.g. anticoagulants, benzodiazepines, beta-blockers, corticosteroids, and antidepressants); in this respect the oral contraceptives are acting as enzyme inhibitors.

Contraceptive steroids may also interact with drugs that cause enzyme inhibition and this delays the metabolism of the hormonal agents. Interactions of this type would be expected to potentiate the action of the contraceptive steroids. It is suggested that the effects of such interactions might be presented in terms of increased incidence of side-effects, including water retention, diabetogenic effects, hypertension, and an increased risk of thromboembolic disorders.

The spectrum of interactions with oral contraceptives is summarised in Table 3. A more detailed account is given in a recent review on drug interactions with oral contraceptives (D'Arcy, 1986).

Table 3 Drug interactions involving oral contraceptives

Drugs implicated (or suspected of implication) in oral contraceptive failure	
Class of drug	**Individual drugs implicated**
Antibiotics	Ampicillin, rifampicin, tetracycline
Anticonvulsants	Phenobarbitone, phenytoin, primidone
Cholesterol-lowering agents	Clofibrate
Non-steroidal anti-inflammatory agents	Phenylbutazone
Hypnotics and sedatives	Barbiturates, chloral hydrate and derivatives, ethchlorvynol, methaqualone
Drug activities modified by oral contraceptives	
Aminocaproic acid	Possible hypercoagulable state; oestrogen augments blood levels of clotting factors VII, VIII, IX, and X
Anticoagulants	Reduced anticoagulant efficacy; oestrogen increases plasma concentration of clotting factors. NB. patients on oral contraceptives should not be anticoagulated and no patient on anticoagulants should take OCs
Antidiabetic agents	Increased requirements for insulin and oral hypoglycaemic agents may occur
Antihypertensives	Reduced efficacy of guanethidine, cyclopenthiazide, and methyldopa possibly due to contraceptive-induced Na and fluid retention
Pethidine (meperidine)	Possible increased analgesia and CNS depression due to inhibition of metabolism of pethidine
Phenothiazines and drugs causing breast enlargement	Phenothiazines, reserpine, imipramine, chlordiazepoxide and chlorprothixene increase prolactin secretion resulting in mammary hypertrophy and galactorrhoea: this effect is potentiated (at the breast) by oestrogen and progesterone combinations
Troleandomycin	Pruitus and jaundice followed combined use of OCs and this antibiotic. Both components have been reported separately to cause jaundice.

Immunosuppressants

Reports of interactions involving immunosuppressant agents have largely centred on cyclosporin (ciclosporin). Such reports include a cyclosporin-methyltestosterone interaction in a kidney graft patient that resulted in severe cyclosporin toxicity. A cyclosporin-erythromycin interaction in a similar transplant patient resulted in a four to five-fold increase in blood cyclosporin concentrations. Also, seriously, five case reports from Jones **et al.** (1986) related to an interaction between cyclosporin and sulphadimidine that resulted in inadequate immunosuppression in orthoptic cardiac transplantation.

The latest interaction reported is between cyclosporin and the calcium channel-blocking agent, diltiazem; the interaction resulted in greatly increased cyclosporin blood concentrations due to interference by diltiazem in cyclosporin clearance. (Grino **et al.**, 1986; Pochet and Pirson), 1986).

It is clear from such reports that cyclosporin is metabolised extensively by hepatic enzyme systems and that drugs which inhibit the P-450 enzyme system will reduce cyclosporin clearance and that drugs which induce liver enzymes will enhance cyclosporin clearance and reduce its immunosuppressant activity (Table 4).

(Cont. on page 35)

Table 4 Drug interactions involving cyclosporin

Corticosteroids Erythromycin Ketoconazole Methyltestosterone	increased cyclosporin serum levels resulting in enhanced graft acceptance, or nephrotoxicity*
Phenytoin Rifampicin Sulphadimidine Trimethoprim	reduced cyclosporin levels and endanger the transplant**

*Less well substantiated reports with: cimetidine, danazol, diltiazem, cotrimoxazole, thiazides and oral contraceptives.

**Less well substantiated reports with: carbamezepine, isoniazid, and phenobarbitone

Aminoglycosides (Gentamicin, Tobramycin) Amphotericin Melphalan Sulphonamides/ Co-trimoxazole Trimethoprim	enhanced/additive nephrotoxicity*

*less well substantiated reports with acyclovir, some cephalosporins, etoposide, frusemide, indomethacin, mannitol and ranitidine.

Interactant	Sequelae
Cyclophosphamide	increased/additive hepatotoxicity; possible leucopenia
Diuretics (K retaining)	possible hyperkalaemia
K supplements	possible hyperkalaemia
Etoposide	increased toxicity and antineoplastic effects
Frusemide	increased/additive hepatotoxicity
Minoxidil	increased/excessive hirsuitism
Oral contraceptives	incerased/additive hepatotoxicity
Phenytoin	increased phenytoin levels due to decreased hepatic metabolism
Prednisolone	increased prednisolone levels due to decreased hepatic metabolism
Propranolol	antagonism of immunosuppressive effect (animal studies)
Ranitidine	increased/additive hepatotoxicity
Vaccines	reduced efficacy of vaccine prophylaxis
Verapamil	increased immunosuppression

ADDENDUM

Pharmacists of old

Chev. Joseph Borg, K.M., Ph.C., L.P.

I am recording the names of our dear fellow-Pharmacists who left to join their Creator. I do hereby offer my and your sincere condolences to their respective families or relatives.

155. Pharmacist Aldo Henry Camilleri born on 20th December 1932 at Sliema, was the son of Maestro Joseph and his wife Maria nee Falzon. He studied at St. Catherine's High School (1937-1939) and at St. Joseph Convent (1939-1944), both at Sliema, at the Lyceum, Valletta (1945-1950) and at the University (1951-1956) whence he obtained his L.P. diploma in 1952 and his B.Pharm. degree in 1956. He was the Managing Apothecary of his 'Ta' Xbiex Pharmacy" in Testaferrata Street, Msida. He lived at No. 40, St. Vincent Street, Sliema. He married Miss Isabel nee Camilleri Galea. His brother is an Assistant-Pharmacist (1959) Herman and his sister Antoinette is the wife of our fellow-Pharmacist Mario Fava while his mother-in-law is Pharmacist Gaiety (sive Gaetana) Camilleri Galea. He died on 8th March, 1987.

156. Pharmacist Tarcisio Vella, from Cospicua was born on 23rd November 1922, son of late Salvatore and his wife Mary nee Cini. He was educated at the Valletta Lyceum (1932-1935), at the Archbishop's Seminary (1936-1939) and at the Royal University of Malta (1944-1947), whence he obtained his Ph.C. in 1948 and B.Sc. in 1946. He was Secretary of the Students' Representative Council in 1947. He married Miss Costanza De Ross on 27th December 1951 and they have a daughter Giorgina and a son Sergio. Sergio is married to Astrid and they have a son Alain. Tarcisio managed his own pharmacy (1950-1956) and subsequently was Assistant-Technical Manager of the Firm Edible Oil Refining Co. (1957-1958) becoming Technical Manager of the Firm Sun Chemicals Ltd. since 1960. He was also Lecturer and Demonstrator of Pharmacognosy at our University during 1957-1960, and Member Examining Board of the Faculty of Science. He was an Associate of Production Engineers of England. He was also Consultant Engineer of the Firm Poultry Products Ltd. During World War II he served in the 21st Battery of the 11th H.A.A., R.M.A.(T). He lived at No. 160/21, "Tower Mansions", Tower Road, Sliema. Tarcisio died aged 64 on the 20th May 1987. May our dear Tarcisio rest in God's peace.

157. Pharmacist Joe Philip Sciberras was born on 9th October 1940, son of Joseph and his wife Josephine nee' Fenech at St. Paul's Bay. He attended the Lyceum and the University, whence he graduated B.Pharm. on 28.3.1962. He married Miss Christina Borg on 7.8.1965 and they had a son, Joseph and a daughter, Penelope. He was the owner of "Mayer Pharmacy", 33, Ta' Xbiex Sea Front Msida. He was a Founder-Member of the Commonwealth Parliamentary Association 1969, President of the Malta Union of Pharmacists (1969-1973) and was a Member of Parliament (Labour) since 1976. He was also Chairman of the Commission for Higher Education, Malta's Permanent Representative to Council of Europe (1982-1986), was chosen Parliamentary Secretary at the Office of the Prime Minister responsible mainly for the Ports and Water Departments (1986-1987) and was Honorary President of St. Joseph Football Club - Msida and the Pietà Hotspur Football Club. He lived at 'Xibobo', Triq il-Għenba, Attard. His recreations were gardening and fishing. Our dear fellow Pharmacist Joe died suddenly, while fishing from his motor-boat, on Sunday 29th November 1987 aged 47 years. May he rest in Peace.

158. Pharmacist Leopold Falzon was born on 26.1.1919 in Valletta. He attended the Pharmaceutical Course 1939-1942 and obtained his Diploma (Reg. No. 7) in 1943.
He married Lily nee' Zammit and had two sons, Joseph married to Doris and Stephen married to Ninette, and three step-daughters, Agnes married to Mr. Joe Mulligan, Vivienne married to Mr. John Gardener of U.K. and Lina married to Mr. Godwin Cauchi.
He was employed in several community dispensaries until he joined the Government Service as Pharmacist at the Health Department on 1.10.1963 and served at the Medical Stores in Gwardamanga and subsequently as Pharmacist-in-charge of the Dispensary at Boffa Hospital at Floriana; and when he went on pension on 26.1.1979 he was employed at Collis and Williams Pharmacy in Republic Street, Valletta until his death. His hobby was the study of and research about the British Naval History since the very beginning of the last century and the commencement of the British stay in Malta: "Magnae et Invictae Britanniae Europae Vox et Melitensium Amor Has Insulas confirmant". My school fellow Puldu was a jolly and happy man and on good terms always with both friend and foe.
He lived at No. 124, St. Ursola Street, Valletta and died aged 69 at St. Luke's Hospital on April 19, 1988. He was older of me by exactly one week 26th January to 1st February, 1919). May he rest in Peace.

159. Pharmacist Emmanuel Attard Bezzina, who obtained his Ph.C. in 1946 was married to Miss Fanny nee' Magri of Birkirkara, who died before him, and they had two sons Charles, married to Marion and Adrian married to Valerie and a daughter Nadya, married to Mr. John Zarb. He

managed his own pharmacy at Zejtun. He was a member of the Labour Party since 1947, was elected to the Legislative Assembly in the 1947, 1955, 1962, 1966 and 1976 General Elections (see my article on 'Pharmacists who were Election Candidates for Parliament', carried in the No. 16 issue of September 1987, pages 32-35), was elected Speaker of the House of Representatives (1971-1976) and then Ambassador to the Federal Republic of Germany, Belgium, Holland, Luxembourg, Austria and the Scandinavian Countries (1976-1981). He lived at No. 40, St. Gregory Street, Zejtun. He died aged 66 at Sir Paul Boffa Hospital, Floriana on 7.10.1988. R.I.P.

160. Pharmacist John Chetcuti Bonavita who was born on 28th October 1910 at Sliema, attended the University whence he graduated as B.Sc. in 1932 and obtained the diploma of Pharmacy in 1933.
He was employed with the Government as Pharmacist in the Medical and Health Department since 10.8.1936, when he was transferred as Analyst of the Milk Marketing Dept. on 20.6.43 when his place as Pharmacist-in-charge of the Central Hospital Dispensary was taken over by myself. He later returned to the Medical and Health Department when he was posted at the Medical Stores where he was soon appointed Senior Pharmacist and Assistant Medical Storekeeper on 30.1.1950 and went on pension on 20.10.1970. Mr. Chetcuti was married to the late Jane nee' Debono born at Gozo, daughter of late Emmanuel and his wife Susanna nee' Abela Carbonese and sister of our late fellow-Pharmacist Emmanuel (see No. 114) and Joseph Gerard (1909-1930-1969; see No. 132), and of the late Archpriest of Floriana the Very Rev. Luigi (1917-1947-1970) and of Captain Frank; they had two sons: Joe married to Carol and Noel married to Miriam. John went into a second marriage with Antoinette and lived at No. 24, Windsor Terrace, Sliema. He died at St. Luke's Hospital on 17th December 1988. R.I.P.

161. Pharmacist William Edward Felice, from Valletta, son of Pharmacist Arthur Robert, M.P.S. (1878-1960; see No. 56 in issue No. 8 of June 1984) and his wife Maria Consiglia nee' Cassar. William was born on 23rd October 1902 and was educated at the Lyceum and our University whence he obtained his Ph.C. in 1947. He married Miss Inez Grech Cumbo on 15.10.1925 and had two daughters, Joan widow of Cecil Agius and Margaret. He was appointed Demonstrator (1957) and later Lecturer (1967) of Pharmaceutics at the University, Acting-Head of the Department of Pharmacy (1968-1970), President of the Chamber of Pharmacists (1960-1968), and was a member of the Royal Society of Health in London. He contested the General Election of 1962 in the 2nd District with the Democratic Nationalist Party when he obtained 329 votes but was not elected.
He managed his pharmacy at No. 95, Sanctuary Street, Zabbar. He lived at No. 37b, Annunciation Street, Sliema and died at St. Lukes' Hospital on 14.3.1989. R.I.P.

(Cont. from page 33)

Conclusion

It must be apparent from this brief account of clinically important drug interactions and the examples that have been cited that most of the drugs involved are those on which patients are carefully stabilised for long periods. Past experience has shown that it is these drug-stabilised patients who are at special risk from any interaction that will influence the potency or availability of their medication. This is especially so for the elderly patient who is at a substantially greater risk than the younger patient of experiencing adverse reactions to medication.

It must be clearly understood, however, that drug interactions **per se** are no threat to the patient; most of the adverse events that they cause are capable of speedy reversal. Their real threat is the practitioners' ignorance either through lack of knowledge of the interaction, or through lack of adequate observation of the patient and the proper interpretation of new events. It is under such circumstances that interactions become dangerous.

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Except for specific points, statements in the text have not been referenced to source largely because of the number that would have been involved. Much of the text has been abstracted from Griffin, D'Arcy and Speirs 'Manual of Adverse Drug Interactions' (1988) and this volume is a fruitful source of more detail and literature references on the whole topic of drug interactions.

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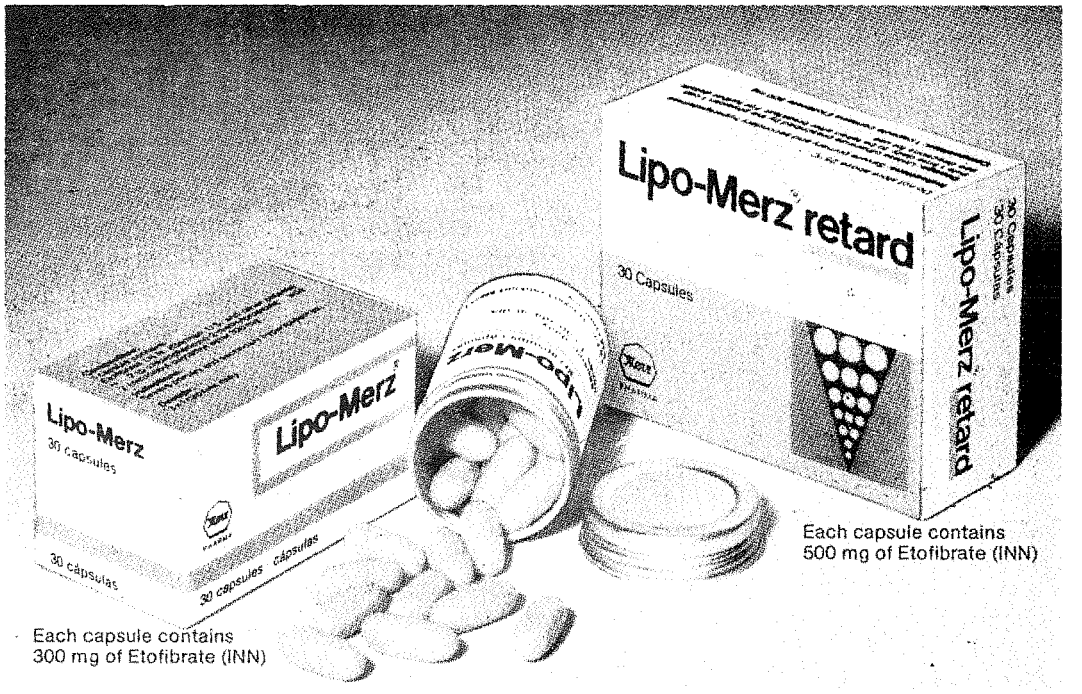

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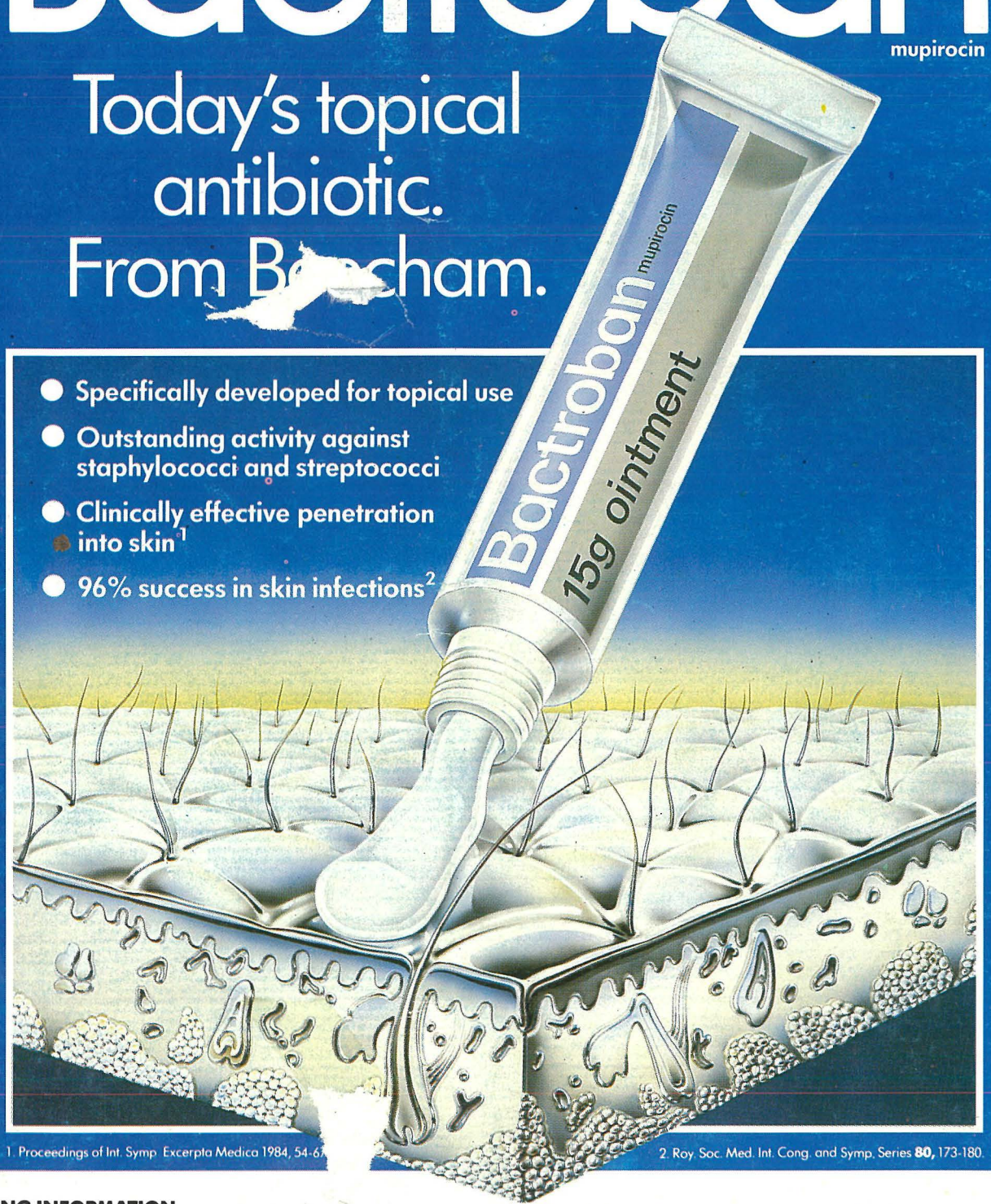

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1. Proceedings of Int. Symp. Excerpta Medica 1984, 54-6[illegible]

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