Role of Gastrointestinal Bacteria in Obesity and Type 2 Diabetes
Negligence and Civil Liability in the Medical Profession
German-Maltese Medical Society Update
Toxicology in the Movies
1492. Christopher Columbus set sail for the first voyage to the New World1

1981. Augmentin® – The first clavulanate-potentiated amoxicillin was launched for oral use2

LEADERS WALK IN FRONT

1. Available at http://www.history.com/this-day-in-history/columbus-sets-sail accessed on 28 May 2014

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Local Presentations: Augmentin 500 mg/125 mg & 875 mg/125 mg
Use Machines:
Marketing Authorisation Holders: Augmentin 500 mg/125 mg & 875 mg/125 mg
Gastrointestinal symptoms may be treated symptomatically. Amoxicillin/clavulanic acid can be removed from the circulation by peritoneal dialysis.
Clinical monitoring should be performed during the combination with mycophenolate mofetil and shortly after antibiotic treatment.
Fertility, Pregnancy and Lactation: Refer to SPCs for full list of undesirable effects
Augmentin SR 1000 mg/62.5 mg prolonged-release tablets: Each tablet contains 1000 mg amoxicillin and 62.5 mg clavulanic acid; Pharmacological form: Augmentin 500 mg/125 mg & 875/125 mg: Film coated tablets; Augmentin SR 1500 mg/62.5 mg prolonged-release tablets: Indications: Augmentin 500 mg/125 mg & 875/125 mg: Acute bacterial sinusitis, acute otitis media, acute exacerbations of chronic bronchitis, community acquired pneumonia, cystitis, pyelonephritis; skin and soft tissue infections, animal bites, severe dental abscess with spreading sepsis, boils, and ear infections; Augmentin SR 1000/62.5 mg tablets: are indicated for the treatment of community acquired pneumonia in adults and adolescents aged at least 16 years, caused or thought likely to be caused by community-acquired Streptococcus pneumoniae. PASSIVITY AND METHOD OF ADMINISTRATION: Oral use. Augmentin 500 mg/125 mg: Adults and children ≥16yrs: Recommended dose of two tablets three times a day. Children ≥12 yrs: Children may be treated with Augmentin tablets, suspensions or paediatric sachets. Augmentin SR 1000/62.5 mg: Adults and children ≥16yrs: 2 tablets daily; children 6-12 yrs: 1 tablet daily; children 2-5 yrs: 1/2 tablet daily. All patients with renal impairment dose adjustments are based on the maximum recommended dose level of amoxicillin. To minimise potential gastrointestinal intolerance, administration at the start of a meal. The absorption is optimised when taken at the start of a meal. Refer to SPCs for further administration and dosage guidance. Children: Limit not indicated. For all young formulations, treatment should not be extended beyond 14 days without review. Concomitant use of probenecid is not recommended. Contraindications: Hypersensitivity to the active substances, to any penicillins or to any of the excipients, patients with history of hypersensitivity to beta-lactam antibiotics, history of amoxicillin/clavulanic acid and associated hypersensitivity reaction. Refer to SPCs for full list of undesirable effects
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DOCTORS AS INTELLECTUALS

The medical profession is arguably the most respected profession, and has been so for centuries. It is seen by the general public as one which can be trusted with the most intimate problems, individual or family, medical or social.

It has also been the case that, particularly in the past, doctors have spread their wings beyond the limits of medical practice and have been involved in politics, literature and various aspects of Maltese culture.

It is true that medical practitioners are considered to be very busy with work within their specialty and have little time or inclination to widen their interests to reach out to the general public. One might also expect that any intellectual input should come primarily from the academic members rather than those involved in the day-to-day work at the coalface.

There is, however, a great need for medical practitioners to become more visible within the framework of society, not just as dispensers of medical advice and medication, but also to become involved in issues of public concern.

One issue of concern is the obvious lack of medical (or even basic biological knowledge) within the community. Science in general, but particularly medical science seems to be at a nadir, neglected to a large extent in schools, and evident not only in the illiterate but even in many of those practicing other professions.

In this respect it is encouraging to see medical students writing about medical matters in the local papers. This is certainly an area where most medical practitioners can be involved, whether in print, radio, television, or the more recently introduced social media which seem to include everybody these days.

Perhaps more worrying are the current changing mores relating to ethical issues. Time was when most of us got our ethical substratum from teaching by the church which used to be so predominant in influencing ethical thinking within society. These days, for better or worse, the influence of the church has diminished very considerably, particularly among the younger members of society, leaving a gaping void.

Everyone seems entitled to express their considered but untutored views on any topic. I believe that the medical profession should be at the forefront in informing the public about ethical issues relating to the many aspects of medical and social problems.

Perhaps related to this is the lack of familiariry with basic issues inherent in an education in the humanities, with its emphasis on elucidation of basic ethical and social issues within the community.

Maybe members of the medical profession may feel diffident in discussing issues which are not strictly and narrowly medical. While medical education is the most essential requisite, it should serve as a springboard to launch into wider societal issues. Who else, professional social workers apart, would be more familiar with the widespread issues which many practitioners face every day, issues such as the effects of poverty, domestic violence, child abuse, old age, single motherhood, reproductive technology, and a raft of other societal issues?

Various definitions of ‘intellectual’ have been proposed. A trivial dictionary definition, ‘a person possessing a highly developed intellect’ is obvious enough but this is just a minimum requirement. It is more important to emphasize the role of such individuals in spreading their knowledge and expertise to the general community, and not merely within the coterie of colleagues and related experts.

We can all be intellectuals if we use our special knowledge to engage with the public to tackle a wide range of educational and social issues. As that wise philosopher/statesman Edmund Burke remarked: “All that is needed for the forces of evil to succeed is for enough good men to remain silent.”

The magazine is distributed free of charge to all Maltese doctors, pharmacists & dentists, as well as students of the aforementioned professions, with a print run of 3500 copies.

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Editor-in-Chief: Dr Wilfred Galea
Managing Editor: Dr Ian C Ellul
Sales & circulation Director: Carmen Cachia
Email: mpla@thesynapse.net
Telephone: +356 21453973/4

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Oil on canvas with painting knife

Our Collaborators

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A maintenance bronchodilator treatment for patients with COPD who are breathless

Anoro® Ellipta® (umeclidinium bromide/vilanterol) Abridged Prescribing Information

This medicinal product is subject to additional monitoring. This will allow quick identification of any new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Kindly consult the full Summary of Product Characteristics (SmPC) before prescribing.

Trade Name: Anoro® Ellipta® Active Ingredients: 55 micrograms umeclidinium bromide and 22 micrograms vilanterol (as trifenatate). Pharmaceutical Form: 55 micrograms/22 micrograms inhalation powder, pre-dispensed.

Indications: Maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD).

Dosage and administration: Inhalation only. One inhalation once daily of Anoro® Ellipta® at the same time of the day.

Contraindications: Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate and magnesium stearate).

Precautions: Anoro® Ellipta® should be discontinued immediately in the event of acute symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). Dosage and administration: Inhalation only. One inhalation once daily of Anoro® Ellipta® at the same time of the day.

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In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

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Malta & Gibraltar: If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi ORM 2458, Malta (Tel: +356 21238131)

Malta: alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADR) reporting system:

Report forms can be downloaded from www.medicinesauthority.gov.mt/adportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D’Argens, Gzira GZR 1388, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA): https://yellowcard.mhra.gov.uk/

ANORO ELLIPTA was developed in collaboration with Theravance
Dr Sarah Caruana Galizia MD
graduated in 2014. She is currently a Foundation Doctor (FY2) at MDH

Dr Clayton John Fsadni B.Pharm.(Hons.) MD
graduated with a degree in Pharmacy and Medicine from the UOM in 2006 and 2014 respectively. He worked for two years in community pharmacies and at MDH. He is currently working as a Foundation Doctor (FY2) at MDH.

Dr Morolayo Owolabi MD
is a Nigerian doctor who graduated from the University of Medicine and Pharmacy – Carol Davila, Bucharest Romania. She is currently a Foundation Doctor at MDH.

Dr Sonia Vancell B.Pharm.(Hons.) M.A. (Eur. Stud.) LL.D
is an associate with MamoTCV Advocates, specialising in Commercial and Civil law. She obtained her first degree in pharmacy and started off her professional experience in 1994 as a project and product manager with various international pharmaceutical companies. Subsequently she obtained a Master’s Degree (Distinction) in European Studies and the law degree. She has been practicing law, since 2013.

Dr Franco Vassallo LLD
is one of the founding partners of MamoTCV Advocates and has been practising law in Malta since 1984. He is greatly respected as a commercial and civil litigation lawyer, having represented corporate and individual clients in the Courts of Malta and having acted on behalf of Maltese Authorities in international proceedings, most notably in the Lockerbie and MV Erika trials.

Prof. Albert Cilia-Vincenti MD FRCPath
is a private consultant pathologist in Malta and Chairman of the Academy of Nutritional Medicine (London) and former scientific delegate to the European Medicines Agency (London). He is a former pathology services director to the British and Maltese health services, and a former teacher of London and Malta Universities. He trained at London’s Royal Marsden, Royal Free, St George’s, Charing Cross and The Middlesex hospitals.

Dr Nikolai P Pace MD PhD
is a lecturer and researcher at the Faculty of Medicine and Surgery, University of Malta. His research focuses on the genomics of type 2 diabetes and obesity.

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 Health, Malta.

Dr Dran Fleming
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The Powerful Amoxicillin + Clavulanic Acid Combination

Forcid Solutab:
- Contains amoxicillin and clavulanic acid in the ratio 7:1, the powerful combination to fight infections in unique Forcid Solutab formulation

Forcid Solutab® indications:
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- Cystitis, pylonephritis.
- Skin and soft tissue infections in particular cellulitis, animal bites.
- Severe dental abscess with spreading cellulitis.
- Bone and joint infections, in particular osteomyelitis.

Forcid Solutab® offers a convenient antibiotic therapy for adults and children:
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- Suitable for a wide range of patients: no sugar, no gluten, no sodium, no lactose.

Forcid Solutab® dosing in adults and children ≥ 40 kg:
- Standard dose of Forcid Solutab 1000 is 2 times a day.
- For infections such as otitis media, sinusitis, lower respiratory tract infections and urinary tract infections, Forcid Solutab1000 is recommended to be given 3 times per day.

Atherosclerosis remains the number one cause of morbidity and mortality in most countries. After almost a century of research, the creation of a huge industry in blood cholesterol testing and marketing of statins, as well as significant advances in interventional cardiology and coronary bypass surgery, the causation and pathogenesis of atherosclerosis remains, as yet, not only poorly understood, but actually controversial.

If the risk factors for atherosclerosis remain poorly understood, and some very controversial, it is no wonder that in spite of improved survival from coronary heart disease (CHD) (due to all the efforts and funds spent on investigations and treatment), there is no good evidence that the incidence of atherosclerosis has significantly decreased.

Many doctors leave medical school with a poor knowledge of physiology and biochemistry and come to rely blindly on information imparted from pharmaceutical companies, the latter also influencing clinical research with their funding. So let’s go back to some basic science and clinical research from as far back as the 1960s which, although apparently largely forgotten, remains valid.

Blood insulin (hyperinsulinemia and insulin resistance) has been claimed to be the most important predictor of CHD. However, this has been largely ignored because the “dietary saturated fat, blood cholesterol and CHD” theory has prevailed and spawned the multi-billion dollar industry, directed at lowering LDL-cholesterol. But around 50% of patients hospitalised with CHD are reported to have total and LDL-cholesterol levels within normal limits.

A study which looked at fasting blood insulin levels compared with conventional risk factors, to see which was more predictive of developing CHD over a 5-year period in clinically disease-free individuals, found that fasting insulin levels were more than twice as predictive compared to LDL-cholesterol (Figure 1). Triglycerides (TRG) were also more predictive than LDL. In fact, one of the first signs of hyperinsulinemia is increased TRG. Although HDL by itself is a less powerful predictor than LDL, when the increase in risk of elevated TRG is multiplied by the increase in risk of decreased HDL, the result is very close to fasting insulin as risk predictor for CHD. The fasting TRG/HDL ratio is in fact a surrogate marker for fasting insulin.

You will remember from previous instalments that what routine laboratories measure as LDL consists of two fractions, one large and light and the other small and dense. The latter is very prone to oxidation and claimed to be related to atherosclerosis. The other fraction is reckoned not to be related to CHD. In routine laboratory estimates of LDL levels one does not know which LDL fraction predominates. However, high fasting TRG/HDL ratios have been associated with high levels of the small dense LDL fraction, and the TRG/HDL ratio is therefore a convenient surrogate marker for the small dense LDL fraction.

A study comparing patients who had survived their first heart attack with matched patients without a history of CHD, found (Figure 2) that those with the highest TRG/HDL ratios were 16 times more likely to have a heart attack than those with lower ratios. This is a dramatic finding. Do you know which drug lowers the TRG/HDL ratio? No, it’s not statins. It’s a low-carbohydrate diet with adequate protein and saturated and mono-unsaturated fats.

The conventional wisdom driving the “dietary saturated fat, blood cholesterol and CHD” band-wagon continues to advise doctors and the general public to reduce dietary fat at all costs. But dietary fat has no direct effect on blood insulin. Even way back in 1997, leading nutritional researchers wrote in the New England Journal of Medicine that there is no persuasive data supporting the hypothesis that a low-fat, high-carbohydrate diet has any long-term benefit in treating obesity, CHD and cancer. Why? Because each of these diseases is associated with hyperinsulinemia. Fat has no effect on insulin secretion, whereas carbohydrates have a major stimulatory effect.

In conclusion, it is most unfortunate that the US governmental nutritional advice continues to recommend severe restriction of dietary saturated fat. Also worrying are, (a) the continuing conventional wisdom that LDL is the prime indicator of CHD risk, (b) the lack of recognition that the TRG/HDL ratio is the most predictive of all the routine blood lipid profiles, and (c) that statin therapy protocols based mainly on routine LDL levels (without knowledge of LDL dense sub-fractions) are of suspect validity. Statins might be a blunderbuss therapy whose positive effect on established CHD may be only via their anti-inflammatory action, similar to the far cheaper aspirin.

Whether adding more expensive predictive tests, such as high-sensitivity C-reactive protein (HsCRP) and the PLACest, improves mortality from CHD (compared to the routine TRG/HDL ratio), is not yet clearly established.
Once-daily ULTIBRO BREEZHALER® is indicated as maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).!

![Image of ULTIBRO BREEZHALER®]

**Once-daily ULTIBRO BREEZHALER®**

**Indications and Usage**: ULTIBRO BREEZHALER® is indicated as maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). It is indicated in patients with mild to moderate COPD, including those who are on short-acting beta-agonist therapy. ULTIBRO BREEZHALER® provides long-acting relief for up to 12 hours, offering additional respiratory benefits compared to other long-acting beta-agonists. ULTIBRO BREEZHALER® should not be used in patients with chronic obstructive pulmonary disease (COPD) who are dependent on short-acting beta-agonists or whose need for treatment of asthma is not adequately controlled by inhaled corticosteroids alone. Use of ULTIBRO BREEZHALER® in patients with severe chronic obstructive pulmonary disease (COPD) may increase the risk of serious cardiovascular adverse events, including unstable angina and myocardial infarction. Use ULTIBRO BREEZHALER® in patients with COPD who are at increased risk of cardiovascular disease should be considered on an individual basis.

**Administration**: ULTIBRO BREEZHALER® is administered via a dry powder inhaler. Each inhalation delivers 50 mcg of umeclidinium (a long-acting anticholinergic) and 4.5 mg of vilanterol (a long-acting beta-agonist) into the lungs, providing sustained bronchodilation for up to 12 hours.

**Contraindications**: ULTIBRO BREEZHALER® should not be used in patients with a history of hypersensitivity to any of its components. It should not be used in patients with severe chronic obstructive pulmonary disease (COPD) who are dependent on short-acting beta-agonists or whose need for treatment of asthma is not adequately controlled by inhaled corticosteroids alone.

**Warnings/Precautions**: ULTIBRO BREEZHALER® should not be used in patients with a history of hypersensitivity to any of its components. It should not be used in patients with severe chronic obstructive pulmonary disease (COPD) who are dependent on short-acting beta-agonists or whose need for treatment of asthma is not adequately controlled by inhaled corticosteroids alone.

**Adverse Reactions**: The most common adverse reactions reported with ULTIBRO BREEZHALER® include upper respiratory tract infections, common cold, pharyngitis, and nasopharyngitis. There is no evidence of serious cardiovascular adverse events in patients treated with ULTIBRO BREEZHALER®.

**Dosage and Administration**: ULTIBRO BREEZHALER® is administered via a dry powder inhaler. Each inhalation delivers 50 mcg of umeclidinium and 4.5 mcg of vilanterol. The recommended dose is one inhalation per day in the morning. The inhalation is followed by at least 30 seconds of breath holding to ensure the drug reaches the lungs. Patients should be instructed to inhale deep and fast.

**Drug Interactions**: ULTIBRO BREEZHALER® does not interact significantly with other drugs, but patients should be advised to avoid concurrent use of other long-acting bronchodilators or other inhaled corticosteroids.

**Patient Counseling**: Patients should be advised to use ULTIBRO BREEZHALER® as directed, to take the medication as prescribed, and to store it at room temperature. They should be advised to avoid swallowing the inhaler capsule as it contains essential ingredients that may be harmful if ingested.

1. **Novartis Pharmaceuticals**: ULTIBRO BREEZHALER® Summary of Product Characteristics.
As referred to in the first part of this article, for an aggrieved party to succeed in his claim he must prove to the satisfaction of the court the three elements of negligence, that is:

i. the physician had a duty of care in that particular situation,
ii. the physician failed to discharge the standard of care required by that duty, and
iii. he has suffered damages in consequence of a breach of that duty.

Reference to the first element, that is, that the medical professional has a duty to provide the patient with care in accordance with an accepted standard, has already been made in the first part of this article.

C.ii.b Breach of Duty

Once the duty of care has been demonstrated, a claimant must then prove that the doctor failed to meet this duty; in other words, that the care provided (or lack of it) has fallen below the minimum acceptable standard. An area that has been extensively debated in the courts is how this standard is to be quantified. Although this is a topic of ongoing debate, the basic test remains the ‘Bolam test’, the best known and often quoted definition of standard of care required from doctors. In the English case ‘Bolam vs Friern Hospital Management Committee’ which was decided by Mr Justice McNair, the applicant contended that the doctor was negligent in the manner the therapy was administered and it was alleged that as a consequence he had a lot of complications. The patient brought an action against the doctor in negligence. The judge declared that a doctor is not guilty of negligence “if he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art.” In other words a doctor is not negligent if his actions are supported by a responsible body of medical opinion; the judgement meant that the act of the doctor had to be examined in the light of the practice followed by a responsible body of medical opinion practicing in a similar field of medicine. In this case, Mr Justice McNair delivered a verdict in favour of the defendant hospital.

To determine whether there has been negligence in medical treatment, courts usually follow the same line of enquiry as they pursue in any other claim based on negligence. Courts usually analyse whether the conduct of the defendant amount to a breach of duty of care which he owed to the injured party. As has been stated above, the ‘Bolam test’ is the standard of the ordinary skilled man professing to have that skill.

There are many cases both in Common Law and Civil Law jurisdictions in which actions for medical negligence have been dismissed on the basis that the doctor conformed to an accepted practice of the profession. It is extremely rare for a commonly accepted practice to be condemned as negligence.

It goes without saying that medicine is not static and is continually evolving. A doctor is expected to keep abreast with the new practices and new treatments and departing from an accepted practice does not, in itself, constitute negligence. Thus, if a doctor can justify why he departed from accepted practice, his actions will not be held to be negligent. The rationale behind this is that the medical profession should not be discouraged from trying new techniques and that there should be the least possible interference with the development of medical science.

C.ii.c Error in Judgment

It is pertinent to note that the Maltese courts have held that an error of judgment does not in itself amount to negligence. In the Asphar case the court held that the medical professional cannot be found liable for an error of judgment as long as the error was not the result of negligence or lack of prudence, diligence, and attention of a bonus paterfamilias.

“Il-Professjonista ma hux tenat ghad-danni rizultanti minn żball professionali, ammenokke’ dan l-iżball ma tkuxx grossolan, u ammenokke’ l-htija ma tkuxx tista’ tigi attributa lilu minhabba nuqqas ta’ prudenza, diligenza u attenzjoni ta’ bonus paterfamilias.”

When faced with such a claim, Courts still looked at whether the action taken by the medical professional was in accordance with standard accepted practices.
C.III LINK OF CAUSALITY

For a person to be held liable for negligence the aggrieved party must also establish a link of cause and effect, that is, that he suffered damage and that damage was a result of the doctor’s negligence. Our courts have continuously upheld this necessity and in the Ellul case the Court of Appeal held that:

“Illi hu elementari li ‘per dare luogo a responsabilita’ e necessario che esista un rapport di causa ed effetto tra il fatto illecito ed il danno”.

The burden of proof lies on the claimant, that is, the person alleging the lack of responsibility of the medical professional.

D. DAMAGES

D.1 Criteria for the imposition of responsibility - ‘culpa’ and ‘dolo’

Culpa has been defined as ‘consisting in the omission of due diligence on account of which one is not aware that one’s act is contrary to a provision of the law or that one’s omission constitutes the breach of a duty imposed by law.’ More often than not, culpa arises out of lack of foresight of the harmful consequences of one’s act, consequences which would be readily foreseeable by the reasonable man.

When a person acts with a high degree of negligence and/or imprudence then such a high degree of culpa approximates to dolus. Dolus consists in the knowledge that one’s act is contrary to a provision of the law or that one’s omission constitutes the breach of a duty imposed by law, and that such an act or omission will cause damage.

D.11 Award of damages

An award of damages is the normal remedy sought by the patient for a breach of duty by a medical practitioner whether the claim is brought in contract or in tort. The central purpose of claims for medical malpractice is to compensate the patient, or his heirs for any loss.

D.11.a Tortious responsibility

The Civil Code establishes that the quantum of damages recoverable as a result of tortious responsibility

shall be assessed by the court having regard to the circumstances of the case, and particularly, to the nature and degree of incapacity caused, and to the condition of the injured party.

Under tort, the damages recoverable, consist in ‘the actual loss which the act shall have directly caused to the injured party, in the expenses which the latter may have been compelled to incur in consequence of the damage, in the loss of actual wages or other earnings’.

These are commonly referred to as the ‘damnum emergens’ which are the actual expenses incurred directly as a result of the injury sustained.

The Civil Code also provides for damages recoverable as a result from ‘the loss of future earnings arising from any permanent incapacity, total or partial, which the act may have caused’. These damages are commonly referred to as the ‘lucrum cessans’.

Both damnum emergens and lucrum cessans can be recoverable irrespective of whether the damage was caused through culpa or dolus.

D.11.b Contractual responsibility

In a breach of contract, there is a difference between the damages recoverable when the obligation is breached due to negligence and the damages recoverable when the breach is due to fraud. In the former case the damages are limited to such damages which ‘as were or could have been foreseen at the time of the agreement’. This limitation is non-existent when the breach is due to fraud.

CONCLUSION

This article has focused on important principles in the field of negligence and a very important conclusion of this study is that as a general rule, a doctor who acts in accordance with the general or commonly accepted practice of other professionals in similar circumstances will not be held to have been negligent. A doctor is under a duty to use that degree of care and skill which is expected of a reasonably competent practitioner in the same class which he belongs, acting in the same and similar circumstances. 

REFERENCES

1. Bolam v Friern Hospital Management Committee (1957) 2 All ER 118; (1957) 1 WLR 582 pg 586-588.

Mamo TCV is a Maltese law firm specializing in a number of areas of law including corporate and commercial practices, litigation and alternative dispute resolution, financial services, intellectual property, shipping and aviation, competition, communication, media and technology and employment and labour.

For the past years MAMO TCV has been top ranked by Legal 500, IFLR 1000, Martindale-Hubell, Chambers Global and Chambers Europe.
Help Poppy by prescribing Seretide

Seretide is the only ICS/LABA proven to achieve guideline-defined asthma control in children.

Safety Information

Very common side effects: Headache and nasopharyngitis.

Common side effects: Candidiasis of mouth and throat, pneumonia, bronchitis, hypokalaemia and hoarseness/dysphonia.

Special warnings and precautions for use: Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids.

It is important that patients are reviewed regularly and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained. Monitor height of children on prolonged inhaled steroid therapy.

59% of children wake at night due to their asthma.

Poppy is 50% less likely to wake at night when using Seretide compared to baseline.

Seretide Diskus: 100 mcg from 4 years

Seretide Evohaler: 50 mcg from 4 years

Common side effects:

- Candidiasis of mouth and throat, pneumonia, bronchitis, hypokalaemia and hoarseness/dysphonia.
- Headache and nasopharyngitis.

Special warnings and precautions for use:

- Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids.
- It is important that patients are reviewed regularly and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained. Monitor height of children on prolonged inhaled steroid therapy.

References:

4. Seretide Accuhaler (fluticasone propionate/salmeterol xinafoate).


In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).

REPORTING ADVERSE EVENTS (AEs):

If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to GSK (Påls Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)) or email: mt.info@gsk.com.

Gibraltar: any suspected AEs and medication errors can also be reported via the National Drug Reactions (ADRs) reporting system:

- Report forms can be downloaded from www.medicinesauthority.gov.mt/adrs and posted to the Malta MedicinesAuthority Post-licensing Directorate, 303, Level 3, Rue D’Argens, Gàrsi Ħaġar 1 368 MALTA, or sent by email to postlicensing@medicinesauthority.gov.mt.


We regularly update our product information and summaries of product characteristics on our website at https://www.gsk.com.

We regularly review the product information and summaries of product characteristics on our website at https://www.gsk.com.

We also welcome feedback from healthcare professionals, patients and carers, and recommend you visit our website at https://www.gsk.com.
Prescribing Information

Presentation: Betmiga™ prolonged release tablets containing 25 mg or 50 mg mirabegron.

Indication: Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome.

Dosage: Adults (including the elderly): Recommended dose: 50 mg once daily.

Children and adolescents: Should not be used.

Contraindications:
- Hypersensitivity to active substance or any of the excipients.
- Should not be used in patients with end stage renal disease, severe hepatic impairment and severe uncontrolled hypertension. Not recommended in patients with severe renal impairment and moderate hepatic impairment concomitantly receiving strong CYP3A inhibitors.
- Dose adjustment to 25 mg is recommended in patients with moderate renal and mild hepatic impairment receiving strong CYP3A inhibitor concomitantly. Caution in patients with a known history of QT prolongation or in patients taking medicines known to prolong the QT interval. Not recommended during pregnancy and in women of childbearing potential not using contraception. Not recommended during breastfeeding.
- Interactions: Clinically relevant drug interactions between Betmiga™ and medicinal products that inhibit, induce or are a substrate for one of the CYP isozymes or transporters are not expected, except for inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga™ is a moderate and time-dependant inhibitor of CYP2D6 and weak inhibitor of CYP3A. No dose adjustment needed when administered with CYP2D6 inhibitors or CYP2D6 poor metabolisers. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. When initiating in combination with digoxin the lowest dose for digoxin should be prescribed and serum digoxin should be monitored. Adverse Effects: Urinary tract infection, tachycardia, palpitation, atrial fibrillation, blood pressure increase, leukocytoclastic vasculitis.

Pack and Prices: Country specific.

Legal Category: POM. Product Licence Number: Betmiga™ 25 mg EU/1/12/809/003; Betmiga™ 50 mg EU/1/12/809/010. Date of Preparation: November 2012. Further information available from: Astellas Pharma Europe B.V. P.O. Box 344, 2300 AH Leiden, The Netherlands. Betmiga™ is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics.
The gastrointestinal tract is home to over $10^{14}$ bacteria that collectively form the intestinal microbiome, and their joint genetic repertoire is larger than the human genome. These symbiotic bacteria establish and maintain the gut immune system, and contribute to the breakdown of complex non-digestible plant-derived polysaccharides. The relatively recent technological advances in genomics have revolutionized the study of the intestinal microbiome. It is now possible to sequence mixed microbial genetic material directly extracted from environmental samples without prior laboratory culture of individual species. This emerging field, known as metagenomics, enables a survey of the different microorganisms present in a specific environment. Several large-scale projects such as the Human Microbiome Initiative have characterized microbial genomes from hundreds of isolated human symbionts and have shed light on the complex interplay between the human host and its microbial populace, and how this changes in health and disease.

This article aims to discuss the emerging body of knowledge that links the gut microbiome to the development of obesity and metabolic disease. The growing prevalence of overweight and obesity is easily linked to the sedentary lifestyles and calorie-dense diets typical of ‘Westernized’ countries. There is, however, growing evidence that there are powerful physiological processes that restrict any cognitive mechanisms to reduce excessive weight by drastic changes in lifestyle. The reason is that those same physiological processes maintain body weight within a narrow range. In this respect, obesity is increasingly recognized as a disease rather than as a willful choice.

**The Obesity Microbiome**

The involvement of the gut microbiome in obesity came to light from studies that compared the microbiota between lean and obese mice and human subjects. Using obese, leptin-deficient ob/ob mice, Ley et al showed a difference in the ratio of the two dominant intestinal phyla – Bacteroides and Firmicutes, between obese mice and their lean counterparts. The reason for using leptin-deficient mice is that they exhibit relatively mild hyperglycemia and obesity. This seminal paper showed that in mice, kinship is a strong determinant of caecal microbial composition. Furthermore, Ley et al showed that regardless of family membership, obesity is associated with a 50% reduction of Bacteroides species and a greater proportion of Firmicutes relative to lean mice. These findings were reproduced by Ley et al in humans and subsequently by other investigators. Other investigators have however failed to fully reproduce these findings, possibly due to methodological differences in determining the composition of the microbiome.

Further insight into the role of the microbiome in obesity comes from germ-free (GF) mice. GF mice are born and bred under special conditions to control their exposure to microbes, and can be inoculated by specific bacterial strains for research purposes (gnotobiotics). Studies have shown that GF mice are leaner and resistant to obesity when consuming a high fat, high carbohydrate diet. Subsequently, Backhead et al showed that the transfer of caecal bacteria harvested from normal mice to their GF counterparts is accompanied by a 60% increase in body fat content and insulin resistance, despite a reduced fat intake. Turnbaugh et al proposed that the gut microbiota of obese individuals are more efficient at extracting calories from the diet when compared to microbes from lean individuals. In a series of elegant experiments, they transferred caecal microbes from obese and lean mice to GF mice, the investigators showed that wild-type GF mice exhibit a greater increase in body fat when colonized by bacteria from obese donors than GF mice colonized by caecal bacteria from lean donors. Similar findings have been reported in human studies, where a randomized controlled trial reported significantly improved insulin sensitivity in male patients with metabolic syndrome who...
received allogenic fecal bacteria from a lean donor compared to those who received an autologous gut microbiota infusion. This study also identified a significant increase in intestinal butyrate-producing bacteria in recipients of microbiota from a lean donor. Comparable results have been reported in two large metagenome-wide association studies. Karlson et al showed that T2DM is accompanied by a decrease in butyrate-producing Roseburia and Faecalibacterium prausnitzii when compared to healthy subjects.

**THE EFFECTS OF MICROBIOME-DERIVED PRODUCTS**

Butyrate, along with propionate and acetate, are short-chain fatty acids (SCFAs) derived from the bacterial degradation of complex polysaccharides in the gut. They have important metabolic roles, with butyrate acting as a metabolic substrate for colonic epithelial cells. Studies have implicated these SCFAs in the pathogenesis of inflammatory bowel disease (IBD). Vernia et al identified low fecal concentrations of butyrate in ulcerative colitis, and butyrate enemas suppress inflammation in distal ulcerative colitis. Other studies have investigated the systemic anti-inflammatory effect of butyrate in IBD, while Gao et al report that oral butyrate administration improves insulin sensitivity and energy expenditure in obese mice.

Butyrate is a histone deacetylase (HDAC) inhibitor. Lysine residues in histone proteins undergo post-translational modification as part of the epigenetic regulation of gene expression. The acetylation of lysine residues in histone proteins leads to nucleosome unfolding and transcriptional activation. Conversely, histone deacetylase removes acetyl groups on lysine in histone proteins, leading to transcriptional repression. Gao et al showed that butyrate administration is associated with increased expression of PGC-1α, which leads to increased fatty acid oxidation, mitochondrial activity and energy expenditure. This directly links microbiome-derived SCFA to changes in host gene expression pathways that promote insulin sensitivity.

SCFA also act on host signaling pathways by binding to G-protein coupled receptors in enterodocrine cells. Butyrate has been shown to trigger production and release of the peptide hormone PYY from intestinal enterocytes. Butyrate is also postulated to play a role in the maintenance of intestinal epithelial integrity, thereby preventing the translocation of endotoxins produced by intestinal Gram-negative bacteria. Obesity and insulin resistance are associated with a chronic subclinical inflammatory response, and studies have shown that high fat diets in mice increase the proportion of endotoxin-producing gut microbes and lead to insulin resistance.

The gut microbiome is intimately linked to the regulation of carbohydrate and lipid metabolism in the host. Specifically, research has shown that butyrate-producing bacteria improve insulin sensitivity in both animal and human subjects. T2DM and obesity are also linked to changes in the composition of the microbiome, although evidence regarding the causality of these changes is not clear, for the observed changes in the microbiome might be secondary to the altered intestinal motility and bacterial overgrowth seen in T2DM. Critically, clinical trials involving SCFA supplementation and microbial transfer are needed in order to evaluate any therapeutic application from this emerging field of research.

**THE EFFECT OF HOST FACTORS ON THE GUT MICROBIOME**

The widespread availability of antibiotics has resulted in a number of public health benefits and a reduced infectious disease burden. However, a growing body of evidence links antibiotic use to the obesity pandemic. Thuny et al link long term (6 week) vancomycin use in infective endocarditis to weight gain in adult males. Short term administration of oral ciprofloxacin has been linked to rapid and permanent changes in the composition and diversity of the gut microbiome. In a cohort of over 28,000 Danish subjects, born from normal weight women, an early exposure to antibiotics before the sixth month of age has been linked to an increased risk of being obese later on in life. These findings reinforce the need for more judicious use of antibiotics, and further emphasize the functional interaction between the gut microbiome and host metabolism.

Host diet is also an important determinant of microbiome composition. Changes in fecal enterotypes, as determined by *Prevotella* and *Bacteroides*, have been shown to occur in response to long term protein-rich vs carbohydrate-rich diets in man.

**CONCLUSION**

The gut microbiome has an intimate relationship with the host organism that is vital for energy homeostasis. Studies suggest that changes in microbial composition can lead to obesity through various mechanisms. Although this area of research is still in its infancy, it opens up a number of potential therapeutic approaches to facilitate weight loss or treat obesity and its complications.
Asthma

Relvar Ellipta is for patients (≥12 years) in need of asthma maintenance therapy.

**Because I simply don't have space for asthma**

For patients like Maria, every day is full on, so even small reminders of asthma can have an impact. So, when they’re uncontrolled on ICS alone, choose new Relvar Ellipta:

- The first ICS/LABA combination to deliver continuous 24-hour efficacy
- In a practical, once-daily dose
- Delivered in an easy to use device that patients prefer to their current inhaler

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Please refer to the full Summary of Product Characteristics before prescribing.

**Trade Name:** RELVAR ELLIPTA.

**Active Ingredients:** 92 micrograms or 184 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifluoroacetate).

**Pharmaceutical Form:** 92 micrograms/22 micrograms or 184 micrograms/22 micrograms microspheres inhalation powder, pre-dispersed indications: The 92 micrograms/22 micrograms dose: for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta, agonist and inhaled corticoesteroid) is appropriate; and for the symptomatic treatment of COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. **Contraindications:** Hypersensitivity to the active ingredient or excipients. Precautions for Use: Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. Drug Interactions: Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). Fertility, Pregnancy and Lactation: Pregnancy: No adequate data available. Lactation: Insufficient information available. Fertility: There is no data in humans. Animal studies indicate no effect on fertility. Effect on Drive or Use Machines: No, or negligible influence. Undesirable Effects: Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). Overdose: There is no specific antidote. Treatment of overdose should consist of general supportive measures. Local Presentations: Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispersed and Relvar Ellipta 184 micrograms/22 micrograms inhalation powder, pre-dispersed. Legal Category: POM. Marketing Authorisation Holder: Glaxo Group Limited, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom Marketing Authorisation Numbers: EU/1/13/116660/16 DATE OF PREPARATION: December 2013.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21288131).

**Reporting Adverse Events (AEs):** Malta & Gibraltar: If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Limited, 1, De la Cruz Avenue, Oppini (QRM) 2013, Malta (Tel: +356 21288131).

Malta: alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adpportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 201, Level 3, Rue D’Argens, Gagà GZR 1388, MALTA, or sent by email to postlicensing@medicinesauthority.gov.mt.

Gibraltar: alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (Mhra): https://safetycard.mhra.gov.uk/igenous.

For a therapeutic comparison of Relvar Ellipta 92/22 micrograms once daily, Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. **Contraindications:** Hypersensitivity to the active ingredient or excipients. Precautions for Use: Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. Drug Interactions: Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). Fertility, Pregnancy and Lactation: Pregnancy: No adequate data available. Lactation: Insufficient information available. Fertility: There is no data in humans. Animal studies indicate no effect on fertility. Effect on Drive or Use Machines: No, or negligible influence. Undesirable Effects: Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). Overdose: There is no specific antidote. Treatment of overdose should consist of general supportive measures. Local Presentations: Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispersed and Relvar Ellipta 184 micrograms/22 micrograms inhalation powder, pre-dispersed. Legal Category: POM. Marketing Authorisation Holder: Glaxo Group Limited, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom Marketing Authorisation Numbers: EU/1/13/116660/16 DATE OF PREPARATION: December 2013.

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**References:**
2. Boeker BR et al Fluticasone furoate/vilanterol 100/25 mcg compared with fluticasone furoate 100 mcg in asthma: a randomized trial. JACI In Practice 2013 (in press).
3. Woepke M et al. Qualitative assessment of a two-strip dry powder inhaler (Ellipta™) for COPD and asthma. EAACI. 2013.
5. MALT_0819756800686_15 Date of preparation: January 2014.

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**References:**
2. Boeker BR et al Fluticasone furoate/vilanterol 100/25 mcg compared with fluticasone furoate 100 mcg in asthma: a randomized trial. JACI In Practice 2013 (in press).
3. Woepke M et al. Qualitative assessment of a two-strip dry powder inhaler (Ellipta™) for COPD and asthma. EAACI. 2013.
5. MALT_0819756800686_15 Date of preparation: January 2014.
MY EXPERIENCES WITHIN MMSA

It has been over a year now since my admission into Medical School. Back then I was still a greenhorn when it came to understanding and appreciating the various extra-curricular activities that MMSA had to offer. Now that I am in my second year of pre-clinical study, I can easily say that MMSA is not only one of the most active student organisations on campus but also serves as a crucial ingredient in the recipe of success for any medical student.

The annual Word Diabetes Day happened to be my first experience as an active member of the organisation. My first health checks were truly memorable as they shed light on my actual life aspirations – that of helping and interacting with those in need.

Later on throughout the academic year, I started to participate in a myriad of events organised by the different standing committees. What fascinated me the most was the fact that although the various committees have different functions, they all share a common goal – that of creating better doctors and educating the general populace.

Participating in events such as the Training Resource and Development Programme, Medic T and the various workshops held on a monthly basis gave me more insight on the various active roles that a student can assume within the MMSA and what personal qualities would be ideal for that particular role.

During the summer recess, I enrolled as an active member in the Finance Team as an External Financial Assistant. I was responsible for obtaining sponsors from various companies and liaising with members of the standing committees within the MMSA. Direct communication with large commercial businesses as well as working in a team setting proved to be very fruitful and greatly enhanced my personality as well as my communication skills which are paramount for my future career.

To sum up, I cannot but thank MMSA for giving us students the opportunity to achieve our full potential in becoming the country’s doctors of tomorrow. To this day, I am still discovering new experiences which MMSA has to offer.

ALCOHOLISM IN THE COMMUNITY

The misuse of alcohol resulted in 2.5 million years of potential life lost each year in the United States from 2006 – 2010. Consequences of alcohol misuse arise in the form of acute and chronic conditions, together with adverse social consequences and possible drunk-driving accidents. It, therefore, stands to question what health care professionals can do in order to reduce the above statistic. Firstly, we should act as role models and not partake in such activities of alcohol abuse in our free time. Additionally, we must educate our patients on the serious adverse effects that could result from alcoholism.

But how does one recognise alcoholic patients in the community?

Since the diagnosis of alcoholism depends on the drinker being willing to honestly answer a series of uncomfortable questions about his or her drinking habits, this can be a delicate situation, particularly because a common symptom of alcoholism is denial.

Essential points to consider when discussing alcoholism, be it with the patient themselves or their loved ones, include the importance of alcohol to the person, the amount of alcohol consumed and the frequency of hangovers and blackouts.

REFERENCE

Symbicort® Turbohaler®
(budesonide/formoterol)

Easy to use¹
Patients do not need to hold their breath after inhalation

High lung deposition
(25-40% of delivered dose)²

Peak Inspiratory Flow from around 30 L/min³

Symbicort® Turbohaler® – For Asthma and severe COPD
Consult SmPC for full information.

AEROSOL PRESCRIBING INFORMATION. Refer to Summary of Product Characteristics (SmPC) before prescribing. Symbicort® Turbohaler® (budesonide/formoterol) microspray inhalation, inhalation powder (Budesonide/formoterol femaleate) dihydrate. Indication: Asthma. Treatment of asthma where use of a combination (inhaled corticosteroid and long acting β2 adrenergic agonist) is appropriate. Symbicort Turbohaler® (budesonide/formoterol) microspray inhalation is not appropriate for patients with severe asthma. COPD (Symbicort® Turbohaler® 2008 only): Symptomatically treat patients with COPD with FEV1 ≤70% predicted normal (post-bronchodilator) and an exacerbation history desires bronchodilator therapy. Presentation: Inhalation powder. Symbicort Turbohaler® 200: Each metered dose contains 100 μg budesonide/formation of microspray inhalation and 6 μg formoterol femalate dihydrate. Symbicort Turbohaler® 400: Each metered dose contains 200 μg budesonide/formation of microspray inhalation and 12 μg microspray inhalation and 30 μg formoterol femalate dihydrate. Inhalation. Symbicort® Turbohaler® is a combination of two drugs: Symbicort Turbohaler® 200 is indicated for the treatment of mild to moderate asthma. The lower dose of budesonide (50 μg) and the higher dose of formoterol (6 μg) are intended to have a synergistic effect. Symbicort® Turbohaler® 400 is indicated for the treatment of moderate to severe asthma. The higher dose of budesonide (100 μg) and the higher dose of formoterol (12 μg) are intended to have a complementary effect.

1. Budesonide is a corticosteroid that works by reducing inflammation in the lungs. Formoterol is a long-acting β2-adrenergic agonist that works by relaxing the muscles around the airways.

2. This means that a larger percentage of the medication reaches the lungs compared to other inhalers.

3. This is the flow rate at which the inhaler is used, which is important for effective drug delivery.

References:
Provides extended antibacterial coverage to include the most penicillin-resistant strains.1

Recommended by leading Guidelines as first-line treatment in AOM.2,3

Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis.4

Indicated for children <40 kg and older than 3 months; dosed at 90/6.4 mg/kg/day in 2 divided doses.4

References:

Prepared: September 2015
Job No: MLT_GIB/AES/0001/15(2)
COLONOSCOPY SCREENING IN MODERATE-RISK FAMILY GROUPS

ABSTRACT
Colorectal cancer is one of the commonest forms of cancer in the Maltese population. It can be treated successfully if detected early. The major components of early detection are education and screening.1 People with a family history of CRC but with no genetic disorder putting them at high risk of CRC are considered to be at moderate risk of developing CRC. These are further divided into high/moderate and low/moderate-risk subcategories. The preferred surveillance mode for patients with a moderate risk of developing CRC is total colonoscopy.2

The aims of this audit are to:

- Evaluate the colonoscopy screening pattern for individuals with a family history indicating moderate risk for CRC in a surgical firm at Mater Dei Hospital.
- Compare this pattern with that recommended by the NICE guidelines.

INTRODUCTION
Colorectal cancer (CRC) is one of the commonest cancers in the Maltese population but can be treated successfully if detected early. The major components of early detection are education and screening.1

A total of 90 patients having one or more first degree relatives (FDRs) affected by colorectal cancer who had undergone at least one colonoscopy between November 2007 - January 2015 were identified. Their respective age, indication for colonoscopy, date of procedure and findings were retrieved from the database. These patients were then phoned and asked about:

1. The number of relatives and degree of relation of relatives affected by CRC;
2. Age of relative/s at time of diagnosis with CRC;
3. Presence of gastrointestinal - related symptoms prior to colonoscopy;
4. Number of colonoscopies and the respective dates at which they were performed;
5. Any other investigative procedures done for the same condition.

A summary of the NICE guidelines for colorectal cancer screening and surveillance is shown in Table 1. Compliance for each parameter was awarded a 25% score. Compliance to all categories was given a 100% compliance. The average percentage compliance was then calculated for all patients within each risk category. Any discordance between the guidelines and actual practice was recorded.

<table>
<thead>
<tr>
<th>High Moderate Risk Category</th>
<th>Moderate risk family history categories</th>
<th>Screening Procedure</th>
<th>Age at Initial screen</th>
<th>Screening Procedure and interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal cancer in 3 FDR in first degree kinship, none &lt; 50 years</td>
<td>Colonoscopy</td>
<td>50 years</td>
<td>5 yearly colonoscopy to age 75 years</td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer in 2 FDR in first degree kinship, mean age &lt; 60 years</td>
<td>Colonoscopy</td>
<td>50 years</td>
<td>5 yearly colonoscopy to age 75 years</td>
<td></td>
</tr>
<tr>
<td>Low Moderate Risk Category</td>
<td>Colorectal cancer in 2 FDR ≥ 60 years</td>
<td>Colonoscopy</td>
<td>55 years</td>
<td>Once-only colonoscopy at age 55 years. If normal – no follow up.</td>
</tr>
<tr>
<td>Colorectal cancer in 1 FDR &lt; 50 years</td>
<td>Colonoscopy</td>
<td>55 years</td>
<td>Once-only colonoscopy at age 55 years. If normal – no follow up.</td>
<td></td>
</tr>
<tr>
<td>All other</td>
<td>Colorectal cancer</td>
<td>Colonoscopy</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Table 1: Summary of NICE Guidelines for colorectal cancer screening and surveillance in moderate-risk family groups. *FDR = First Degree Relative.

The guidelines used were the NICE Guidelines for colorectal cancer screening and surveillance in moderate-risk family groups. These were updated by The British Society of Gastroenterology (BSG) and the Association of Coloproctology for Great Britain and Ireland (ACPGBI) in 2002.

Data analysis
All data were processed using Microsoft Excel 2013 and analysed by comparing the number of colonoscopies performed between November 2007 - January 2015 for every patient, with the screening procedure and respective interval recommended by the NICE Guidelines. The parameters required to assess compliance with guidelines included:
1. The number of first degree relatives affected;
2. Age of diagnosis of such relative(s);
3. Age of patient at which colonoscopy was first undergone;
4. Number of colonoscopies within a 5-year interval.
Any discordance between the guidelines and actual practice was recorded.

Ethical approval and consent
The study was approved by the Audit and Data Protection Act Committee and the Mater Dei Hospital data protection Unit. Consent was obtained from the Consultant Surgeon of the Firm.

Results
As shown in Figure 1 the greatest number of patients fell in the ‘other Family history of CRC category’, (35 from 90 patients; 39%). Average compliance to the NICE guidelines was greatest in the low/moderate-risk category (75%) while the lowest compliance was observed in the other family history of CRC category (25%), as shown in Figure 2.
There was 100% compliance in all categories to the NICE recommendations pertaining to the screening process of patients with FDR having a history of CRC (Table 2). Compliance to mean age at which relatives were diagnosed with CRC was 100% in the high/moderate-risk and low/moderate-risk categories. All the patients screened had one or more first degree relatives with history of colorectal cancer, so compliance to this parameter was fulfilled in all categories. The mean age at which the affected relatives were diagnosed with colorectal cancer was also complied with in the low/moderate-risk category and high/moderate-risk category. However, compliance to the recommended frequency of screening and age at which to start screening was low in all categories. Overall percentage compliance to the NICE guidelines across all categories was 11% (Figure 3).

Discussion
Family history categories and recommendations
A positive family history of CRC confers an increased risk for the development of CRC.

The study considered the moderate-risk category which is further divided into high/moderate-risk and low/moderate-risk. The remaining patients fell into the ‘other family history of CRC’ category.

i. The high/moderate-risk category includes:
1. Patients with 3 or more affected relatives in a first degree kinship with each other (none <50 years old as otherwise they would fulfil high risk criteria).
2. Two affected relatives with a mean age <60 years in a first degree kinship.

Recommendation
In this category patients merit low intensity surveillance comprising 5-yearly colonoscopy commencing at age 50 and continuing till 75 years of age. Polyps must be snared and histologically characterised. If adenomas are present, surveillance should be instigated as per adenoma surveillance guidelines.

ii. The low/moderate-risk category includes:
1. Patients with only one affected relative <50 years old.
2. Patients with only two affected first degree relatives aged 60 years or older.

Recommendation
Once only colonoscopy at 55 years of age. Polyps must be snared and histologically characterised. If adenomas are present surveillance should be instigated as per adenoma surveillance guidelines.

Figure 1. Number and percentage of patients in each moderate risk category

<table>
<thead>
<tr>
<th>High Moderate Risk</th>
<th>Low Moderate Risk</th>
<th>Other Family history of Colorectal cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>28%</td>
<td>32%</td>
</tr>
<tr>
<td>35</td>
<td>39%</td>
<td>33%</td>
</tr>
</tbody>
</table>

Table 2: Compliance to the presence of FDR with history of CRC, mean age at which relative was diagnosed with CRC, number of colonoscopies performed within 5 years and age at which first colonoscopy was performed in the 3 moderate risk categories.
iii. All other family history of CRC

Recommendation
No need for screening.

COMPLIANCE WITH SCREENING RECOMMENDATIONS

Most patients screened had a family history of CRC but did not fit the criteria for low or high moderate-risk. The highest average percentage compliance (75%, n=22.5) was found in the low/moderate-risk category (Figure 2).

a. Compliance in the High/Moderate-Risk Category

In the high/moderate-risk category, full compliance was observed with regards to the NICE criteria relating to the screening of patients that had first degree relatives with a history of CRC as well as the mean age at which the relatives were diagnosed. Compliance was not observed with regard to the number of recommended colonoscopies as there was a tendency to screen every 2 years rather than the recommended 5-year interval. When it came to the age of first colonoscopy, delayed and early screening initiation were equally observed. Unawareness of the guidelines, practice of defensive medicine and pressure from patients could all be reasons for non-compliance.

b. Compliance in the Low/Moderate-Risk Category

Most patients in this category had more colonoscopies than recommended by the guidelines. Reasons for this may be similar as for the high/moderate-risk category, that is inadequate history taking leading to improper categorisation of patients, unawareness of the guidelines and the practice of defensive medicine by the clinician. Pressure from the patient and/or relatives, mainly due to anxiety and insecurity may also have contributed to this.

With regards to the age at which screening was initiated, non-compliance was due to delayed screening initiation rather than early screening initiation. Delayed screening initiation may occur if the patient is not under the care of a primary health care provider at the time at which screening is supposed to start. Primary health care providers have

an important role to play in advising patients when they should have their first screening colonoscopy as advised by guidelines and according to which risk category they are in. Another reason for delayed screening initiation is that the patient may be older than the recommended age for screening initiation by the time CRC is discovered in his/her relatives. Health care providers’ lack of knowledge of the screening guidelines may also contribute to delayed screening initiation.

c. Compliance in Patients with ‘Other Family History of CRC’

According to the NICE guidelines, screening is not recommended for those patients with a family history of CRC that did not fall into either of the above categories. Hence, these patients should not have had a colonoscopy. The study showed that screening was mainly conducted on the basis of whether the patient had a first degree relative with a history of CRC or not. The main reasons for non-compliance in this category are the same as the ones mentioned for the previous categories, that is, limited sampling units, pressure to perform screening by the patient or relatives, the practice of defensive medicine and the possible belief of some clinicians that the guidelines for screening are not stringent enough and that following them may lead to missed cases of CRC.

As for any other guidelines, dissemination, accessibility, clarity and regular updating of guidelines is essential to ensure clinician awareness and to improve compliance.

OUTCOMES OF THE SCREENING COLONOSCOPIES PERFORMED

Across all categories, in 50% (n=45) of the colonoscopies carried out, no abnormality was detected (Figure 4). Of the patients that did not fall into low or high/moderate-risk categories, only 14% had polyps on colonoscopy. This supports the recommendation of the guidelines that screening is not to be performed in this category of patients.

It is suggested that left-sided hyperplastic colonic polyps (generally within the reach of a screening sigmoidoscopy) serve as a marker for neoplastic polyps.4

Figure 2. The average percentage of compliance in each moderate risk category

Figure 3. Overall compliance to the NICE guidelines
Relvar Ellipta is for symptomatic treatment of patients with a FEV1 <70% predicted normal (post-bronchodilator) and an exacerbation history1

Because I just don’t have space for more COPD

For many patients like Joe with a history of exacerbations, COPD already takes up too much space in their life, yet they fear losing even more.

So, when they need maintenance therapy, choose new Relvar Ellipta:

- The first ICS/LABA combination to deliver continuous 24-hour efficacy2
- In a practical, once-daily dose1
- Delivered in an easy to use device that patients prefer to their current inhaler1

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Please refer to the full Summary of Product Characteristics before prescribing.

Trade Name: RELVAR ELLIPTA. Active Ingredients: 92 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate).

Dosage and Method of Administration: For Asthma: One inhalation of Relvar Ellipta 92/22 micrograms or 184/22 micrograms once daily. Patients usually experience an improvement in lung function within 15 minutes of inhaling Relvar Ellipta. However, the patient should be informed that regular daily usage is necessary to maintain control of asthma symptoms and that use should be continued even when asymptomatic. If symptoms arise in the period between doses, an inhaled, short-acting beta-agonist should be taken for immediate relief. A starting dose of Relvar Ellipta 92/22 micrograms should be considered for adults and adolescents 12 years and older who require a low to mid dose of inhaled corticosteroid in combination with a long-acting beta-agonist. If patients are inadequately controlled on Relvar Ellipta 92/22 micrograms, the dose can be increased to 184/22 micrograms, which may provide additional improvement in asthma control. For COPD: One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. Contraindications: Hypersensitivity to the active ingredient or excipients. Precautions for Use: Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. Drug Interactions: Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). Fertility, Pregnancy and Lactation: Pregnancy: No adequate data available. Lactation: Insufficient information available. Fertility: There is no data in humans. Animal studies indicate no effect on fertility. Safety, Pregnancy and Lactation: Fertility, Pregnancy and Lactation: See section 6.1 for full information available. Undesirable Effects: Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). Overdose: There is no specific antidote. Treatment of overdose should consist of general supportive measures. Local Presentations: Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispensed and Relvar Ellipta 184 micrograms/22 micrograms inhalation powder, pre-dispensed.

Legal Category: POM.

For Athsma:

One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day.

For COPD:

One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day.

To report any suspected adverse reactions and/or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi (QRM 2158, Malta) (Tel: +356 21238131)

Relvar: alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADR) reporting system Report forms can be downloaded from www.medicinesauthority.gov.mt/adreport and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 1, Rue D’Argens, Gzira GZR 1388, MALTA, or sent by email to postlicensing.medicinesauthority@gmail.com.

Gibraltar: alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (DHRA) https://yellowcard.mhra.gov.uk/
LIMITATIONS
The main limitations were:

a. The cohort of patients all belonged to the same surgical firm;
b. The small sample size;
c. The patients may have forgotten certain details by the time of interview;
d. Time constraints limited the assessment of the overall survival in all referrals according to their risk category.

CONCLUSION AND RECOMMENDATIONS

The tendency is to screen more aggressively than recommended by the NICE guidelines, possibly due to inaccurate history taking and improper patient categorization, unawareness of the guidelines, the practice of defensive medicine and pressure from anxious patients and relatives. To improve compliance, it is recommended that the NICE guidelines should be easily accessible, clear, well-disseminated and regularly updated. There should be more clinician awareness of the unnecessary stress, inconvenience and discomfort that excessively aggressive screening can cause to patients. In patients that fell into the ‘other family history of CRC’ category, polyps were only found in 14%, supporting the guidelines’ recommendation that screening is not necessary in these patients.

Figure 4. Outcome of colonoscopies performed

Figure 3. Overall compliance to the NICE guidelines

GERMAN-MALTESE MEDICAL SOCIETY UPDATE

SIGNING OF MOU BETWEEN THE MINISTRY OF ENERGY & HEALTH AND RED CROSS HOSPITAL

A delegation from Malta visited the Red Cross Hospital (RCH) in Kassel, Germany on the 14th of December to review an ongoing co-operation and to discuss areas in which further co-operation can be carried out. Accompanying his Excellency Mr Albert Friggieri, who in his capacity as Maltese ambassador in Germany had already visited the RCH, there were Dr Chris Fearne, Parliamentary Secretary of the Maltese Ministry of Energy & Health (MEH), Dr Ray Galea, Head of Specialist Medical Education at the University of Malta, and Dr Antoinette Calleja Director of International Relations at the MEH. In addition to the successful Clinical Clerkship Project for Maltese medical students which started in 2013, further expansion in other fields are planned, including specialist exchange in the sphere of medical technical services. Within the framework of this visit an agreement was signed by the MEH of Malta and the RCH with a view to reach these objectives.

Also present at the signing of the memorandum were
Prof. Dr Rudolf Hesterberg Medical Director, Mr Michael Gribner CEO and Mr Christian Collard Human Resources Manager at RCH
DUAC (CLINDAMYCIN/BENZOYL PEROXIDE) IS AN EFFECTIVE TREATMENT THAT HELPS YOUR MILD TO MODERATE ACNE PATIENTS TO SEE IMPROVEMENTS FAST1,3

DUAC HAS A DUAL MODE OF ACTION2

Benzoyl Peroxide

• Keratolytic2
• Treats comedones2 and inflammatory lesions2
• Bactericidal action against P. acnes strains2

Clindamycin

• Suppresses P. acnes 2
• Anti-inflammatory action3

Duac2 once daily gel on the affected area, not just the individual spots

DUAC UNDERSTANDS WHAT’S IMPORTANT TO PATIENTS

• Thoroughly wash the affected area of skin
• Gently pat dry
• Apply a thin layer of Duac gel on the affected area,

DUAC INDICATIONS & USAGE ADVICE2

• Duac Once Daily Gel is indicated for the topical treatment of mild to moderate acne vulgaris, particularly inflammatory lesions in adults and adolescents from 12 years of age and above2
• Formulation contains added moisturisers, glycerin and dimethicone, for better tolerability1

YOUR EXPERT ADVICE CAN SHOW ON THEIR FACE

Duac comes ready-mixed, and is easy for your patients to use. It is recommended that you offer the following guidance4:

Once-daily, in the evening, your patients should2:

• Duac works fast, starting to work in just 2 weeks3
• Duac is a once daily treatment2
• Duac is generally well-tolerated4,5

Most common side effects include erythema, peeling, dryness, burning sensation, photosensitivity and headache

TIPS4

• If your patient’s skin peels or becomes dry, they can try:
  • Using an oil and fragrance-free hypoallergenic moisturiser
  • Using Duac less often, or stopping for one or two days before starting again


DATE OF PREPARATION: January 2016

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STAR TREK SYMPOSIUM 2016

The Star Trek academic symposium will be held at the Faculty of IT, UOM between 15-16th July 2016. This event will be a platform for academics from across many disciplines and Star Trek fans to meet and explore the intersection of the humanities and the sciences. There will be inspirational presentations from national and international speakers, with the programme tailored to attract a wide audience. Contributors will be encouraged to explore and present contemporary issues in medicine, science and technology as well as philosophical, psychological and sociological issues relating to the humanities with a specific focus on and a direct correlation to Star Trek.

The following is a link to the website which is continuously updated with new information: startreksymposium.com

TOXICOLOGY IN THE MOVIES: ‘ERIN BROCKOVICH’

Erin Brockovich is a very poignant movie which highlights medical issues in relation to environmental toxicology, specifically hexavalent chromium. Hexavalent chromium is a genotoxic carcinogen that was found to be contaminating drinking water in Hinkley, California.

The dramatized events narrated in this award winning movie are based on a true story. The character of Erin Brockovich is portrayed by the famous actress Julia Roberts. She is the unemployed mother of three children, desperately looking for a job. Eventually, she manages to take up an assistant position at a legal office. The index case is first presented to the viewer when we see her go through a set of laboratory results and later conduct a home visit to better understand the situation. In the movie, Donna Jensen (Marg Helgenberger) tells her that their medical bills are being taken care of by the Pacific Gas and Electric company who had also offered to buy her house. Soon after, we see her speak to a toxicologist who explains to her that there is a difference between, for example, trivalent chromium (Cr(III)) and hexavalent chromium (Cr(VI)), the latter being highly toxic and carcinogenic. An example of hexavalent chromium’s practical use is for its anticorrosive properties. The Hinkley chromium level in water exceeded the maximum contaminant level stipulated by regulation. The fictitious Jensen family are said in the film to have had Hodgkin’s lymphoma, uterine cancer, chronic nosebleeds etc. Erin Brockovich later meets another family, who used to live across the road to the index family, who had five miscarriages. As the story progresses she meets many more families in the area who were also affected.

Hexavalent chromium exposure, such as in this case, also forms part of the wider remit of ecotoxicology and occupational medicine, and remediation strategies have been devised. The effects of exposure to hexavalent chromium can be diverse, and have also been studied in cell lines and animal models.

References can be accessed via thesynapse.net
You are presently living and working in Copenhagen - can you explain more about this post?
I have been employed with WHO since 1998 and this is my 4th duty station to date. I started off with two years in Fiji, then six years in Manila, then four years in Geneva and have now been in Copenhagen for five years.

What was your specialisation in Malta before you left?
I specialized in public health and held two posts. The first was Head of the Health Education Unit, which is now incorporated into the Health Promotion & Disease Prevention Services. I spent six years in this post. Afterwards I became the first Executive Director of the Institute of Healthcare, now Faculty of Health Sciences. I held this post between 1992 and 1998.

How did you come to relocate abroad?
The public health discipline is characteristically dependent on social, cultural, behavioural and other determinants of health and disease, all of which are often connected with international influences. Consider, for instance, migration, disease outbreaks, cultural influences such as advertising, trade and cross-border relations ... it is all much larger than what happens in a single country. In Malta, I was very aware of the influences of public health on small island nations. In fact, Malta is a key leader in the study of sociology, economics, administration, and public health amongst small island nations. I began writing about the topic and presented a paper to the WHO. That basically started it all.

What has been your most pleasantly surprising experience during these years?
Living in the small islands of the Pacific. I was offered the post in Suva, Fiji at the end of 1997, to manage a programme called ‘Healthy Islands’ which concerned itself with non-communicable epidemics. It was a very different context to Malta, of course. I was pleasantly surprised to find a good level of technical competences and much of my Maltese experience in public health was directly relevant to the work I conducted there.

Can you explain more?
In the mid-late 1990’s the Pacific islands started exploring health promotion. I was lucky to be given the chance to contribute to a number of initiatives. By 1998, several projects were running in parallel and I had the chance to work in Fiji, Tonga, Papua New Guinea, Nauru, Marshall Islands, Cook Islands, Samoa, Micronesia and others. I travelled to 13 of the 22 Pacific countries and territories. Epidemiological studies showed very high levels of risk and burden related to a number of noncommunicable diseases. This meant that one had to take into account health systems, trade patterns and behavioural influences, alongside genetic and demographic issues. Consider the presence of certain types of imported foods - turkey tails and mutton flaps – which are all extremely high in fats and which, over a relatively short time period, came to form part of “traditional food”. Furthermore, fishing rights are leased as a source of foreign revenue. This led to a situation, where ironically, island people primarily accessed canned fish, rather than atolls and the sea. These trends (among other influences) resulted in a high incidence of diabetes, obesity and heart disease which exerted a toll on services, well-being and life expectancy. I must say that during these years I was privileged to work with many leaders who guided the islands in the implementation of innovative programmes to combat such a situation.

What about your present role in Europe?
I am Director of Noncommunicable Diseases and Promoting Health through the Lifecourse within the Regional Office of Europe at the WHO. Briefly, my division covers the fifty-
three Member States of Europe, ranging from Central Asia to Western Europe. Technical units under NCDs include tobacco and alcohol control, diet and physical activity, NCD management, mental health and the prevention of violence and injury. Under the life-course programme, an area that was the subject of a Ministerial Conference in Minsk, Belarus in 2015, we cover the gamut from neonatal health to healthy ageing. A fairly broad remit in a very diverse Europe.

What was it like, travelling and relocating in such different surroundings?
There were definitely plenty of radical lifestyle changes, actually less dramatic than one might think. I moved with my wife, Ann, who is also a physician and our two children; with a family, adjustments are not always simple. However, it was all a very enriching experience. We researched each location, searched the best schooling at every level and with careful planning, managed it all. These are normal experiences to many of my peers who are expatriate.

Let us move away from the islands for a moment and concentrate on your involvement here in Malta with the set-up of The Synapse. What are your memories on that?
It all began as a joint partnership with Dr Wilfred Galea. We were young medical doctors interested in programming and IT. The technology was very limited back then, as was the awareness of the medical community on the riches of the World Wide Web. We wanted to change that and provide available resources to medical students and professionals. Our plan was to kick off the project with a bulletin board, carrying info such as Department of Health circulars, for instance. The idea of a bulletin board was suddenly overtaken by the introduction of Internet in Malta. We found we could run our own server and the new technology proved to be a huge but rewarding learning curve for us. Wilfred built a network of contacts with colleagues and companies, whilst I tackled web development and design. The Synapse embraced new partners such as Keith Gauci and Aldo Calleja who took on the management and technical side of the project. I had to leave the partnership when I moved abroad. I am happy to see the project progressed successfully thanks to Wilfred’s able guidance. Truly, those early days in our discovery of the potential of the internet were extremely exciting for us. Since then, I have kept abreast with technology, including the exploration of new languages and recent trends towards “big data”, data visualisation, machine learning, and becoming familiar with a range of open source statistical computing software … all tools which have the potential to transform the face of public health itself.

I READ THE SYNAPSE BECAUSE...
Mostly for the nostalgia of remembering where we started, and am pleased to see, on occasional visits, that The Synapse is still going strong, that it has incorporated new channels – print, web and app – and that it is still providing a sterling service to the profession.
Incorporates proven Air-Stirrup® ankle brace features with additional compression and stabilization provided by the Airsport's patented ATF cross-step and integral midfoot and shin wraps.

- The unique “step-in” design (toes first into the back of the brace) and automatic heel adjustment simplify application.

**Indication:** Ankle sprains; Chronic instability; Prophylaxis

<table>
<thead>
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<th>Size</th>
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<th>Shoe Size</th>
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<tr>
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<td></td>
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**Indication:** Acute ankle sprain; Post-op (tendon rupture and ankle fracture); Chronic instability; Prophylaxis
Ultrasound (US) has become the most commonly used imaging method to assess musculo-skeletal (MSK) injuries. In addition to the high soft tissue image quality it provides, MSK US has the advantage of providing a rapid mode of evaluation that avoids the use of ionising radiation, allows dynamic assessment and can guide targeted treatment. Use of high quality scanning equipment to diagnose and treat MSK injuries is of the utmost importance. Without the necessary high image resolution, most injuries will be missed. Sonographer experience also has a major influence on diagnostic accuracy.

In children, tendons and ligaments are usually stronger than the growth plate. Thus, growth plate injuries are more common than tendonous/ligamentous injuries. Consequently, overuse injuries in a tendon that attaches to an un-united apophysis are more likely to affect the apophysis than the tendon. Such injuries were previously referred to as osteochondrites or apophysites, however they are now recognised as overuse injuries. The most common type of apophyseal overuse injury is Osgood-Schlatter’s disease (OSD), which affects the insertion of the patellar tendon into the tibia. In the past, a child or young adult presenting with pain below the patella would promptly be referred for a lateral X-ray of the knee (Fig 1a) to detect OSD. Today, an ultrasound of the knee will not only depict the fragmented ossification centre seen on X-ray, but will also provide more detailed information on the state of the soft tissues, including the presence of any fluid collections or adventitial bursae, while confirming or otherwise the integrity of the patellar tendon (Fig 1b).

Other common sites of apophyseal injury include the proximal patellar tendon insertion (Sinding-Larsen-Johansson’s disease) (Fig 2), the insertion of the Achilles’ tendon into the calcaneus (Sever’s disease) (Fig 3) and the insertion of the triceps muscle into the olecranon.

In adolescents, after growth plate closure, injuries at tendon attachment sites are generally referred to tendinopathies; the term tendinopathy refers to a combination of pathologies that include tendinosis (collagen degeneration, fibre disorientation and accumulation of mucoid substance), tendinitis (findings of tendinosis and the presence of inflammatory cells) and paratendinitis (inflammation of the paratenon). Unlike MRI, which shows healthy tendons as homogeneous dark bands in all imaging protocols (Fig 4a), ultrasound is able to distinguish a fibrillar pattern running longitudinally through the tendon that correlates with collagenous fibre bundles (Fig 4b).

US findings of tendinosis include focal thickening with heterogeneous decreased echogenicity and loss of the normal fibrillar pattern (Fig 5a). Assessment of the area of abnormal texture with Colour Doppler US may show an area of increased blood flow (Fig 5b). Detection of these findings is not only useful for diagnosis of tendinosis but also for guiding treatments. Such treatments may include needling or fenestration, which induces haemorrhage and inflammation, both of which stimulate production of growth factors to promote healing. Platelet Rich Plasma (PRP) infiltration has the same effect. On the other hand, sclerotherapy - which is achieved by injecting a sclerosant such as polidocanol to occlude the vessels (Fig 6) - results in a decrease in inflammatory response. Although the latter is contradictory to other techniques mentioned earlier, which rely on an inflammatory response to induce healing, sclerotherapy has been shown to have positive results particularly in patellar tendinosis, lateral epicondylitis of the elbow and Achilles’ tendinosis.

Continued overuse in the presence of tendinosis can result in progression to a partial or complete tear. Partial tears may be longitudinal or transverse. Longitudinal tears (also called longitudinal splits) course along the length of the tendon and may resemble tendinosis on US. Longitudinal tears are best seen when the tendon is imaged perpendicular to its course (along the short axis) (Fig 7). Transverse tendon tears are best seen when imaged parallel to the course of the tendon. Partial
thickness transverse tears may appear as an irregularity along one margin of the tendon or as a partial cleft within the tendon (Fig 8). A full thickness tear will present as a fluid-filled gap in the tendon with retraction of the proximal and distal segments (Fig 9). Dynamic US assessment during muscle contraction may improve visibility of a transverse tendon tear on ultrasound by opening the gap.

Tenosynovitis is an inflammatory reaction of the tendon synovial sheath, which is the most common type of overuse injury and is readily detected with US. It may present alone with pain located over the tendon and accentuated by tendon movements. Tenosynovitis may also present itself in association with tendinosis and tendon tears. US is highly accurate in detecting tenosynovitis (Fig 10) and in guiding treatment with injection of long acting steroids or PRP into the tendon sheath.

In summary, US has become the first line of management for acute soft tissue injuries. It provides immediate and accurate results in a safe and dynamic fashion. Tendon injuries are frequently better seen on US than with more complex imaging such as MRI. US also provides a means to deliver immediate and targeted treatment to decrease convalescence times.

Part II of this article will discuss imaging and treatment of ligamentous injury.

(to be continued ...)

Figure 1a. Lateral X-ray of the knee showing the fragmented ossification centre (arrow) at the site of insertion of the patellar tendon into the tibial tuberosity as well as soft tissue swelling (Osgood-Schlatter’s disease)

Figure 1b. Sagittal US image showing the fragmented ossification centre (grey arrow), soft tissue swelling over the ossification centre (white arrow) and fluid deep to the patellar tendon (arrowhead)

Figure 2a. Lateral X-ray of the knee showing a fragmented apophysis at the inferior margin of the patella (Sinding-Larsen-Johansson’s syndrome)

Figure 2b. Sagittal US image in a patient with Sinding-Larsen-Johansson’s syndrome showing fragmented ossification at the insertion of the patellar tendon into the inferior pole of the patella

Figure 3a. This lateral X-ray of the calcaneus shows sclerosis of the posterior apophysis of the calcaneus (arrows) as well as widening of the epiphyseal plate (arrowheads), classic features of Sever’s disease, an overuse injury at the insertion of the Achilles’ tendon

Figure 3b. Sagittal US image in a case of Sever’s disease showing a fluid collection (arrow) at the insertion of the Achilles’ tendon into the calcaneus
Figure 4a. Sagittal Proton Density-weighted MRI scan of the normal patellar tendon, which appears as a dark uniform band (arrows).

Figure 4b. Sagittal US of a normal patellar tendon showing a fibrillar internal structure (arrows) that correlates with collagen bundles running in a longitudinal direction parallel to the course of the tendon.

Figure 5a and b. Sagittal US scans through the proximal patellar tendon showing tendon thickening and loss of fibrillar pattern (a) with increased blood flow seen on Colour Doppler Imaging (b).

Figure 6a and b. Synchronised US scans in conventional (a) and Doppler (b) modes showing a guided sclerotherapy for patellar tendinosis.

Figure 7. Transverse US scan of the long head of the biceps tendon (arrow) showing a split (arrowheads) within the tendon.

Figure 8. Longitudinal US scan of the supraspinatus tendon showing a partial cleft (arrow) on the deep aspect (articular side) of the tendon.

Figure 9. Longitudinal US scan of the Achilles’ tendon showing a full thickness transverse tear (arrow).

Figure 10. Transverse US scan through the extensor tendons of the index, middle and ring fingers at the level of the proximal metacarpal bones. Dark rings around each of the tendons (arrows) represent the thickened synovial sheaths.
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✓ Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis.

✓ Indicated for use in adults & adolescents aged ≥16 years; 2 tablets BD for 7-10 days.

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### References:


2. Anthony R. White et al. Amoxicillin (as trihydrate) and potassium clavulanate. PRESENTATION: 1000 mg/62.5 mg prolonged-release tablets. Supplied in 28 tablet packs. INDICATION: Treatment of community-acquired pneumonia in adults and adolescents aged at least 16 years, caused or thought likely to be caused by penicillin-resistant Streptococcus pneumoniae. POSOLOGY & ADMINISTRATION: Oral use. Recommended dose of two tablets twice daily for seven to ten days. To minimise potential gastrointestinal intolerance, administer at the start of a meal. CONTRAINDICATIONS: Hypersensitivity (and past history of) to the active substances, to any penicillins or to any of the excipients. SPECIAL WARNINGS & PRECAUTIONS: Before initiating therapy careful enquiry of previous hypersensitivity reactions to beta-lactams. Where an infection is proven to be due to an amoxicillin susceptible organism, a switch to an amoxicillin-only preparation should be considered. Convulsions may occur in patients receiving high doses or who have impaired renal function. Concomitant use of alopurinol increase likelihood of allergic skin reactions. Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Contains 29.3 mg (1.3 mmol) of sodium per tablet. Refer to SPC’s for full list of precautions. INTERACTIONS: Penicillins may reduce the excretion of methotrexate causing increased toxicity. Mycophenolate mofetil and shortly after antibiotic treatment. Penicillins may increase the risk of methotrexate being converted to active metabolites causing possible increase in toxicity. Concomitant use of probenecid is not recommended. If co-administration occurring. Please refer to full Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131). REPORTING ADVERSE EVENTS (AEs): If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131). Alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system: Report forms can be downloaded from www.medicinesauthority.gov.mt/adportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D’Argens, Gzira GZR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt.

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