NEWSPAPERPOST

TheSynapse

The Medical Professionals' Network

Issue 06/12

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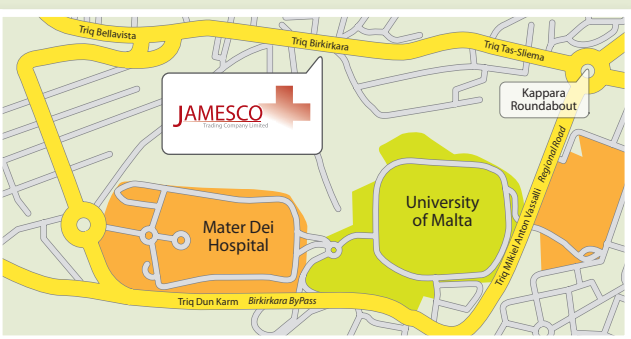

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Equipoise

Clinical practice may be defined as the continuously evolving practice of communicating and applying research-based knowledge. Part of this is what I call 'the challenging factor'. Researchers and clinicians have to continuously challenge what is currently known with new findings heralded by joint collaborations between man and technology. The following are two such examples, both pertaining to oncology.

In the past few weeks we have witnessed the roll-out of the national HPV vaccination programme, which has followed other screening programmes including breast cancer. Interestingly during this period The Lancet published an interesting article 'The benefits and harms of breast cancer screening: an independent review'. The primary research objective was to compare the benefits of screening ie reducing mortality, with any possible harm incurred ie over-diagnosis. Over-diagnosis has been defined as 'cancers detected at screening that would not have otherwise become clinically apparent in the woman's lifetime.' The review was commissioned by the UK's Cancer Research and Department of Health and involved UK women aged between 50 and 70 years who are invited for breast screening every 3 years. The study found that there is a 20% relative risk reduction for women who accept to do the screening. It has also been estimated that for every 10,000 women (aged 50 years) who are invited for screening in the next 20 years, there would be 43 preventable deaths. However, interestingly during this period, there would also be 129 cases of breast cancer which would be over-diagnosed and treated. So apparently the ratio stands at 1:3. Obviously these findings have clinical and ethical repercussions. Hopefully a similar study is carried out locally since it would add to the knowledge repository in this important area.

Another interesting article has been published in December in Peptides, 'Nullomer derived anticancer peptides (NulloPs): Differential lethal effects on normal and cancer cells in vitro.' Nullomers are essentially amino acids which the human body does not code for, possibly because they are too toxic or useless. The research team at Boise State University in Idaho have analysed several possible DNA sequences which could give rise to promising nullomers, finally arriving at 9R and 9S1R. These have been found to switch off breast and prostate cancer cells through mitochondrial impairment but do not have an overall sustained detrimental effect on healthy cells. What is more exciting is that whilst cancer cells became more sensitive to nullomers with time (possibly overcoming the question of resistance), exactly the opposite happens with healthy cells.

Ian C Ellul

WIN a weekend break for two at the Calypso Hotel

We at TheSynapse are continuously working to improve our services. We therefore interact regularly with our subscribers and target audience to assess how we can give them a better service.

We would like to announce and invite all DOCTORS, PHARMACISTS, DENTISTS and MEDICAL, PHARMACY and DENTAL students working or studying in Malta to participate in a survey which is intended to gather information on use of media by professionals and students in the medical field. The data will be used to provide better services by TheSynapse. All data will be anonymous.

The survey is divided into two sections - Section 1 is anonymous whereas you can use section 2 to participate in a draw and win a weekend break at the Calypso Hotel in Gozo. Filling Section 2 is optional.

Please complete this survey ONLY if you are either a medical doctor, pharmacist, dentist or a medical, pharmacy or dental student practising or studying in Malta. **You will find the survey on http://tinyurl.com/ts2012survey**

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Daniela Attard
is an M.Pharm student carrying out research on oral conditions. The research was carried out under the supervision of Professor L. Azzopardi and Professor A. Serracino-Inglott from the Department of Pharmacy.

Dr Alfred Grech MD
graduated from the University of Malta in 1985. He has been working in Primary Health (specifically at Paola Health Centre) for these last 24 years. His special interests are molecular biology and epigenetics. As a pastime he cultivates bonsai trees. The co-author of the article is Dr Sandra Baldacchino.

Massimo Azzopardi
is an independent catering consultant and event specialist with over 20 years experience in delivering successful events, quality catering and bespoke services designed to reach and exceed guest expectations.

Professor Albert Cilia-Vincenti MD FRCPath
is a pathologist in private practice and a scientific delegate to the European Medicines Agency. He is a former pathology teacher at London and Malta Universities, and pathology services director to the British and Maltese health services. He trained at London's Royal Marsden, Royal Free, St George's, Charing Cross and The Middlesex hospitals.

Dr Pierre Vassallo MD PhD FACA Artz fur Radiologie
specialised in radiology at the Institute of Clinical Radiology at the University of Muenster, Germany and the Memorial Sloan-Kettering Cancer Center, New York, US. He is currently Consultant Radiologist and Managing Director at DaVinci Hospital, Malta.

Dr Charmaine Gauci MD MSc Dip(Fit&Nut) PhD FRSPH FFPH
is the Director of the Health Promotion and Disease Prevention Directorate. She is a senior lecturer with the University of Malta and delivers lectures in the field of public health with special interest in Epidemiology and Communicable Diseases. She is active in the field of public health and is currently also the President of the Malta Association of Public Health Medicine.

contents

COVER:
Celebrating Christmas at Bighi Hospital, December 1917
Staff and patients posing for a picture in a decorated ward on Christmas Day 1917. Many of these decorations and parties were organized by the Malta branch of the British Red Cross. Red Cross volunteers looked after the welfare of the patients by reading to the wounded, writing letters home and providing home comforts such as birthday cakes and knitted mittens The volunteers came from different walks of life, many were wives of service personnel stationed in Malta or Maltese wives predominantly from the professional and business classes. Richard Ellis was an active member of the British Red Cross offering his photographic services free of charge. He was also instrumental in organizing a number of fund-raising concerts and teas.

Photography:
Richard Ellis

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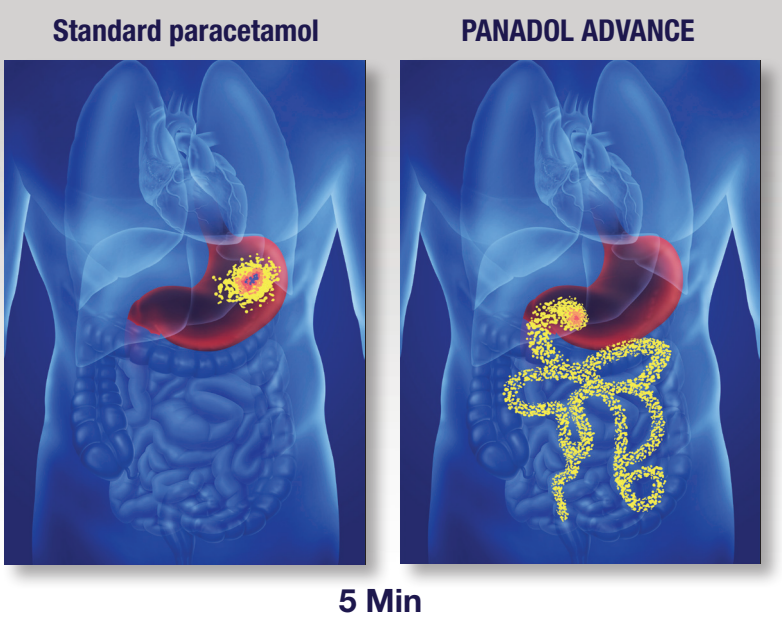

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*Representation of actual gamma scintigraphy images of paracetamol in the gastrointestinal (GI) tract.

References

1. Wilson CG, Clarke CP, Starkey YY, Clarke GD. Comparison of a novel fast-dissolving acetaminophen tablet formulation (FD-APAP) and standard acetaminophen tablets using gamma scintigraphy and pharmacokinetic studies [Epub ahead of print January 11, 2011]. *Drug Dev Ind Pharm.* 2. GSK. Data on file. Bioequivalence Studies A1900260, A1900265. 3. Clarke GD, Adams IM, Dunagan FM. Using suitability profiles to better inform consumers' choice of commonly used over-the-counter analgesics. *Int J Pharm Pract.* 2008;16(5):333-336. 4. Singh G. Gastrointestinal complications of prescription and over-the-counter nonsteroidal anti-inflammatory drugs: a view from the ARAMIS database. Arthritis, Rheumatism, and Aging Medical Information System. *Am J Ther.* 2000;7(2):115-121.

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PRIMA

Science today offers greater promise for finding new treatments than ever before, thanks to new knowledge and new technologies. Today, European citizens can expect to live up to 30 years longer than they did a century ago. Huge reductions in mortality (e.g. in HIV/AIDS, many cancers or cardiovascular disease) and significant progress in the quality of life are the results of some large and many small steps in biopharmaceutical research.

The key contribution of the research-based pharmaceutical industry to medical progress is to turn fundamental research into innovative treatments that are widely available and accessible to patients. European citizens can expect not only to live longer, but to live longer and healthier lives. High blood pressure and cardiovascular disease can be controlled with antihypertensive medicines and cholesterol-lowering medicines, knee or hip replacements reduce immobility, and some cancers can be controlled or even cured thanks to newer targeted medicines.

Yet, there remain huge challenges in many disease areas such as Alzheimer, multiple sclerosis, many cancers and orphan diseases.

The Pharmaceutical Research Based Industry Malta Association, PRIMA, is affiliated with the European Federation of Pharmaceutical Industries and Associations (EFPIA). EFPIA is the representative body of the pharmaceutical industry in Europe. Its members are the national industry associations of thirty countries in Europe and over forty leading pharmaceutical companies.

PRIMA's primary mission is to promote pharmaceutical discovery and development in Malta and to bring to the market medicinal products in order to improve human health.

As PRIMA, we aim to foster an environment which encourages the availability of newly researched and developed medicinals and intellectual property protection. We also aim to work in collaboration with the government and non-governmental bodies to allow patients rapid access to medicinal products.

PRIMA represents the R&D pharmaceutical companies operating in Malta with respect to government organizations. Our aim is to make such bodies aware of the views of the R&D pharmaceutical industry on all matters that are of interest to it and concern public health, especially international legislation and regulations. Furthermore we endeavour to maintain close relations with both governmental bodies and non-governmental bodies in order to enhance an understanding of the various problems affecting the R&D pharmaceutical industry.

PRIMA is responsible to co-ordinate policies of member companies particularly as regards rules of conduct and self-regulatory ethical codes specific to the industry and organize any exchange of information and views among members. It also co-operates with international organizations having similar objectives and activities.

This association was founded by AstraZeneca, Eli Lilly, GlaxoSmithKline, Novartis, Sanofi-Aventis and Wyeth on 3rd May 2006. Today PRIMA represents 10 R&D pharmaceutical companies operating in Malta. These are the founder members together with Boehringer Ingelheim, Janssen-Cilag, Lundbeck and MSD. The current board officials are Mr. Mark Mallia as President, Mr. Alan Mulligan as Vice President, Mrs. Margot Pisani as Executive Secretary, Mr. Hilary Agius as Treasurer, Mrs. Vicky Grima as Compliance Officer and Mr. Niki Falzon as Public Relations Officer. The Public Relations Officer can be contacted on 99822169 or niki@associateddrug.com. Mailing address for PRIMA is P.O. Box 34, Naxxar.

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References: 1 Terpstra IJ, Acne treatment with 4% erythromycin and 1.2% zinc acetate Cardiff 1988; 255-259. **2** Stainforth J et al. Dermatol Treat 1993 4: 119-122. **3** Schachner L et al. J Am Acad Dermatol 1990; 22(3): 489-495.

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2012-ZNT-003

HERVs, Transposons and Human Diseases – Part I

ALFRED GRECH
SANDRA BALDACCHINO

Abstract

It has been found that the human genome is full of relic retroviral DNA sequences called HERVs (Human Endogenous RetroViruses). A HERV is a type of a transposon, the latter being a piece of DNA sequence that can move from one position to another position in the genome, hence its other name of 'jumping gene'. HERVs and other transposons are held in check from doing havoc in the genome by several mechanisms, one of which is epigenetic in nature (namely DNA methylation and histone modifications). HERVs and other transposons are being implicated to have physiological and pathological functions in the genomes of the cells that host them. Accumulating evidence is showing that they may be associated with certain human diseases, specifically in some autoimmune diseases (e.g. rheumatoid arthritis, psoriasis, systemic lupus erythematosus, insulin-dependent diabetes mellitus), neurological diseases (e.g. schizophrenia, multiple sclerosis, motor neuron disease) and cancer. Understanding how these relic viruses and other jumping genes bring about these human diseases could help in their prevention and treatment.

Definitions

A **transposable element** (**TE**) is a DNA sequence that can move and change its position (transpose) within the same chromosome or from one chromosome to another. These mobile DNA sequences are also called **mobile elements** and have been discovered single-handedly way back in 1956 by **Barbara McClintock** in her work on maize.[1] Since then, similar mobile elements have been also shown to exist in mammalian genomes, including that of humans, and some of them are exclusive to our own species.[2] Indeed, almost half of the genome in mammals consists of transposable elements that have gained access to the genome by infecting the germline in the distant evolutionary past (millions of years ago!). Moreover, these transposable elements have been found to exist in almost all living species, including bacteria (here they are called **Insertion Sequences (IS)**).[3]

These transposable elements were regarded as 'selfish DNA parasites' or 'junk DNA'. But these 'terms' for these transposable elements are no longer suitable since their role in the genome is now being uncovered. Infact, one could say that they might have been parasitic when they were integrated into the genome but with time they entered into a kind of symbiosis with the host. Also, for some transposable elements, 'junk' is inappropriate because they are being found to have physiological and pathological significance on cell processes and functioning. Moreover, some believe that these transposable elements had and still have a role in the advancement and structure of the genome and hence to evolution itself.[4]

The focus of this paper is on such transposable elements (with specific emphasis on **human endogenous retroviruses (HERVs))** and their implications in some human diseases.

History

It was believed that genes, likened to 'beads on a string', were static and that they were passed from one generation to the next without being changed. This notion prevailed until Barbara McClintock, studying the **mosaic colouration in maize**, single-handedly found out that pieces of DNA, which she called **Dissociator** and **Activator** 'mutable loci', were capable of moving around in the genome.[1,3] She described them as **'controlling elements'** since they appeared to regulate the expression of certain genes. Her idea was not received well, and it was only when transposable elements were discovered in plants and bacteria that biologists started to acknowledge her findings. Those biologists that did not recognize McClintock notion were responsible for the era of such terms like 'selfish DNA' and 'junk DNA'. They envisaged such TEs as molecular parasites that seize and take over the cellular mechanisms for their own propagation.

But evolution biologists pointed out that the processes of evolution dispose of that which is useless or harmful for a species and the fact that many species harbour so much 'junk' DNA in their genome was surely an implication of a very valid reason. It is now believed that **genomes have co-evolved with TEs** and have devised ways to control them from running out of control while at the same time developed biological functions from their presence.

With the advent of **genomic sequencing studies**, TEs were found to be present in abundance in eukaryotic genomes. Indeed, they are a major determinant of the genome size (Table 1).

It is a known fact that the mining of the data in genome databases (**computational analysis**) has led to the discovery of new genes. But not only this, it also led to the finding of TEs and has proved useful to explore their function in the genome.

Classifications

The two main classes of transposable elements are **DNA-transposons** and **retrotransposons** (also called **retroelements**).[5] This classification is based on whether an RNA intermediate is involved during transposition.[6] Indeed, the main difference between a retrotransposon and a DNA-transposon is the way they amplify in the genome. A retrotransposon uses an RNA intermediate that is retro-transcribed into DNA using reverse transcriptase. A DNA-transposon does not use an RNA intermediate.

Table 1: Percentages of TEs sequences in eukaryotic genomes

Plants	80%
Fungi	3-20%
Metazoans	3-52%

Table 2: Main classes or types of transposable elements

Transposable Element	% in Mammalian Genome
Class I Retrotransposons (or type 2 TEs)	42.2%
Class II DNA-Transposons (or type 1 TEs)	2.8%

Table 3: Classification of retrotransposons

Non-LTR retrotransposons	LTR retrotransposons
SINE Alu repeats MIR repeats LINE L1 autonomous sequence L2 autonomous sequence	ERV (classes I, II, or III) MST MLT

Abbreviations:
LTR: Long Terminal Repeats, SINE: Short INterspersed Elements
LINE: Long INterspersed Elements, ERV: Endogenous RetroVirus

Figure 1: Typical DNA sequence of a HERV

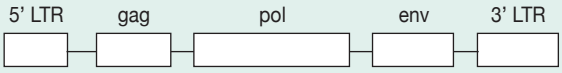


Table 4: Classification of DNA-transposons

TIR DNA transposons	The classical 'cut and paste' terminal inverted repeat (TIR) transposons
Cryptons Helitrons	Lack terminal inverted repeats
Mavericks (also known as Polintons)	The largest and most complex transposons; have terminal repeats

Table 5: Typical DNA sequence of infectious retroviruses

Sequence	Function
LTR (long terminal repeats) sequence	Contain promotors, enhancers, and regulatory sequences
gag gene	Codes for structural proteins
env gene	Codes for surface envelope proteins
pol gene	Codes for viral enzymes, including reverse transcriptase

In mammals, only less than 0.05% of retrotransposons have the ability to transpose and the LINE-1 and SINE subfamilies are mainly implicated. Again, in mammalian genomes LINE-1 accounts for about 20% of the genome.[7,8] The *Alu* elements belong to the SINE subfamily of retrotransposons. These *Alu* elements are the most abundant elements in the human genome reaching more than one million copies. LINEs are autonomous[9] i.e. they can self-propagate and transpose. SINEs like *Alus* are not autonomous and can only transpose using LINE's machinery.[10]

The DNA structure of an exogenous infectious retrovirus is shown in Figure 1 and the functions of the same sequential parts of an infectious retrovirus are explained in Table 5.

Knowing this sequence, researchers started to find similar sequences in the genomes of many species, including our own. Focusing on HERVs, their classification (Table 6) was based on the similarity of the sequence of the *pol* gene to that of the exogenous retroviruses.

Researchers use the divergence of HERVs LTR sequences from those of the exogenous counterpart retrovirus to estimate the age of HERVs in the genome. Thus LTRs act as a 'molecular clock'.[11] Class I and Cass III HERVs appear to be the oldest ones, while class II includes HERVs that have been most recently active.

So the question arises. Is the human germline still being infected? Compared to the evolutionary past or to the rate of infection in other mammals,[12] the rate of new human germline infection with evident insertions is extremely low. Indeed, presently only a small percentage of the 'youngest Alu elements and LINE-1 are still transposing in humans'.[6]

(to be continued)

References may be accessed at www.thesynapse.net

Table 6: The three classes of HERVs

HERV class	HERV example	Class of the related (exogenous) infectious retrovirus	Example of related exogenous retrovirus
Class I	HERV-W HERV-H	Gamma-retroviruses	Murine leukemia virus
Class II	Several types of HERV-K	Beta-retroviruses	Mouse mammary tumour virus
Class III	HERV-L HERV-S	Spuma-retroviruses	Primate foamy virus

Entertaining guests successfully

MASSIMO AZZOPARDI

You might be wondering what this subject has to do with the medical professionals` network. Well, that's what I thought too when I was called by the editor to include my contribution as a catering consultant. However, it did not take much to realise that TheSynapse keeps aiming high in offering its members valuable news, resources and services even in their day-to-day life. So here I am catering for TheSynapse with my first contribution.

Does it necessarily have to bring all that stress in planning and running around to bring together a successful event to your guests? Absolutely not, and if it does, it will lose its purpose. Always easier said than done, but here are 7 tips from my experience in catering for domestic and large scale events ranging from 3 to 3,000 guests.

Budget

Set your costs and stick to them. Establish before- hand an estimated breakdown of costs and allocate a contingency. Nevertheless keep looking into cost saving opportunities that in return can be utilised to enhance areas that have been left out or had a low cost allocation.

Date

I consider the date as the do or die factor of any event. Where possible, take ample time to plan the date considering other activities that might fall on the same date. And do inform your guests at least 10 days in advance if you are keen on a good turnout.

Venue

Selecting the venue depends primarily on the size of the event. Your personal preference is irrelevant but considering comfort, accessibility and practicality whether at home or at an establishment is crucial to the success of your event. The type of event you are organising determines the area size required: cocktail, stand up, seated, buffet, family style, fork buffet and live cooking are different events with different space requirements.

Type of Event

Most probably you would know all guests invited, so you would know what appeals to them and what are their likes and dislikes, maybe not on an individual basis, of course, but you can always recall past events that were successful. If the majority of guests are being invited for the first time, keep it as simple as possible and take time to assess the preferences of your guests for the next possible event.

Food and Drinks

Again this will primarily depend on your allocated budget. If you are preparing food at home, there are various practical, cost-effective party food solutions that come handy. Look out for cooked frozen items rather than cooked chilled items as these can be stored for a much longer time. Go for IQF (Individually Quick Frozen) food items so you can cook the required units without defrosting in bulk. You would also need to consider any food intolerances of your guests and to make sure that you detail your ingredients both verbally and if necessary in writing on the day. A simple tag informing that a recipe contains nuts can avoid a fatality. On the other hand hiring a quality catering company can save you time, if not cost. Asking for actual food sampling before the event avoids last minute surprises. For drinks one can anticipate a straightforward easy option by having a welcome punch for the first hours of the event. This not only empties those left-over spirits from previous events, but avoids you asking your guests one by one to prepare their individual drink.

Wow Factor

Whatever your event, the highlight should be the occasion being celebrated. Ensure that the venue is decorated for this and consider having some type of entertainment. Lights do also play an important factor at any event, so ensure your lights are not too dim or too bright. Hiring out some light effects do add to that wow-factor required to impress.

Good Planning

Like any other project, failing to plan is planning to fail, and organising an event is a project in itself. Get yourself well prepared in advance by listing down your requirements, costs, shopping, scheduling, set-ups, equipment, decorations and do allocate a day to try out some samples and go through some dummy runs beforehand especially if the event is the first of its type.

From a professional point of view I can assure you that organising an event is an exciting time every time. Keeping the focus on the outcome desired, creating the gathering and exceeding your guests` expectations are factors that will give you confidence to spend quality time with your guests and ultimately, as the host, enjoy your event.

Dear Doctor,

I am Sephorah Falzon, a third year pharmacy student and as part of my undergraduate training I am working on a project entitled "Chronopharmacology in Hypertension".

This project aims to assess the influence of antihypertensive medications, namely Calcium channel blockers and Angiotensin 2 receptor blockers (ARB's) on blood pressure levels over a period of 24 hours when administered in the morning or in the evening.

This will be assessed by performing two separate 24 hour Ambulatory Blood Pressure readings in patients who have primary hypertension and are taking once daily Amlodipine or Valsartan. For this to be carried out, a group of patients has to be recruited. As part of the study I would like to invite you to help me recruit patients who would be willing to participate.

Patients who participate in this study will benefit from two 24 hour Ambulatory Blood Pressure assessments. You will obviously be given a copy of each examination so you can better manage your patients. The protocol for this study will be as follows:

An appointment will be set up where the patients shall be asked to wear an ambulatory blood pressure monitor (ABPM) for 24 hours. For the following 7 days the patients will be asked to take their medication at the opposite time of day that they usually take it. A second appointment will be set up where the ABPM shall be attached again for another 24 hours.

The results obtained will help me determine the optimum time of administration for each antihypertensive drug in a 24 hour time period; when it is most likely to produce a therapeutic effect and less likely to produce side effects.

As a student, I need the help of consultant cardiologists and physicians who can help me identify patients satisfying the above mentioned criteria and who would also give me the permission to approach their patients.

I would really appreciate it if you would kindly accept this invitation to participate. Any assistance given will be acknowledged in the thesis and in any publication.

I can be contacted via e mail at seph.falzon@gmail.com or by phone on 7930 9671 / 2763 4165.

We would like to thank the following reviewers for their help:
Prof Albert Fenech
Dr Abigail Cassar Parnis
Dr Bridget Ellul
Dr Chris Barbara
Dr Nigel Camilleri
Dr AnneMarie Scerri

DID YOU KNOW

Nitrous Oxide (laughing gas) which is an anaesthetic was the by-product of a theory which advocated that oxygen caused tuberculosis.

(Source: Spitting Blood – The History of Tuberculosis, authored by Helen Bynum and published by Oxford University Press, December 2012)

Principles of fluid balance and IV fluid therapy in the adult surgical patient - Online learning module

The Malta Foundation Programme in collaboration with TheSynapse is pleased to announce the launch of the 5th online e-learning module – **"Principles of fluid balance and IV fluid therapy in the adult surgical patient".** The e-tutor of this online course is Dr Victoria Bonello. Dr Bonello obtained an MD from the University of Malta in 2007 and became a member of the Royal College of Surgeons in 2010. She obtained a Postgraduate Certificate in Medical Education from the University of Cardiff in 2012. She is currently holding an academic post as a Clinical Teaching Fellow within the Epsom and St Helier University Hospitals NHS Trust which is affiliated to St George's University of London Medical School.

The aim of this new online course is to improve junior doctors' understanding of the indications and uses of intravenous fluid therapy in surgical patients, based on the 2011 British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients.These online courses are available to all Foundation Students and also to TheSynapse online members. If you wish to participate and you are not yet a registered online member of TheSynapse, please visit TheSynapse Website – www.thesynapse.net and click on the register button which is located at the top right-hand corner. If you need any support, please send an e-mail to mpl@thesynapse.net or contact the Administration on telephone number 21453973/4.

We encourage you to participate and wish you success!

How to access this online course

Log on
www.thesynapse.net

Login in with your username and password
that you normally use to access TheSynapse website
or
If you do not have TheSynapse username and password please click on the tab Register located on the top right menu

Click on TS Learn in the top menu

Click on Courses

Click on Principles of fluid balance and IV fluid therapy in the adult surgical patient
Use the enrolment key Adult_Surgical1

All five courses are sponsored by an unrestricted educational grant by Actavis Malta

Compliance with Protocols in Dental Conditions

DANIELA ATTARD
LILIAN M. AZZOPARDI
ANTHONY SERRACINO-INGLOTT

Key Words

Compliance, protocols, dental conditions, local community pharmacies

Abstract

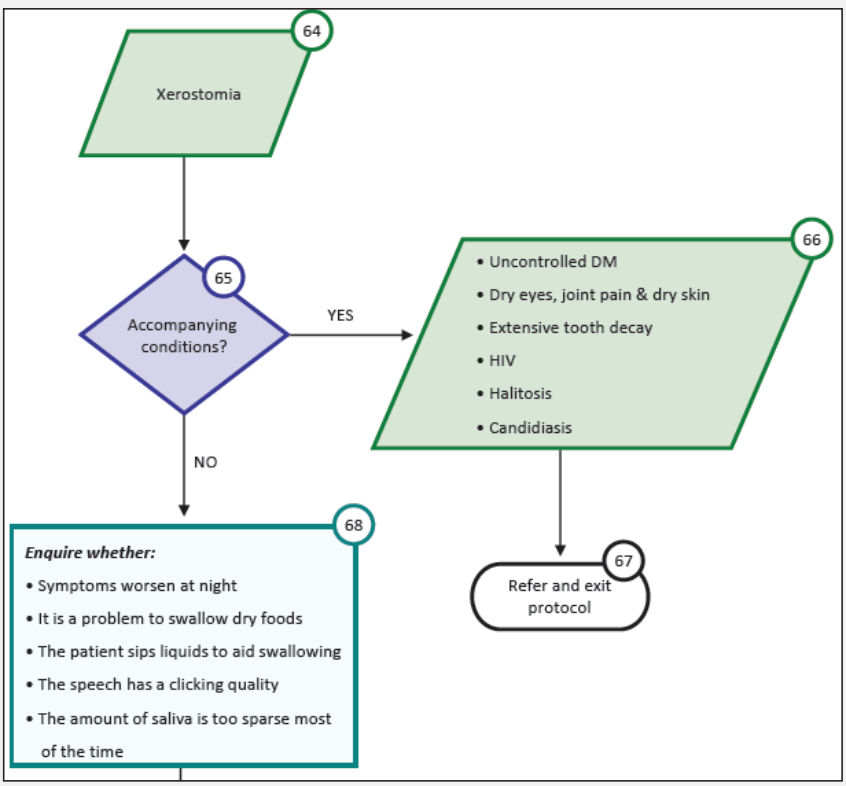
The aims of this study were to assess compliance with the developed treatment protocols through the dissemination of case studies. Out of 203 questionnaires distributed, 125 (62%) were collected. Community pharmacists were asked to complete case studies within a fortnight to indicate their line of action in three conditions presented. Average percentage compliance with the protocols was 73%.

Introduction

Evidence-based practice dates back to the 1980s following the establishment of 'evidence-based medicine',[1] and it was best defined by Sackett and colleagues as "The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients".[2] The intervention of the community pharmacist and other healthcare professionals is shifting towards this practice, implying that daily practice is strongly based on evidence, rather than traditions.[3]

Multiple factors may hinder the process of evidence-based practice, including inadequate knowledge and skills by healthcare professionals, misconceptions, lack of time and lack of counsellors to help guide along the change.[4] These barriers are faced by all healthcare professionals, irrespective of the motivation,[5] however knowledge can constantly be improved through continuing professional development.

Figure 1: Excerpt from the Xerostomia protocol, illustrating the colour-coded scheme for easier interpretation



Protocols and guidelines should be based on the latest information ensuring that they provide evidence-based practice. Using high quality evidence will increase overall quality care.[3]

A survey conducted in Scotland in 2002 illustrated that many patients with oral problems seek the help and advice of a pharmacist before that of a dentist. It was further established that the majority of conditions presented could easily be managed successfully within the pharmacy setting.[6] A study performed locally in 1998 by Caruana[7] demonstrated that all pharmacies that took part in the study (n=103) were consulted as first line of treatment for oral problems. The course of action taken by pharmacists when presented with an oral complaint varies, but immediate referral was not generally recommended, except for scenarios presenting with trauma to the anterior teeth or abscesses. In other circumstances, the patient was referred only if the complaint was severe or persistent, or after dispensing an emergency medication.

The aims of this study were to develop treatment protocols for recurrent aphthous ulcers, xerostomia and dental abscess, and to assess compliance of the pharmacists with the protocols through dissemination of case studies.

Method

An extensive literature review was carried out and three treatment protocols on recurrent aphthous ulcers, xerostomia and dental abscess were designed for community pharmacists when responding to oral symptoms.

Three corresponding case studies were also created to evaluate the pharmacists' compliance with the protocols. The case studies were kept concise and open-ended questions were used so that the pharmacist would not be automatically guided to follow

the protocols. Referral was included as an option only in the recurrent aphthous ulcers and xerostomia case studies, as cases of dental abscess require initial and immediate referral to a dentist since their management require specialized treatment by a qualified healthcare professional.

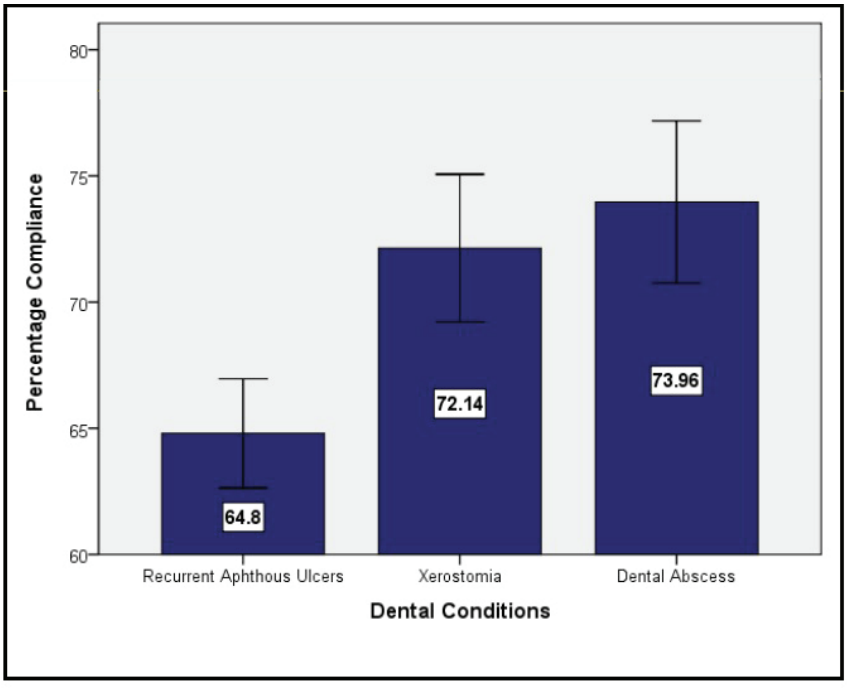
Both the protocols and the case studies underwent validation by a panel of six experts in the medical and dental field. Subsequently, the protocols were modified according to suggestions made during the validation process.

The validated protocols were then formulated into an A5 booklet, which along with the explanatory text and case studies were distributed by hand to 213 local community pharmacies. Ten pharmacies out of the total declined to take part in the fieldwork and thus the pharmacy population was taken as 203.

A scoring system was adapted from Aquilina, 2004[8] whereby a score of '1' was awarded for every step followed which complied with the protocol, and a score of '0' was awarded for steps which were not followed or which were omitted. Steps omitted as required by the protocol were awarded no score and thus were not considered during statistical analysis.

Data collected was analysed using Microsoft® Office Excel 2007 and Statistical Package for the Social Sciences (SPSS®) software version 17. Compliance with the individual protocols was calculated as percentage compliance.

Figure 2: Comparison of compliance, at the 95% Confidence interval, if all pharmacies (n=203) had to participate in the study



Results

The validated booklet consists of 40 pages and it was divided into 4 different sections. The first section titled 'Introduction' starts off with a list of the abbreviations found throughout the whole booklet, a glossary and a table which explains the interpretation of shapes. The second section, 'Treatment Protocols', includes the three treatment protocols in a flowchart format (Figure 1), along with an introductory protocol. The introductory protocol mainly deals with patients who present in the pharmacy with a prescription, highlighting the intervention of pharmacists in dispensing medication. For example, it highlights the need for pharmacists to check for any cautions, contraindications and drug-drug interactions, and to offer advice on the prescribed medication at the end of the pharmacist-patient interraction. This protocol consists of 20 steps, the Recurrent Aphthous ulcers protocol consists of 43 steps, the Xerostomia

protocol has 40 steps while the Dental Abscess protocol is 20 steps. The next section entitled 'Appendix' contains relevant information that complements the protocol flowcharts, such as the predisposing factors of recurrent aphthous ulcers, along with management of cases which warrant referral, a list in table format of the most common drugs that cause dry mouth, and an emphasis on how to maintain good oral hygiene. Finally, the last section 'References' contains a list of references that were used to compile the content of the booklet.

A total of 203 case studies were distributed, and a total of 125 were collected, giving an average response rate of 62%. An average compliance of 73% was obtained. It was highest for dental abscess (77%), followed by xerostomia (74%), and recurrent aphthous ulcers (68%) (Figure 2).

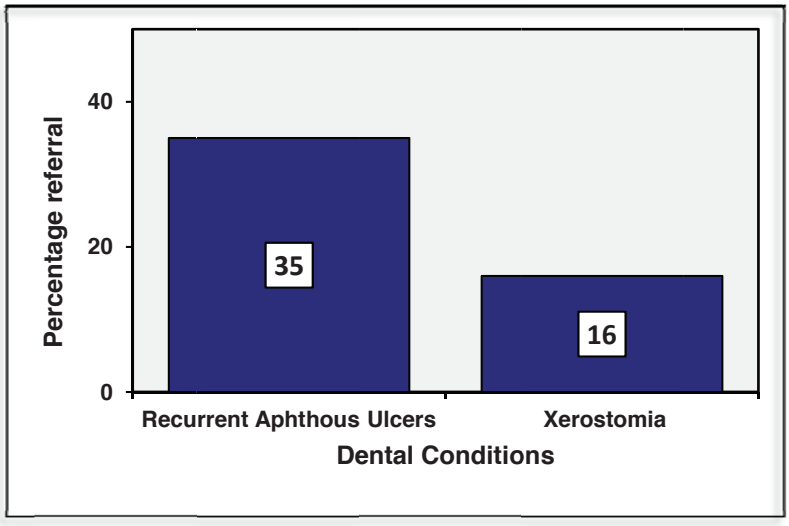
Limitations

The main limitation was the time period allocated for data collection. If the study was conducted over a longer time period, it may have given the opportunity of the collaboration of more pharmacists. Other limitations were the increased workload on pharmacists created by the Pharmacy of Your Choice scheme, giving them less time to evaluate the protocols and participate in the study. Another limitation to the study could be that pharmacists replying to the questionnaire referred to the adjoining protocol before filling in the case study leading to a higher number of correct answers.

Discussion

The overall percentage compliance obtained (73%) indicates that pharmacists found the protocols of value when presented with such conditions. The higher compliance obtained with the dental abscess protocol (77%) shows that pharmacists tend to be more cautious when dealing with more severe conditions, which usually require referral. The lower compliance obtained with the recurrent aphthous ulcers protocol (68%) reflects referral, mostly when it was unnecessary (Figure 3).

Figure 3: Pharmacists referral for recurrent aphthous ulcers and xerostomia



There was a misconception perpetuated by several pharmacists in the recurrent aphthous ulcers case study. The case study specified that the patient was suffering from painful recurrent bouts of mouth ulcers, lasting up to a few days. The majority of pharmacists that took part in the study would refer such a patient since the ulcers were recurrent and painful, to establish an appropriate diagnosis, however, literature explains that the presence of pain is a good sign, since it excludes more serious underlying diagnoses. Furthermore, step 23 of the recurrent aphthous ulcers protocol indicates that in the absence of pain or discomfort, the patient should be referred immediately, but essentially this step was either ignored or not considered to be of significant importance.

Implementation of the use of protocols and guidelines in the community and clinical scenario may be hindered by several factors. Simple and easy-to-use protocols are preferred, and may enhance their utilization. Healthcare professionals may be unfamiliar with the contents, and both environmental and patient characteristics may affect the implementation of their use. Predominant environmental characteristics include time and lack of staff, while the most common patient characteristic is the presence of comorbidities, where most protocols and guidelines are not customized for such patients.[9] The developed treatment protocols aimed to overcome these barriers, by taking into consideration possible comorbidities.

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CHARMAINE GAUCI

Stroke prevention

Strokes are sudden and have an immediate effect. They are a leading cause of long term disability in adults. In 2010, strokes accounted for 8.7% of total deaths in Malta. In addition there were six hundred and fifteen discharged cases of stroke in Malta and Gozo in the year 2011. Stroke is also the second leading cause of death in the Western world after ischaemic heart disease, with an exponential increase in its occurrence with increasing age.

Some risk factors cannot be modified by medical treatment or lifestyle changes:

- Age
- Gender
- Family History
- Ethnicity/race

However other risk factors **can be modified.** These can be split into:

Medical risk factors
Lifestyle risk factors

- Hypertension
- Smoking
- Hypercholesterolaemia
- High alcohol consumption
- Diabetes
- Physical inactivity/obesity
- Heart disease
- Unhealthy diet

The Health Promotion and Disease Prevention Directorate is embarking on an initiative to reduce the risks of stroke.

1. A balanced diet

A diet low in saturated fats and cholesterol and high in dietary fibre:

- Include plenty of fresh vegetables and fruits
- Avoid adding salt to food during its preparation or at table
- Avoid processed foods that are high in salt
- Read food labels to help you choose foods that are low in salt, fat and sugar

2. Be active

Thirty minutes for at least five days per week of moderate intensity activity (such as brisk walking or riding a bike at ground level) is recommended. Some physical activity is better than none. Any amount of physical activity gives health benefits. Physically active men/women generally have a 25-30% lower risk of stroke or death than the least active people.

3. Tobacco

Smoking doubles the risk for stroke. Smoking cessation is also associated with a rapid reduction in risk of stroke to a level that approaches but does not reach that of those who never smoked.

4. Alcohol

Heavy drinking multiplies the risk of having a stroke by more than three times. One gram of alcohol is equivalent to seven calories and therefore may lead to weight gain.

General practitioners have an important role in making people aware of stroke and the possible consequences. Regular measurement of blood pressure, cholesterol levels, blood glucose levels, weight ,waist circumference and Body Mass Index (BMI) can help identify risk factors and take measures to limit their impact.

A stroke can cause temporary or permanent disabilities which include:

- Paralysis
- Dysarthria, aphasia
- Memory loss or thinking difficulties
- Emotional problems
- Central pain syndrome
- Changes in behaviour and self-care

The rates of reported medical complications of stroke are high with 50% of deaths after stroke being attributed to medical complications. An autopsy series found that the most common cause of death after ischemic and hemorrhagic stroke was cerebrovascular disease in the first week, pulmonary embolism in the second through fourth weeks, bronchopneumonia in the second and third months, and cardiac disease after three months.

Early treatment when stroke happens is essential. Hence it is **important to understand stroke warning signs and get the patient to hospital fast**.

The FAST test helps recognise the signs:
FACE: Does one side of the face droop? Ask the person to smile
ARMS: Ask the person to raise both arms. Does one arm drift downwards?
SPEECH: Is the speech slurred? Ask the person to repeat simple sentences
TIME: Act Fast. Dial 112 immediately

For more information on the campaign contact the Directorate on 23266000.

MARIKA AZZOPARDI

Richard Ellis

THE MAN, HIS TIMES & HIS PICTURES

We've all seen them – pictures of Malta from days gone by, from centuries gone by. All signed by a man who photographed Malta like no other – Richard Ellis. Meeting his great grandson Ian Ellis in the Ellis photographic archives which house somewhere between 36,000 and 40,000 images, allows me some insight on the man, his times and his pictures.

Richard Ellis was born in London in the year of the Lord 1842. One of 13 children, his parents thought fit to send him off to see the world at age 10 when he was apprenticed to James and Sarah Conroy. This couple worked in a circus and henceforth, Richard was officially part of a travelling troupe which toured Europe to thrill the crowds with the show. He eventually found himself in Paris.

It was in this city abuzz with novelty and fashion that Mr Conroy noticed how photography was becoming all the rage and decided to invest time and money to study this new and amazing image-making technique. The young Richard tagged along and as he did all the odd jobs around Conroy's initiation in photography, the bright young boy learnt the tricks of the trade and mastered the art of photography, slowly but surely.

In 1861, the circus headed for Naples, intending to perform on the Italian peninsula, but whilst en route, Italy experienced its internal unification upheaval and the Conroys decided it was safer to head further south to Malta. Richard Ellis therefore, at age 19, ended up in Malta. Mr Ian Ellis explains further, "It was in Malta that Richard met a young woman called Fonza Curmi from Cospicua and they got married. In the meantime, Conroy had established himself as a professional photographer in Malta and it seems the man and Richard eventually parted ways since we know that Richard opened his first photography shop and studio in Strait Street, Valletta in 1871."

Ellis had several advantages in Malta – for one thing he was British, had an English surname and this made him popular with the English settlers and visitors in Malta. He was also married to a Maltese girl, so his local connections were firmly entrenched as well. He was highly inventive and enterprising and whilst he was continuously commissioned by the British forces and its members to take pictures and portraits, he routinely came up with novel ways of making money. A picture shows two men rowing a 'dghajsa' sporting the 'Ellis' flag on the waters of the Grand Harbour. "This was one of his money-spinners apparently. He rented out the boat and took pictures of fleet ships as they entered the harbour. Then he would show the pictures to the sailors who came with them, offering to take each man's photograph which he super-imposed on the ship's image. It all turned into a souvenir postcard of Malta's Grand Harbour, of the ship and of the sailor who proudly sent it back home to the family. Simple and ingenuous, it seems to have been pretty successful as an idea."

Ian Ellis explains that whilst all this happened quite a long time ago, it has proved relatively straightforward to trace back events and to find things out as they happened in Richard Ellis's life,

The studio camera which was used by Richard Ellis

At the archives

from research, old documents and from his pictures. “He was very meticulous in documenting all his photos with the date, location, and the person/company commissioning the picture if this was the case. The first picture he took in Malta is of an English ship berthed at Senglea Point, a picture taken from Marsa.” Leafing through one of Richard Ellis’s large hand-written registers proves to be quite a treasure-throve of names of the gentry of his time, and Ian Ellis shows me related images which he managed to dig out of the archives and ‘develop’ from the old glass negatives and then transfer onto the computer. The variety is staggering – portraits of beautiful women, house interiors, hospital wards, equipment, roads, landscapes, people …

“I became involved in the care of this collection and in the eventual publication of his pictures quite perchance and quite late in life. I am by profession an engineer. I was pretty close to my uncle so that when he passed away aged 82, I was landed the responsibility of taking over his photography shop. Actually photography had been phased out of the business because by that time (1990s), photography was pretty much accessible to everybody and there was no scope in keeping the photography services going. My uncle had shifted to frame-making and in 1993, I decided to take over the business. I knew of the archive and over the past 10 years I have been sifting through it

His main difficulty was to scan the negatives to be able to view the actual pictures they produced. “I had visited a photography fair in Germany and asked about purchasing equipment to carry out the process. The price of it was exorbitant and the time it would have entailed me to see through the project would have taken me three lifetimes. So back home, I drew on my engineering prowess and came up with a solution whereby I have found an effective, fast and relatively cheap method to transfer the images from the old glass negatives onto the computer. This way I can see all the pictures, compare notes with the registers and add a caption to each and every one.”

It was this process which allowed him to publish the four books with images from the Richard Ellis collection, the first one showing images of Floriana and Valletta, a second one about the Grand Harbour and the Three Cities, a third about the St Julian’s/Sliema area, and a fourth one with generic views of Malta and Gozo. Presently he is working on the fifth and sixth publications. “My dream is to open a Museum of Photography of Malta because my great grandfather’s pictures truly document Malta as it was in his days and as it morphed over his lifetime. The pictures give us an opportunity to step back in time and see Maltese life as it was in all its aspects. There are his pictures, his equipment, his cameras … Yes, the books are one way of financing such a museum and I hope to find other funding for this scope. It is a dream which will hopefully materialise.” S

PIERRE VASSALLO

Endometrial Imaging

The endometrium demonstrates a wide spectrum of normal and pathologic appearances throughout menarche as well as during the prepubertal and postmenopausal years and the first trimester of pregnancy. Characteristic morphologic changes take place in the uterus and endometrium over time.

At birth, the uterine body is smaller than the cervix, and the endometrium generally appears as a thin, echogenic line (Fig 1). However, fluid may be present in the uterine cavity; this is due to the effects of transplacental maternal hormones.

The most common endometrial abnormalities in neonates include hydrocolpos and hydrometrocolpos. Hydrocolpos is characterized by distention of the vagina and hydrometrocolpos is characterized by dilatation of both the uterine cavity and vagina with serous fluid and sometimes urine if a vesico-vaginal fistula is present. Both hydrocolpos and hydrometrocolpos in neonates result from cervical or vaginal stenosis, hypoplasia or agenesis.

In contrast, hematocolpos and hematometrocolpos in adolescent girls are generally associated with an imperforate hymen without an increase in associated congenital anomalies. Ultrasound demonstrates an echogenic, tubular, cystic midline mass with internal echoes representing fluid and debris (Fig 2).

During the reproductive age, the appearance of the endometrium will change with the phase of the menstrual cycle. This is best analysed on endovaginal scans. During menstruation, the endometrium appears as a thin, echogenic line 1–4 mm in thickness. Endometrial thickness is measured from echogenic border to echogenic border across the endometrial cavity on a sagittal midline image (Fig 3). During the proliferative phase of the menstrual cycle (days 6–14), the endometrium becomes thicker (5–7 mm) and more echogenic relative to the myometrium, reflecting the development of glands, blood vessels, and stroma. In the late proliferative (periovulatory) phase, the endometrium develops a multilayered appearance with an echogenic basal layer and hypoechoic inner functional layer, separated by a thin echogenic median layer arising from the central interface or luminal content (Fig 4). In this stage, the endometrium may measure up to 11 mm in thickness. The layered appearance usually disappears 48 hours after ovulation. During the secretory phase, the endometrium becomes even thicker (7–16 mm) and more echogenic (Fig 5). This increased echogenicity is thought to be related to stromal edema and glands distended with mucus and glycogen. The endometrium typically reaches a maximum thickness during the midsecretory phase. The appearances of normal and abnormal endometrium, such as in the setting of endometrial hyperplasia, may overlap, so imaging of the endometrium is best performed during or immediately following menstruation.

The MR imaging appearance of normal endometrium during the reproductive age is best demonstrated on T2-weighted images. T2-weighted images delineate the uterine zonal anatomy. The normal endometrium is of uniformly high signal intensity, with the inner myometrium, or junctional zone, of uniformly low signal intensity and the outer myometrial layer showing higher signal intensity than the inner layer (Fig 6).

Transvaginal Ultrasound is the primary modality for evaluation of an

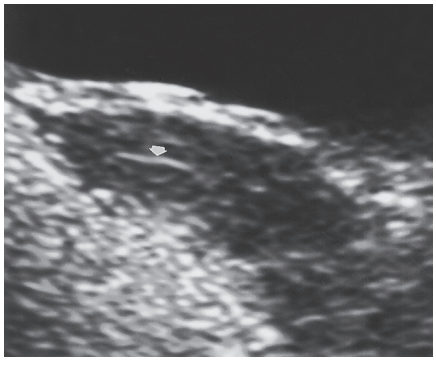


Figure 1. Normal pediatric endometrium. Sagittal Ultrasound image of the uterus in a 2-year-old girl demonstrates a thin endometrium (arrow).

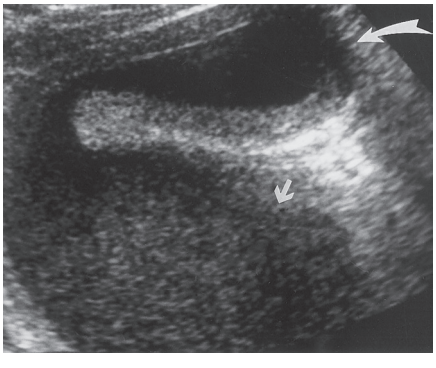


Figure 2. Hematometrocolpos in a 12-year-old girl with abdominal pain. Sagittal ultrasound image demonstrates a markedly distended vagina (straight arrow) and uterine cavity (curved arrow).

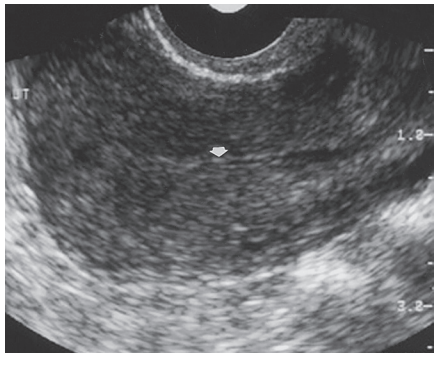


Figure 3. Normal reproductive age endometrium. Sagittal ultrasound image of the uterus obtained during menstruation shows a thin endometrial lining (arrow) with a trace of fluid.

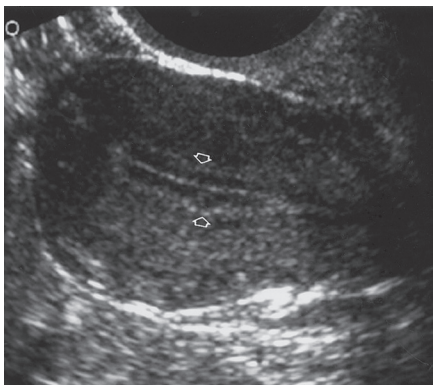


Figure 4. Normal reproductive age endometrium. Sagittal ultrasound image of the uterus obtained during the late proliferative phase of the menstrual cycle demonstrates the endometrium with a multilayered appearance (arrows).

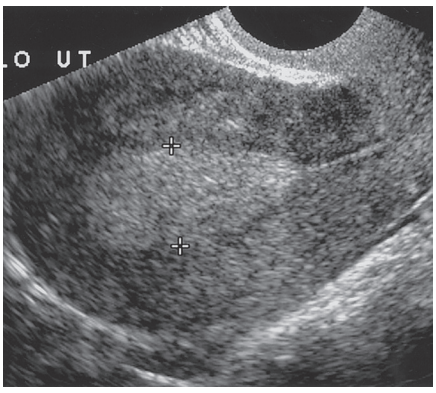


Figure 5. Normal reproductive age endometrium. Sagittal ultrasound image of the uterus obtained during the secretory phase of the menstrual cycle shows a thickened, echogenic endometrium (cursors).

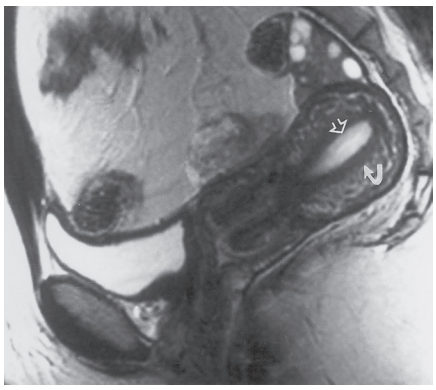
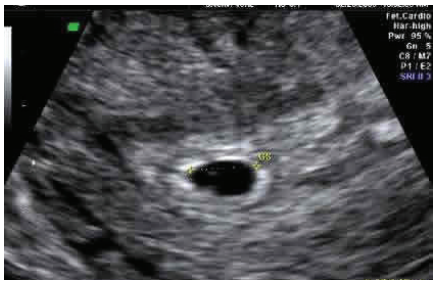


Figure 6. Normal reproductive age endometrium. T2-weighted MR image shows the normal endometrium (straight arrow) and junctional zone (curved arrow).



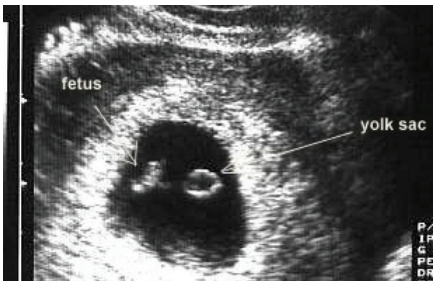


Figure 7. (a) Normal 5 week intrauterine gestation. (b) Normal 6 week gestation showing a yolk sac and the foetus.

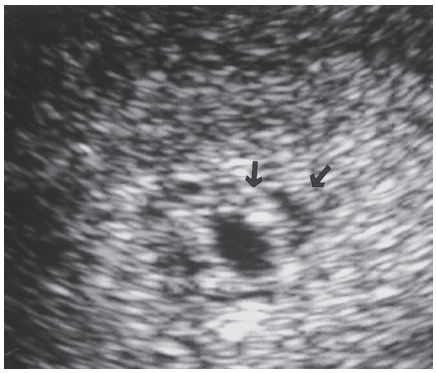


Figure 8. Double decidual sac sign appears as two hyperechoic rings (arrows). The inner ring represents the combined chorion-decidua capsularis, and the outer ring represents the decidua parietalis.

early intrauterine pregnancy, which varies in appearance depending on gestational age. At 4.5 weeks gestation, the normal gestational sac appears as an oval or rounded anechoic space measuring 5mm in diameter located within the endometrium and surrounded by a hyperechoic rim at least 2 mm in thickness. The sac should grow at a rate exceeding 1.2 mm per day (Fig 7). The yolk sac should be visualized between 5 and 6 weeks gestation, and an embryo may be seen before 6 weeks gestation. The gestational sac should be located in the upper or middle uterine segment, midway between the two apposed uterine walls. A low position in the endometrial cavity suggests an impending or ongoing miscarriage, a cervical ectopic pregnancy, or a fundal fibroid compressing the sac downward. The presence of placental blood flow on Color Doppler Ultrasound in a cervical ectopic pregnancy or low-lying sac is useful in distinguishing these entities from an abortion in progress.

The hyperechoic ring surrounding the gestational sac represents the decidual reaction before 5 weeks of gestation. After 5 weeks gestation, a double decidual sac sign may be seen, the inner sac representing the chorion-decidua capsularis and the outer layer the decidua parietalis (Fig 8). Both the decidual and double decidual signs help distinguish a normal intrauterine pregnancy from a pseudosac that may occur in up to 20% of ectopic pregnancies (Fig 9). Prior to visualization of a yolk sac or embryo, these two Ultrasound signs assist in the diagnosis of a normal intrauterine pregnancy.

Apparent endometrial thickening in the setting of a positive pregnancy test may in fact represent an echogenic decidual cast in the endometrium (Fig 10), although retained products of conception may have a similar appearance. A decidual cast is suggestive of an ectopic gestation.

A thin decidual reaction of less than 2 mm, an abnormally shaped sac, or a gestational sac in a low uterine location suggests an abnormal pregnancy. An empty gestational sac may represent a blighted ovum, particularly when the mean gestational sac diameter is >10 mm (Fig 11). A blighted ovum is an anembryonic gestation.

Gestational trophoblastic disease is a proliferative disease of the trophoblast that may manifest as a complete or partial hydatidiform mole,

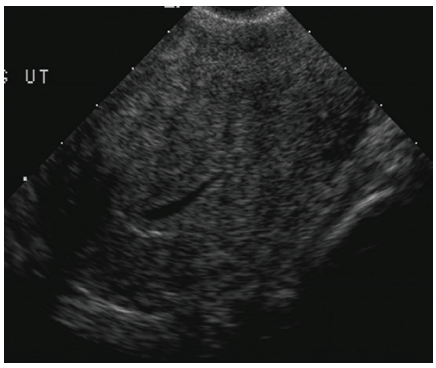


Figure 9. Pseudosac appears as a collection of fluid in the endometrial cavity with no decidual or double sac signs in a patient with a positive pregnancy test.

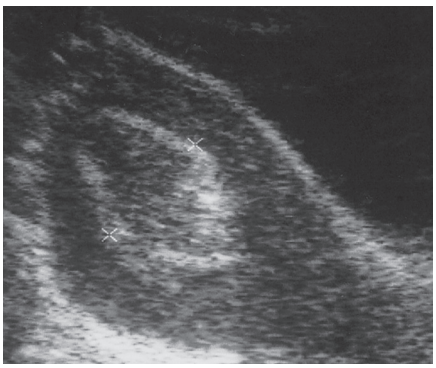


Figure 10. Decidual cast. Transabdominal ultrasound image reveals echogenic material within the endometrium (cursors) with no gestational sac.

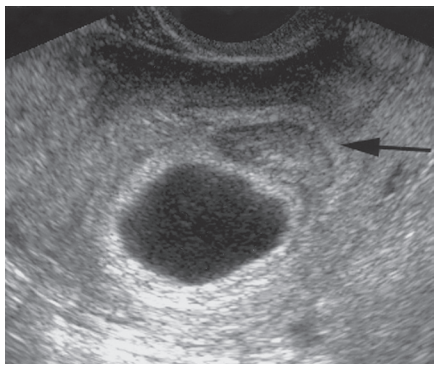


Figure 11. Blighted ovum. Ultrasound image shows the gestational sac with no visible embryo or yolk sac. A small subchorionic hematoma is noted (arrow).

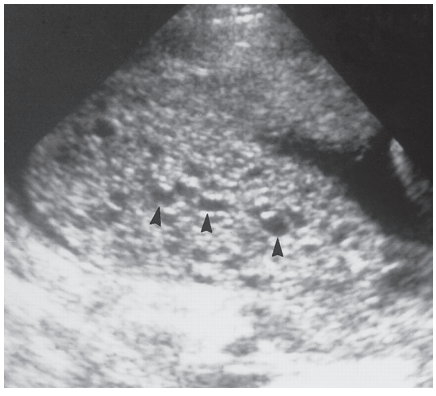


Figure 12. Molar pregnancy. Ultrasound image demonstrates an echogenic mass in the uterine cavity with multiple small, hyperechoic areas (arrowheads).

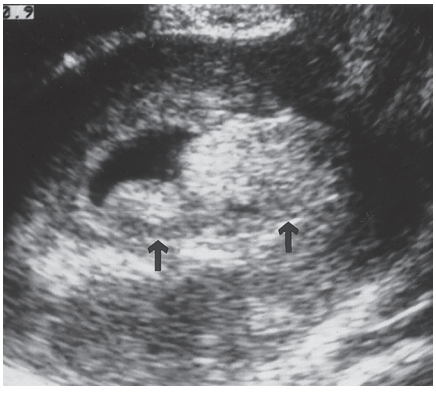


Figure 13. Retained products of conception seen as echogenic material within the endometrial canal (arrows).

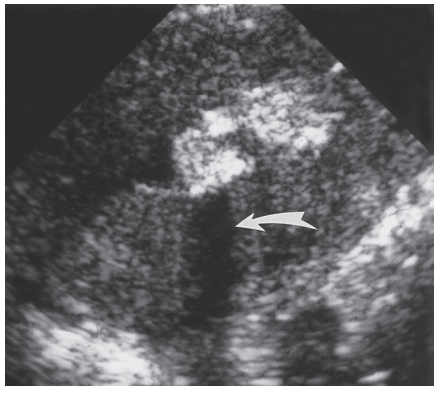


Figure 14. Endometritis. Ultrasound image demonstrates multiple echogenic foci within the endometrium (arrow) representing gas.

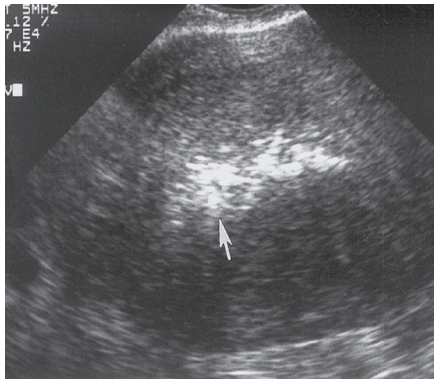


Figure 15. Ultrasound image shows echogenic material with posterior acoustic shadowing (arrow), a finding that is consistent with calcified retained products of conception.

invasive mole, or choriocarcinoma. A hydatidiform mole, the most common form of gestational trophoblastic disease, is noninvasive and usually manifests in the second and third trimesters. This type of mole distends and fills the endometrial cavity without invading the myometrium. Ultrasound demonstrates a uterus that is enlarged for gestational age and filled with multiple small, hyperechoic areas 3–10 mm in diameter with posterior acoustic enhancement (Fig 12). The cysts represent grossly swollen villi from trophoblastic hyperplasia.

Normal ultrasound findings in the postpartum uterus include uterine enlargement and an endometrial cavity less than 2cm in thickness. The cavity wall has a variable appearance ranging from smooth, well-defined borders to irregular, heterogeneous linings, with considerable overlap between normal and abnormal cases. Small echogenic foci within the endometrial cavity may not be pathologic. Abundant intrauterine echogenic material may however represent retained products of conception (Fig 13), while the presence of gas bubbles may indicate endometritis (Fig 14), the latter being more common after caesarian section. Air in the uterus may be present in up to 20% of normal postpartum women, so clinical findings must also be considered when considering treatment. Retained products of conception that are seen late after delivery may contain calcifications (Fig 15). S

ALBERT CILIA-VINCENTI

Diagnosis of Coeliac Disease – an Update

Overall prevalence rate of coeliac disease in both children and adults in the western world is quoted at 1% although some groups have reported a five-fold increase in children when compared to adults.[1] The disease is more prevalent than first thought in Eastern Europe and Asia, with as many as 1% of Latvians and 1.44% of north Indians testing positive with routine screening serology.[2,3] The rise is largely attributed to increased awareness and education resulting on average in 16% annual increases in serological testing for coeliac disease.[1] Large scale studies of healthy school children from Eastern Europe and North Africa have reported prevalence rates similar to those in the western world of between 0.4 and 1.1%.[4,5,6]

In contrast to whites, only one in 300 urban African-Americans investigated for iron deficiency anaemia (IDA) was found to have coeliac disease, although this might be an underestimate of coeliac disease in black communities.[1] European-American differences have also been reported with refractory coeliac disease (RCD), with a lower incidence in North America (1.5%) and a higher type I:II RCD ratio compared to Europe.[6]

Recent prevalence studies in children with type 1 diabetes (T1DM) and adults with irritable bowel syndrome (IBS) have reignited the debate of the timing and frequency of coeliac disease screening in these conditions.

Depending on the use of serology and/or biopsy, the prevalence of coeliac disease in T1DM ranges from 7.2 to 8.6% in Europe[7-9] and even reaches 11% in India.[1] These are almost double the mean prevalence reported in the 1990s,[10] and strongly advocate the need for routine screening of all T1DM patients for coeliac disease, regardless of presence or absence of symptoms. In 2009, the UK's NICE guidelines recommended that children with T1DM should be screened for coeliac disease at the time of diagnosis.[1] But Babiker et al[11] have pointed out that, judging by Cardiff's experience,[12] if the 2009 guidelines were adhered to, only half of the possible childhood coeliac disease cases would be detected, and up to one-third of asymptomatic cases would remain undetected over a 7-year follow-period. Annual screening has, therefore, been suggested, but larger supportive studies are needed.

The need to screen all cases of IBS has recently been challenged by a large American study that found that despite a common finding of coeliac disease antibodies in non-constipated IBS sufferers (7.3%), the presence of histological coeliac disease was almost identical to that of healthy controls (0.41 vs 0.44%, $P>0.99$).[13]

Serological antibody screening and small bowel histology remain the 'gold standard' for coeliac disease diagnosis. Large-population studies have continued to highlight the accuracy of sequential serological antibody testing – high sensitivity of tissue transglutaminase (tTG) and specificity of endomysial antibodies – in detecting symptomatic and asymptomatic coeliac disease.[1] A recent Dutch study of symptomatic children and teenagers suggests that a positive (>100 U/ml) tTG antibody plus symptomatic response to a gluten-free diet (GFD) avoids need for diagnostic biopsy.[1] Infants with chronic diarrhoea and normal serology remain a challenge without a biopsy, but the discovery of a new class of antibodies against deamidated gliadin peptides (α-DGP)[14] have high sensitivity and specificity for coeliac disease in this clinical setting.[1] These α-DGP antibodies can be used to monitor compliance with GFD to a high degree of accuracy in this age group.

Attempts to find non-invasive markers have resulted in novel methods of human leukocyte antigen (HLA) typing techniques. Furthermore, confirming coeliac disease with pre-existing self-prescribed GFD is difficult because both serology and histology can normalise with GFD. In these circumstances, HLA genotyping is of value, but traditional HLA typing methods are costly and labour intensive. Cost-effective HLA typing methods that accurately distinguish risk alleles for coeliac disease have now been reported,[15-17] and they offer promise for screening and diagnosing coeliac disease in developing countries.

To further tackle the problem of detecting a diagnostic immune response to gluten in patients already self-established on GFD, a new subset of peripheral blood gluten-specific T-lymphocytes with better specificity for gut mucosal antigens have been described.[18-19]

Villous atrophy is patchily distributed and the optimal site and number of duodenal biopsies continues to be debated. There is increasing support for duodenal bulb biopsy in addition to D2.[20-22] Furthermore, the diagnostic accuracy of the histological distribution of intraepithelial lymphocytes along the villus for detecting mildly active coeliac cases with otherwise normal villus architecture, has been confirmed.[23-24]

However, the gold-standard status of the histological diagnosis of coeliac disease is under increasing scrutiny and doubt because of the variability of reporting between pathologists, with claims of up to 20% histopathological underdiagnosis of coeliac disease, particularly so with milder forms of the disease. Misinterpretation of poorly oriented biopsies may also lead to overdiagnosis of coeliac disease, mistaken initiation of gluten-free diet, and subsequent unnecessary assessment for misinterpreted failure to respond to the diet.[25]

The author's suggested take-home message is that with the increasing sophistication of serology, where the serological and histological diagnoses do not match up, doubts should be raised about the accuracy of the histological diagnosis. Some authors have recently also put forward the possibility of making the diagnosis and treating patients purely on the basis of serological findings.[26]

References may be accessed at www.thesynapse.net

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