MINIMA MEDICA

2020 ISSUE

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The Role of the Doctor at this Day and Age

I was very delighted when I was invited by the Malta Medical Students' Association (MMSA) to write the editorial for this issue of Minima Medicamenta. Twenty-three years ago, in my role as the Medical Education Officer for MMSA, I myself was the Editor of the 'Murmur', which at the time was the MMSA's student magazine, the content of which was more of a lighter nature. MMSA has made giant leaps, and as evidenced by this particular issue, from an early stage, medical students are getting involved in authoring high quality scientific work such as the literature reviews and case reports.

This is of vital importance, because as doctors, our role is not just to diagnose and manage patients, but to inform and educate society. This is in spite of the fact that we live in an age where 'information' is available at the click of a button, and yet it has become overwhelmingly delugedby 'misinformation' which is packaged in such a way that it may heavily influence the unwary. Medical students must be very well-equipped in order to fullfill their role as future medical doctors in modern society and learn to be unafraid to state facts and help point their patients in the right direction. At the time of writing, society is facing two major health-related issues on a national and international level: domestic violence and the novel coronavirus infection.

There is a significant amount of hidden domestic violence, even on our little tiny rock. Doctors from the Accident and Emergency Department at Mater Dei have recently warned that there are "too many" domestic abuse cases that go under the radar, as the victims are either afraid of the perpetrators or feel helpless in their fight for their rights. As the ones on the frontline, doctors deal with domestic abuse victims on a regular basis. They are victims of all ages, of any gender, coming from all social strata and hailing from all different cultural and racial origin. Apart from medicating the physical injuries, doctors play a crucial role as the point of reference of multidisciplinary management in order to defend the 'voiceless'. We have seen many success stories in the international media how women have been saved from a domestic violence trap by reaching out to all kinds of service workers, even fast food chain employees. Just imagine how much heavier is the responsibility on our shoulders as trusted professionals to help these individuals escape their silent traps. It is therefore our role to be sensitive to these issues and be well-informed in order to be the advocates to influence authorities, stakeholders and lawmakers, in the interest of the most vulnerable in society.

As concern grows over the coronavirus, which was first diagnosed in Hubei province in China, fake news and scams capitalising on people's fears have been also spreading into what WHO has named an 'infodemic'. Given that the world is hooked on social media, viral misinformation can worsen any global public health emergency creating damage and hurting people far more than the fatality rate of the disease itself.

While there is no doubt that the social media is a powerful tool in spreading public health news, education and debunking myths, unfortunately the myth-makers tend to outnumber the educators. It is causing waves of racism and xenophobia. Misleading videos are instantly viewed and shared by numerous users, and even after deleting the original post, reactions and responses to video-duets still linger on, emphasizing how difficult it is to kill digital falsehoods (check out the measles vaccine 'infodemic' which is still raging despite the original paper having been retracted for ages). As doctors and frontline workers, we have a duty to inform ourselves from authoritative and peer-reviewed scientific sources. We have the obligation to correctly inform and educate both ourselves and the public at large. The damage wreaked by a doctor spewing misinformation on the media is indeed incalculable.

In conclusion, quoting Rudolf Virchow (1821-1902), one of the 19th century's foremost leaders in medicine and pathology, as well as a public health activist, social reformer and politician: "Medical education does not exist to provide students with a way of making a living, but to ensure the health of the community."

Prof Jean Calleja Agius
MD, FRCOG, FRCPI, MSc Clinical Embryology (Leeds), PhD (London)

Foreword Message
President, Omar Chircop

The Malta Medical Students' Association is there to support students in all their skills and talents and bring them out in a practical way. Minima Medica is a perfect example of this. It is a platform that allows our members to write scientific articles as a way of showcasing the importance of research, give an opportunity to our members to work in research and be a learning tool that teaches students both the common and uncommon diagnoses that we will encounter as future doctors.

It is with great pride and joy that during my term as president we are launching the sixth edition of Minima Medicamenta again after several years of not being published. Minima is the product of a lot of preparation, hard work and a collaborative team effort. Congratulations to everyone involved, the writers, media team, the publishers and the whole SCOME team.

These past years MMSA has been working within the field of research, having organized three annual research conferences in a row, the publishing of Minima is a major step forward towards our efforts as a student organisation to inform students of how important research is and how as students we can do our own research.

Looking forward to see MMSA keep on publishing Minima on a yearly basis with innovative initiatives in the field of research.

I hope all readers both professors, clinicians and health science students enjoy this publication, find it an interesting read and aid their current studies and future work.

Omar Chircop
MMSA President 2020

Foreword Message
SCOME Officer, Gloria Montebello

MMSA, through the platform of SCOME, has been working throughout the past years to restructure its impact, by harmonizing medical students' involvement in their own Medical Education. As Medical Education Officer for the term 2019-2020, I have witnessed a transformative attitude whereby students are getting more intrigued to be active in their academical enhancement and also in the remit of advocacy.

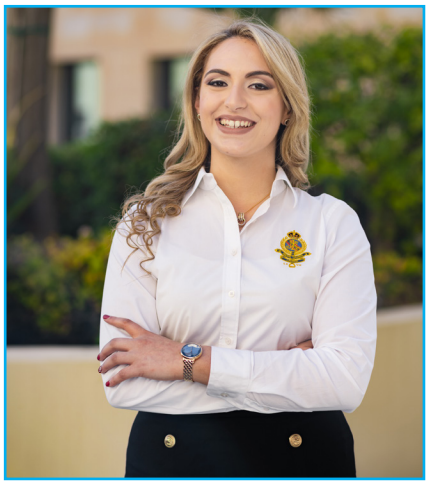
A positive energy has transcended upon me following influential SCOME Officers and this has put upon me a great responsibility – a promise to continue to provide more learning opportunities for all students to succeed. This vision fueled in me the idea to again recommence MMSA SCOME's own publication - Minima Medica.

Minima Medica, formerly named Minima Medica, is the first opportunity offered to medical students to step into the world of academical publications whilst rekindling the passion towards medicine. A holistic student seeks a continuous developmental approach through critical thinking with a prospect of becoming a reflective professional who progresses every day. Last published in 2016, Minima Medica is now back on track thanks to my Minima Medica Coordinators Ms Gabrielle Grixti and Ms Daniela Chatlani who have been instrumental in assisting our 6 budding writers until the publication of this final project.

''Your task is not to foresee the future, but to enable it"- Antoine de Saint Exupery

Within SCOME this year, we have worked tirelessly to provide multiple platforms whereby all interested students can find their voice or improve a skill. We have not only created concept notes but we have enabled goals and objectives that are within our reach as enthusiastic Medical Students. Having all the tools, now it is our turn to make great use of them.

I encourage you to approach this publication with open minds and a passionate heart towards medicine and learning! I hope that you'll enjoy reading as much as we have enjoyed preparing this project for you – our beloved MMSA member.



Gloria Montebello
Medical Education Officer 2019-2020
Board of Studies Representative 2019-2020

Editors' Message
Gabrielle Grixti and Daniela Chatlani

Dear readers,

Before applying to become Minima's editors, we had no idea that this publication existed. It is a shame that for the last 3 years students have not had a chance to publish their work. We were therefore very excited to revive this journal!

In this journal one can find an array of both literature reviews and clinical cases, which are sure to peak your interest. The aim of including both was to provide equal opportunities to all medical students. The work of the original authors went through a long process in order to achieve the greatest accuracy possible. Their work was initially reviewed by their tutor, followed by further suggestions from external professionals found by MMSA, and finally reviewed by an English professional. One can see that this journey would not have been possible without the contributions of various people from all walks of life, and this was our original vision, when we became coordinators.

It was no coincidence that Minima Medica was launched during the SCOME Research Conference 2020. Minima acts as a bridge between us as medical students and the potential research we can do. We hope this journal encourages you to pursue further opportunities in the field of research and publication.

We hope you enjoy this journal as much as we enjoyed putting it together!

Gabrielle Grixti
Minima Medica Editor 2020

Daniela Chatlani
Minima Medica Editor 2020

Research: Hierarchy of Evidence

It is heartening to witness a display of papers written by medical students. It may be salutary for the younger colleagues to read a reminder as to how the hierarchy of evidence is viewed by clinicians and researchers alike and for this reason, the editorial will briefly outline this pyramid.

1.1. Observational studies

Observational studies describe a naturally occurring variation within a given population. Types of observational studies include:

- Case report or case series
- Ecological studies
- Cross-sectional studies and surveys
- Case-control studies
- Cohort studies

2.1.1 Case series

A case report or series is a descriptive study that does not involve any hypothesis testing. Instead the study observes subjects with a known exposure (such as a type of medication) and records outcome data - selection bias is inherent.

2.1.2 Ecological studies

Ecological studies describe the associations between an exposure and an outcome at a group level such as by time trends or by geographical location. However, such studies cannot confirm associations.

2.1.3 Cross-sectional studies

Cross-sectional studies record data at one point in time, a snapshot. This type of study is easy to conduct and relatively cheap. Conducting regular cross-sectional randomised population studies may provide useful health information on exposures and outcomes. However, temporal relationships between the exposure and the outcome cannot be confirmed.

2.1.4 Case-control studies

Case-control studies retrospectively explore an exposure between the individuals with a disease (case) and those without the disease (control). This is relatively quick and cheap but susceptible to selection and recall bias, and temporal relationships between exposure and the outcome cannot be assessed.

2.1.5 Cohort studies

Cohort studies (or longitudinal studies) follow a group of people (healthy or otherwise) over a period of time, in order to measure the incidence of a particular disease (if healthy) or to

the natural history, survival rate etc of those with the condition. This permits the establishment of temporal relationships between exposure and outcome/s. These studies are expensive and time-consuming and the latter may result in losses to follow-up and non-participation.

2.2 Experimental studies

Experimental studies the researcher's can control/alter various factors/s, and then measuring the variation/s in outcome/s. The controlling interventional factors include but are not limited to: medication, vaccinations and behavioural change programmes. The commonest type of experimental study in medicine is a clinical trial 1.

2.2.1 Clinical trials

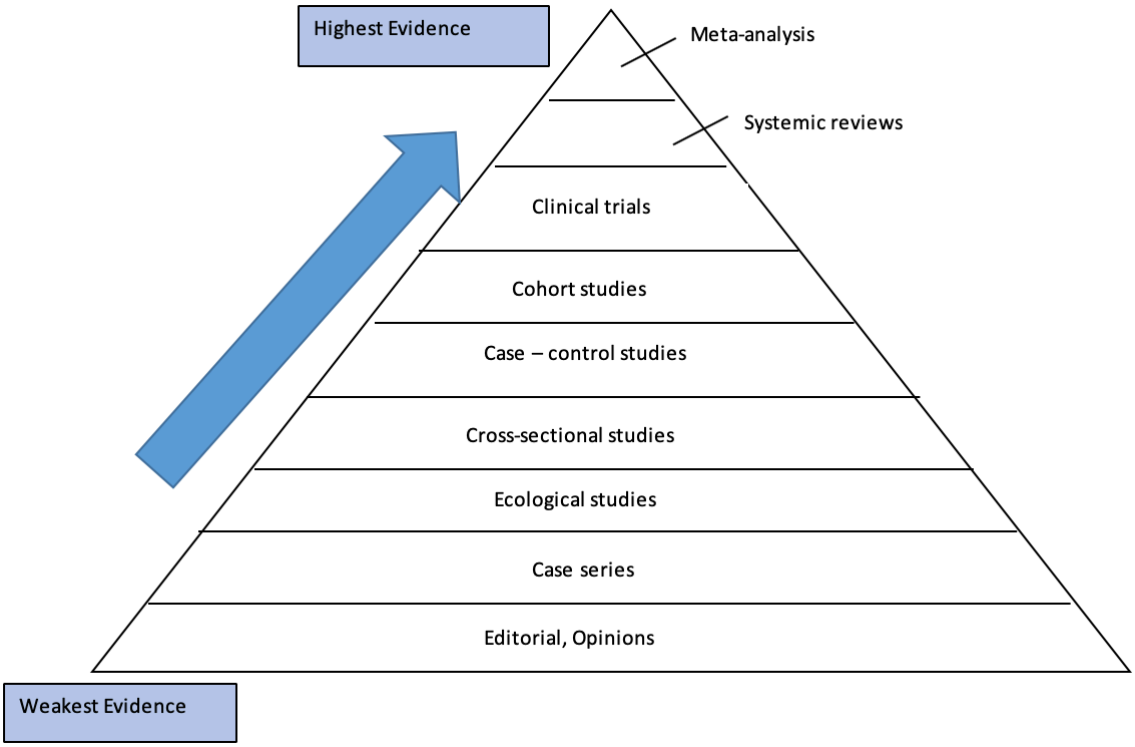
A clinical trial is an experiment designed to measure the effect of an intervention, prospectively, using an interventional and a control group.
Randomised control trials (RCTs) are the commonest type and this avoids bias i.e. individuals are randomly allocated to either the intervention group or the control group. It is best to blind i.e. the best is a double-blinded trial wherein both the investigators and the participants are unaware which is the intervention group, and which is the control group.

2.3 Other type of studies

A systemic review of the literature review collects published research data on a topic and formulates a summary. It is a common for a systemic review to precede a meta-analysis.
A meta-analysis statistically collates and combines a number of published scientific studies on a topic in order to achieve a higher statistical power.

2.0 Hierarchy of evidence

The study design chosen will depend on the question being investigated and the funding available. Clinical guidelines and policies are based on the highest evidence-based data available. Figure 1 illustrates the hierarchy of evidence for research studies.



It is accepted practice for medical guidelines to provide the level of evidence on which each and every part is based as per table 1.

Conclusion

At this stage in a medical student's career, you will (at best) almost certainly only be creating work at the lowest level of evidence. You should not be disheartened. We all started out like this, with the odd case report and audit, and slowly built up to strong studies and important papers. The important thing is "to strive, to seek, to find, and not to yield." I wish you all the best of luck not only in your medical careers but also in your academic (teaching and research) careers.

Table 1. Level of evidence in published research material

Grade of recommendation	Level of evidence	Research design
A	1a	Systemic review of RCTs
	1b	Individual RCT
B	2a	Systemic review of cohort studies
	2b	Individual cohort study
	3a	Systemic review of case-control studies
	3b	Individual case-control study
C	4	Case series
D	5	Expert opinion without any critical appraisal

Acknowledgments

The inspiration for this papers arises from the international Write a Scientific Paper course (WASP - http://www.ithams.com/wasp) and indeed, this summary is based on a paper in the WASP series.

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Prof. Victor Grech
Associate Professor, University of Malta and Consultant Paediatric Cardiologist, Mater Dei Hospital, Msida Malta

Literature Reviews

Face Blindness

External Reviewer
Prof. Richard Muscat

Tutor
Dr. Christian Zammit
M.D.,M.Sc.

Overview on Face Blindness

Facial recognition is a complex task, often done immediately and readily, involving discrimination of subtle differences in facial structures with differences in facial expressions, ageing, perspectives and lighting. Facial recognition requires fast identification of stimuli which are then correlated against reservoirs of faces which are accumulated throughout life (Barton and Corrow, 2016).

The facial recognition system is extremely complex, and if impaired, cannot be fully remedied by other areas of the brain. When such injury occurs early on in life, juvenile brain plasticity has been shown to be potentially inadequate to restore facial recognition functions, thereby suggesting that such an impairment can have severe, permanent implications, even at an early age (Barton et al., 2003)

Damage to any part of the facial recognition mechanism may result in the development of face blindness. Such dysfunction results in the development of selective face-recognition and visual learning deficits, a condition called prosopagnosia. Prosopagnosia can be either acquired or congenital. The acquired form of prosopagnosia is considered to be a rare consequence of occipital or temporal lobe damage, possibly due to stroke or lesions occurring in adulthood. Congenital prosopagnosia, on the other hand, is usually not found associated with any gross abnormalities, and no clear underlying causative agent is found to be associated with the development of the disease (Grüter et al., 2008).

Nevertheless, face blindness in children may also be associated with inherited or acquired brain lesions, and may not be exclusively of a congenital/hereditary aetiology. Moreover, prosopagnosia can also occur in association with other disorders, which may be psychiatric, developmental or associated with multiple types of visual impairment (Watson et al., 2016).

Impact on Social Behaviours

The impact of face recognition is of crucial importance in human social interaction. Face recognition allows the determination of identity of third parties and self, and permits the gathering of information on age, health status, gender and mood of an individual. Facial features are a considerable aspect in sexual attraction, and also play a vital role in the interpretation of speech via the observation of lip movements and in determination of direction of gaze (Grüter et al., 2008). The discovery of neurons associated with facial recognition in primates suggests that this process has evolutionary implications (Tsao et al., 2006).

Prosopagnosia may sometimes be associated with autism spectrum disorders (ASD). The link between autism and prosopagnosia may be two-fold. The lack of interest in social interaction characteristic of autism may result in a deficit in the development of facial recognition. In this case, the anatomical and functional features of facial recognition would be working normally, but prosopagnosia would ensue due to the lack of facial recognition

experience (Grüter et al., 2008). On the other hand, dysfunctions in the amygdala and the fusiform face area may result in an anatomical basis for the development of autism and ensuing prosopagnosia (Sasson, 2006). Both instances may in turn lead to a detrimental impact on social development and interaction.

However, a direct correlation between ASD and facial recognition dysfunction is still to be determined (Grüter et al., 2008). The causative agents in the development of ASD (Santangelo and Tsatsanis, 2005), and therefore, of associated symptoms of prosopagnosia remain unclear (Wang et al., 2015).

Different degrees of severity of prosopagnosia may lead to social and occupational deficits, together with problems in daily functioning. These may include an inability to recognize self, mistaking familiar faces such as family members as strangers when there are changes in hairstyles and an excessive reliance on verbal cues for identification (Barton and Corrow, 2016).

Incidence, Prevalence and Aetiology of Face Blindness

Recent data has shown a considerable prevalence of congenital prosopagnosia, with levels comparable to those of dyslexia and dyscalculia (Kennerchnecht et al., 2006), affecting 2.5-2.9% of the Caucasian population (Bowles et al., 2009). On the other hand, although purely acquired prosopagnosia is a rare condition, many individuals suffering from brain lesions tend to suffer from ranging degrees of visual impairments affecting facial recognition together with other cognitive disorders (Bate and Bennetts, 2014).

Acquired prosopagnosia is usually the result of localized tissue damage usually to the occipito-temporal lobe, whereas congenital prosopagnosia is due to a problem in neural development. In acquired prosopagnosia, together with an occipito-temporal lesion, adjacent areas of the cortex may also be involved in the damage. This could potentially explain the association between prosopagnosia and colour blindness, as well as other visual field defects including quadrantinopias or hemianopias (Bouvier and Engel, 2006). Emotion recognition can also be impaired in acquired prosopagnosia, but was thought to be absent in hereditary face blindness; however, recent data has proven otherwise. Acquired prosopagnosia is usually characterized by a loss of familiarity, whilst hereditary prosopagnosia usually is associated with a loss of confidence in the feeling of familiarity, brought about by a generalized visual impairment which mostly affects the facial recognition process (Grüter et al., 2008).

Feeling of familiarity	Lasting uncertainty	Lost
Colour Blindness	No association	Frequent association
Quadrantanopsia	No association	Frequent association
False-negative and false-positive recognition events	Constant	Inconsistent, rare
Emotional expression recognition	Normal	Inconsistent
Gaze contact	No	No data
Impaired visual recognition of objects and scenes	Constant	Inconsistent

Table 1: Major differences in the presentation and characteristic features of Hereditary and Congenital Prosopagnosia (PA) (Grüter et al., 2008).

Facial Recognition Process

Facial recognition and memory involves multiple areas of the brain, which include the middle temporal lobe, amygdala, inferior frontal and parahippocampal gyri, the hippocampus and orbitofrontal cortex. The process of facial recognition is dependent on a number of factors, including orientation, attention, age and emotional demeanour. Throughout the years, research has shown that the facial recognition mechanism is brought about by a specialized neuronal network, rather than forming part of a larger recognition process (Grüter et al., 2008).

The normal face recognition process involves multiple stages. Primarily, the face is recognized as being a face. Following the initial detection phase, generalized facial information is gathered, including the gender, age, health status, and emotional demeanour. This process involves a correlation of the facial information with stored images. The original model of facial

recognition by Bruce and Young (1986) [Figure 1] does not include cortical involvement in the process (Grüter et al., 2008). A later model developed by Ellis and Lewis suggests the parallel involvement of facial recognition and cortical involvement in the process of familiarity (Ellis & Lewis, 2001). Disconnection between the two systems could potentially result in a feeling of unfamiliarity (Grüter et al., 2008).

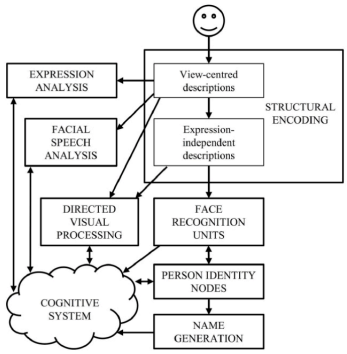

Figure 1. Illustration of the cognitive model of facial processing as proposed by Bruce and Young in 1986. (Taken from Bates and Bennetts, 2015.)

A functional model of facial recognition was developed in association with specific areas of the cortex. This model suggests the presence of a core component which involves the occipital face area in the inferior occipital lobe, the fusiform face area in the fusiform gyrus (also called the extended system) and the face area in the dorsal superior temporal gyrus (Grüter et al., 2008; Towler et al., 2017).

The dorsal superior temporal gyrus is thought to be involved in dynamic facial information, whereas the occipital face area and the fusiform face area is thought to be associated with constant facial features in facial recognition (Grüter et al., 2008). It has been proposed that facial recognition is initiated by the occipital face area and is then transmitted to the other two areas of the cortex. On the contrary, the extended system is thought to be involved in the emotional response and the information perceived by the individual. A correlation between facial and vocal recognition has also been determined via an association between the fusiform face area and the dorsal superior temporal gyrus (Gobbini and Haxby, 2007).

Any damage to these three areas of the cortex may result in the development of prosopagnosia. Damage to the occipital face area may result in a deficit in the obtaining of facial information. A deficit in the fusiform face area may result in a reduced adaptation to familiar faces. Lesions to the dorsal superior temporal gyrus may lead to reduced processing of dynamic facial data (Grüter et al., 2008).

Electrical current stimulation in the occipital face area of pre-surgical epileptic patients resulted in the development of temporary prosopagnosia, where the patients failed to recognize famous faces (Jonas et al., 2012) Stimulation of the fusiform face area resulted in perceptual facial disorders, whereby facial features appeared to be moving, and experienced changes in facial identity from a third-party individual to another. These results suggest a confirmatory link between these areas of the cortex and facial processing (Rangarajan et al., 2014).

Facial recognition is present in neonates; however, it is finessed over the years. There are a number of strategies utilized in the recognition and learning of faces. Faces may be viewed as whole or as the identification of individual facial features, the latter being more prominent in upright faces (Grüter et al., 2008). The process of configural recognition, namely the piecing together of individual features to make up a whole face is lost when faces are upside down (Carbon and Leder, 2006).

This is evident when selective facial features such as the eyes and mouth are turned upside down in an upright and inverted picture. The change is immediately noticed in the upright picture but is lost in the inverted one. This has led to a hypothesis that faces are stored and pieced together against a reservoir of what counts as a typical face to the individual (Valentine, 1991). When faces are rotated from their normal, upright orientation, holistic processing, that is, the piecing together of facial features against a whole face, is diminished, resulting in the aforementioned

inverse effect (Watson et al., 2016).

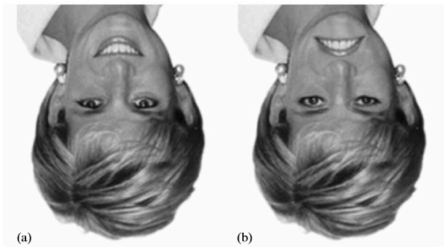

Figure 2. Pictorial representation of the original face (a) and 'Thatcher' face (b) used in the original experiment determining the role of featural and holistic facial information. (Taken from Carbon, C. C., 2005.)

This phenomenon could also potentially explain the 'other-race' effect, whereby an individual is more confident in recognizing faces of his or her own race. This could possibly occur because the reservoir of faces mostly stored by an individual against which a new face is compared to are those of own-race (Grüter et al., 2008). When an individual stores more other-race faces, this discrepancy eventually lessens considerably (Sporer, 2001).

A recent study has shown that prosopagnosia can occur due to damage on both sides of the brain, with a prevalence on right-sided damage. This suggests that there is a right lateralization of the process of face recognition after birth which persists. Although damage to the right-side of the brain can be compensated for, conspicuous damage to this area may lead to permanent deficits in face recognition (Watson et al., 2016).

The exact pathophysiology of this condition is still unclear to date. However, Harris et al., 2005 proposed that patients suffering from prosopagnosia were found to have an abnormality in the N170 wave on electroencephalography (EEG). This wave is considered to be the hallmark of face processing in the temporal lobe and functional MRI scans have associated this wave abnormality with potential damage to the occipital face are and smaller anterior fusiform gyri (Grüter et al., 2008; Towler et al., 2017).

Acquired Prosopagnosia

Acquired prosopagnosia may be considered as a lingering condition following brain tissue damage. The presentation of the disorder may be extremely varied, depending on the extent and location of damage. This condition may be viewed as a deficit in image and object recognition which leaves a detrimental effect on the facial recognition process.

Acquired prosopagnosia is an extremely rare disorder, which in most cases is not present in patients with occipito-temporal lesions. When present, it is mostly associated with patients who have other severe symptoms, including hemi-spatial neglect and visual field defects. The varied presentation of the disorder adds another level of complexity to the diagnosis of the disorder (Grüter et al., 2008).

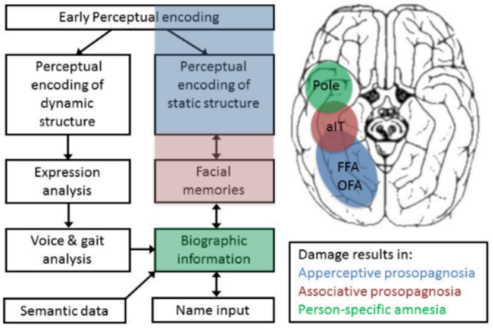

Figure 3. The three variants of acquired prosopagnosia and their anatomical correlation. (Taken from Davies-Thompson et al., 2014.)

There are three major variants of acquired prosopagnosia. Appreciative prosopagnosia involves the loss of ability to derive sufficient data about a face from visual cues results, and is characterized by a lack of activation of the familiarity signal. In associative prosopagnosia, one loses the ability to associate the acquired facial information to the reservoir of stored facial images (Davies-Thompson et al., 2014). In cases where the reservoir of stored images is lost, and the individual cannot correlate new images to stored ones, the amnesic form of the disorder, termed amnesic prosopagnosia follows (Damasio et al., 1990).

Congenital Prosopagnosia

Congenital prosopagnosia is characterized as a selective facial processing deficit in the absence of any intellectual disability or brain lesion (Towler et al., 2017). Usually, individuals with this type of prosopagnosia first report any

symptoms during adolescence or adulthood, potentially due to the increased social demands during these life-stages (Towler and Eimer, 2012; Susilo and Duchaine, 2013).

In cases where prosopagnosia is not associated with any brain lesion, and manifests itself early in life, a familial, and hereditary component of this condition has been reported. A study of pedigrees has shown a characteristic autosomal dominant manner of inheritance, potentially due to point mutation in a single or multiple genes. This could also suggest that within the context of a single family, the causal defect could potentially by the same mutation (Grüter et al., 2008). However, this does not exclude the development of prosopagnosia due to uterine environment or de novo mutations (Barton & Corrow, 2016).

Contrary to acquired prosopagnosia, congenital prosopagnosia has a number of analogous and common symptoms. The diagnostic hallmark present in all patients with congenital prosopagnosia reported during a study was found to be a lack of confidence about facial familiarity (Kennerknecht et al., 2006). Rather than the inability of recognizing faces, it was the determination of familiar faces which was found to be dysfunctional. This could in turn translate in unfamiliar responses to familiar faces, and hyper-familiarity to strangers (Grüter et al., 2008).

Other features of congenital prosopagnosia are prolonged recognition of familiar faces and learning of new ones. A modified pattern of scanning facial features was found in congenital prosopagnosia. Congenital prosopagnosia also allows more time for coping mechanisms. Individuals with the disorder usually behave in a preventative, apologetic and compensating manner to avoid any unfavourable situations (Grüter et al., 2008).

A recent study has also shown that contrary to popular perception, congenital prosopagnosics also display emotion recognition deficits, when asked to follow changes in emotional display from whole-face, or ocular regions. This further highlights the heterogeneity present in this condition (Biotti and Cook, 2016).

Diagnosis

The diagnosis of facial recognition impairment is challenging. To date, there is no test which can accurately determine any dysfunction of the system. Moreover, there are currently no set standards for the levels of facial recognition which should be reached by an individual at specific ages, and skills associated with facial recognition are not taught in the education system (Grüter et al., 2008).

The current process of diagnosis of facial blindness is the use of behavioural test questionnaires. This may result in problems with the diagnosis of specific conditions, since it simply elucidates a score which is below a set criterion, thereby indicating the presence of a problem with facial recognition. Diagnosis is usually established via the utilization of neural, biochemical and genetic markers which may contribute in an additive manner to the results of behavioural test questionnaires (Barton & Corrow, 2016).

To add another level of complexity to the diagnosis of the condition, there is a range of abilities that even healthy individuals have in the recognition of faces (Zhu et al., 2010). Healthy individuals may either never forget a face or may find problems in remembering faces (Russel et al, 2009). This in turn translates to a difficulty in the determination of the definition of prosopagnosia, and what segment of the population actually suffers from the condition. Moreover, certain behavioural mechanisms adopted by prosopagnosics may also hinder the determination of the severity of the disorder (Barton and Corrow, 2016).

Several markers are usually used to dissociate between individuals suffering from prosopagnosia and individuals who are at the lower end of the spectrum with respect to facial recognition. These include an absence of face-inversion effect (Behrmann et al., 2005),

absence of holistic dispensation (Avidan et al., 2011), irregular scanning of the face (Schwarzer et al., 2007) and a paradoxical better processing of the buccal than ocular regions (DeGutis et al., 2012). These tests usually show a reduced rather than absent features, and may be solely indicative of a potential problem rather than a hallmark diagnosis (Barton and Corrow, 2016).

The diagnosis of acquired prosopagnosia could potentially be easier than that for congenital prosopagnosia, primarily because the individual can recognize a discrepancy and a decline in the ability to recognize faces, and secondarily because this decline in facial recognition can be correlated to a condition, such as a stroke or trauma (Barton and Corrow, 2016).

Treatment and Coping Mechanisms

A number of individuals with developmental prosopagnosia tend to develop individual coping mechanisms to allow them to identify the people around them, mostly via non-facial cues such as voice, clothing, gait and hairstyle recognition (DeGutis et al., 2014, Bate and Bennetts, 2014).

The paucity of data surrounding effective remedies for prosopagnosia could suggest an important, and currently missing link on how to better enhance knowledge on the disorder both on a theoretical and practical levels (Bate and Bennetts, 2014).

The general consensus on the development of facial recognition throughout the lifespan is that the general holistic skills on facial recognition are generally developed at a very early age, with no considerable qualitative changes beyond the ages of 4-5 years. This in turn implies limited plasticity beyond early childhood with respect to face processing, and that rehabilitation of such patients may be difficult (Nelson, 2001). However, the mechanisms involved in face recognition may be finessed and transformed beyond childhood, possibly even during adulthood (Bate and Bennetts, 2014).

The determination of the best mode of rehabilitation of prosopagnosia requires the determination of the timing, location and extent of injury, if present. The locus of the injury, that is, whether the manifestation of the disorder is perceptual or semantic should be determined, and the rehabilitation tailored for the specific case (Bate and Bennetts, 2014).

Two types of rehabilitation methods may be used: compensatory and remedial. The compensatory model enhances the behaviours which allow coping with the condition. The remedial one focuses on reinstating normal facial recognition behaviours. Due to the lack of data available, and the variable manifestations of the disease, no rehabilitation data has yet proven to be more efficient than the other, but possibly depend on the parameters of individual cases (Bate and Bennetts, 2014).

Spontaneous recovery and neuronal remodelling have been reported in some cases of acquired prosopagnosia (Bate and Bennetts, 2014; DeGutis et al., 2014). This could suggest a potential niche for treatments and rehabilitation modalities to considerably improve facial processing.

Conclusion

Facial recognition is an essential process in functional social development and interaction. It involves multiple areas of the brain, and involves a complex mechanism involved in the acquiring of multitude information gathered from facial features. Specific areas of the brain have been found to be associated with facial recognition. Any lesions in these areas of the brain may lead to acquired prosopagnosia, a rare condition which causes a deficit in facial recognition. Another form of prosopagnosia, not associated with any gross brain abnormalities, with a much higher prevalence is congenital prosopagnosia, which usually manifests early in life and follows an autosomal dominant mode of inheritance.

Although the data on prosopagnosia and its potential treatment or rehabilitation is

very scarce, there have been some potential improvements in the rehabilitation of the disorder. This could in turn translate in application of treatment for other populations with face processing and cognitive deficits.

Despite being acknowledged as a neurological disorder, prosopagnosia has received little attention within the clinical field. This could be potentially due to a lack of formal diagnostic standards, lack of awareness about the condition and considerable difficulties in the diagnosis of such patients. Increased inter-disciplinary awareness of the condition, and introduction of formal, standardized diagnostic criteria could potentially improve the current situation considerably, thereby improving efficacy in managing and treating patients with this condition and other related conditions.

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Charmaine Cordina
5th Year Medical Student at the Faculty of Medicine & Surgery, University of Malta.

Phage Therapy: Its Uses and Flaws Pertaining to Pseudomonas aeruginosa Infections

External Reviewer

Dr. Rodianne Abela
M.D.(Melit),F.R.C.Path.(UK)

Tutor

Dr. Christopher Barbara
Chairman of the Mater Dei Pathology Department M.D.,M. Sc.(Lond.),D.L.S.H.T.M.

As cases of antibiotic resistant bacteria increase, possible alternatives to antibiotics have often been sought. One alternative discussed in literature is phage therapy. While this procedure has been studied for many decades, there is still much to learn for such a practice to become commonplace. For the purpose of this review, Pseudomonas aeruginosa will be discussed, since it often exhibits antibiotic resistance in hospitals.

Phage Therapy Explained

Bacteriophages are the most abundant 'organisms' on Earth.Phages are viruses that specifically attach to and infect bacteria. Each virus is specific to a particular strain/s of the bacterium and can either be lytic (infects and kills the cell) or lysogenic (incorporating its genetic material into the genetic material of the bacteria) (Clokie et al., 2011). Bacteriophages are an extremely diverse group of viruses with vastly different morphologies and families. While siphoviruses, for example, have no envelopes and have long tails, ampullaviruses are enveloped and bottle-shaped (Kulikov et al., 2007).

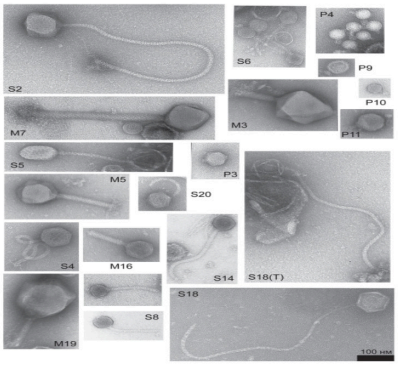


Figure 1: Bacteriophage morphology. M refers to myoviruses, P to podoviruses and S to siphoviruses. Adapted from: Kulikov et al., 2007

Phage therapy targets bacterial infections in the body by making use of bacteriophages (Lin et al., 2017).The process was discussed as far back as 1915 (Twort., 1915) but following the discovery of penicillin, research was mostly stopped except in the Soviet Union and Eastern Europe, where it has occasionally been used (Wittebole et al., 2013).

Only lytic bacteriophages (i.e. those that cause quick bacterial cell death) are used in phage therapy. Lysogenic phages make their genetic material available to the bacteria to be transcribed. Such genes may actually help the bacteria by producing virulence factors (like botulinum toxin) or antibiotic resistance genes (Ohnishi et al., 2001).

Advantages of Phage Therapy over Antibiotic Treatment

Phage therapy has a number of strengths over antibiotics. Primarily, they are very specific to one or a few bacterial strains that carry their complement receptor and will not attack other important bacteria such as gut flora. Therefore, side effects are typically minimal and chances of opportunistic infections are reduced.Phages are mostly proteins and nucleic acids and are therefore nontoxic (Loc-Carrillo et al., 2011). They also self-amplify (so very small doses are needed) and are very useful in biofilm degradation (Donlan., 2009).Phages can be administered in many different ways and are versatile even with regards to formulation development. They are easy to discover as they are usually found in waste products with high bacterial concentrations (Kutateladze et al.,

Immediate Problems Associated with Phage Therapy

The specificity of phagescan sometimes be problematic since the strain of bacteria must be specific too and thus, a 'phage cocktail' of multiple phages is often used to ensure adequate treatment (Watanabe et al., 2006). Phagescan sometimes cause immune system activation including possible cytokine release though little evidence exists that this could happen during phage therapy. Still, in order to prevent anaphylaxis, highly purified phages must be prepared and complete isolation of bacteriophages can be difficult (Loc-Carrillo et al., 2011).

P.aeruginosaInfection Characteristics

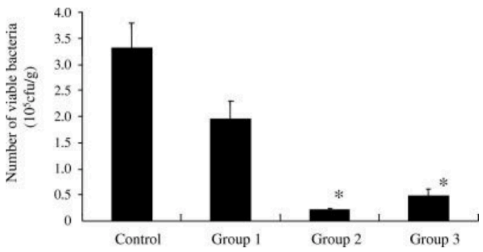
Pseudomonas aeruginosa (PA) is a gram-negative, opportunistic, environmental pathogen. It especially infects patients in hospitals and can be a life-threatening infection since some strains have shown resistance to a large number of antibiotics(CDC., 2019).It can lead to infection of critical body organs, as well as sepsis and is notably often found in patients suffering from cystic fibrosis. (Rossitto et al., 2018). The infection is also associated with mechanical heart valves, grafts, sutures and catheter-associated urinary tract infections. The bacterium can survive on many different environmental surfaces (Remold et al., 2011) andresistance to antibiotics has been linked to increased hospital stay and morbidity (de Kraker et al., 2011). PA owes its antibiotic resistance to a series of multi-drug efflux (Mex) systems which pump antibiotics out of the bacterial cell (Masuda et al., 2000).

Using Phage Therapy to Treat PA Infections

Phage therapy has shown mixed results when applied to PA infections. Phage OMKO1 is an example of a bacteriophage targeting PA. It uses the outermembrane protein M associated with the multidrug efflux systems MexAB and MexXY to bind to its host. One study involved an aortic graft infected with PA. Following endotoxin removal from the phage solution, 10 ml of phage OMKO1 (10e7 PFU/ml) and ceftazidime (0.2 g/ml) solution was administered into the mediastinal fistula. The next day, the patient had improved markedly and soon was able to return home. Biofilms grown with P.aeruginosa isolated from the graft showed that treatment with OMKO1 both alone and with antibiotic significantly reduced bacterial densities compared to the antibiotic alone. (Chan et al., 2019).

PA phage therapy has also been successfully used to prevent intestinal colonisation and overgrowth in young children in Georgia (Chanishvili et al., 2008) as well as prevention and degradation of biofilm in a hospital setting (Motlagh et al., 2016).5 podoviruses and a myovirus have also been used to treat chronic otitis infections with no observed serious side effects (Kutter et al., 2010).

Another study showed that fish embryos infected with P.aeruginosa showed a strong reduction in lethality when administered both phages and ciprofloxacin compared to either one of the two (Cafora et al., 2019). Yet another bacteriophage (KPP10) was administered to mice suffering from gut-derived sepsis due to PA. Intravenous and intraperitoneal administration were found to be more effective but whilst KPP10 did reduce mortality, it did so best if administered 1 day after inoculation with the bacteria (Watanabe et al., 2007).



2: Effect of KPP10 on PA concentration in the mouse intestinal tract. Group 1 received phage therapy a da inoculation. Group 2 received phage therapy 1 day after and group 3 received it 6 days after. (*, P < 0.05 Adapted from: Watanabe et al., 2007

That being said, phage resistance has often been put forward as a possible problem associated with phage therapy. Indeed, OMKO1 binding to its MexAB and MexXY systems pushes for selection of bacteria to evolve phage resistance. However, a study did note that such resistance actually causes changes in the Mex systems causing the bacterium to lose some

antibiotic resistance. As such, a bacteriophage cocktail administered with an antibiotic is ideal (Chan et al., 2016). Another approach involves the isolation of endolysins like artylisins from bacteriophages. Once again, this has been shown to kill PA in situ (Briers et al., 2014).

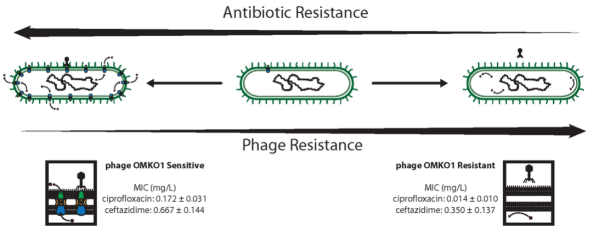


Figure 3: Resistance to the OMKO1 phage causes loss of resistance to antibiotics such as ciprofloxacin and ceftazidime. Adapted from Chan et al., 2019

Whilst so far, most studies on phage therapy have been case studies carried out in Eastern Europe, the European Commission is now funding a project called 'Phagoburn' which will be organising the world's first multicentre, randomised controlled trials (Phagoburn., 2019). The first such study took place with patients who had infected burn wounds. A phage cocktail or PP1131 was found not to be as effective as silver sulfadiazine at treating the wound. That being said, the therapy was also associated with less side effects than the silver sulfadiazine. It is possible that this negative result was obtained because too little phage was used. More research is required (Jault et al., 2019).

Discussion:

Phage therapy certainly has the potential to become a more commonplace procedure in infection treatment. That being said, a lot more research (especially controlled, unbiased trials) in the field is merited. Whilst most research traditionally took place in Eastern Europe, researchers in countries like the United States (Furr et al., 2018) and Belgium (Jennes et al., 2017) are also seriously beginning to take an interest. Only further study about safety concerns, costs and efficacy of phage therapy can lead to the possibility of such a procedure becoming more mainstream.

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Miguel Vella
3rd Year Medical Student at the Faculty of Medicine & Surgery, University of Malta.

Case Reports

Guillain-Barré Syndrome

External Reviewer
Prof. Richard Muscat

Tutor
Dr. Josanne Aquilina
M.D.,F.R.C.P.(Lond.),F.R.C.P.(Edin.)

Mr G.B. presented to casualty with bilateral weakness in distal lower limbs which was progressive. He had a history of gastrointestinal illness with severe diarrhoea. On examination he had decreased deep tendon reflexes (ankle jerk) and an unsteady gait. A lumbar puncture was done and the findings were unremarkable. An EMG was also done and confirmed Guillain-Barré Syndrome. He was treated with intravenous immunoglobulin and physiotherapy and he is currently still in hospital recovering well.

Fact file on Guillain-Barré Syndrome:
Guillain-Barré Syndrome (GBS) is a neurological disorder characterised by weakness, most prominently in the distal extremities at first and which progresses proximally. Absent or decreased myotactic reflexes are also an important feature of this syndrome (Walling & Dickson, 2013). It was first described by Guillain, Barré and Strohl, back in 1916 (Guillain et al, 1916). GBS is a rare condition with incidence estimated at 1.1/100,000/ year – 1.8/100,000/year. The incidence also increases with age; over 50 years incidence is between 1.7/100,000/year – 3.3/100,000/year (McGrogan et al, 2009). Sejvar et al also noticed that males have a higher tendency to develop GBS; the ratio is 3:2 (Sejvar et al, 2013). Some complications of this disorder include breathing difficulties due to weakness or paralysis of the respiratory muscles, blood clots and pressure sores due to immobility, cardiac arrhythmias, dysphagia and also relapse (Alshekhlee et al, 2008).

Some criteria that must be present for GBS diagnosis are: bilateral symptoms, reduced myotactic reflexes and weakness with decreased or absent reflexes. Moreover, there can be autonomic and cranial nerve involvement and some sensory disturbances. Cerebrospinal fluids obtained through lumbar puncture usually reveal a high protein content in the fluid but normal amount of white blood cells (Walling & Dickson, 2013).

GBS have 5 subtypes. The most common is acute inflammatory demyelinating polyradiculoneuropathy (AIDP) with demyelination of peripheral nerves causing a symmetrical weakness, hyporeflexia or areflexia. Acute motor axonal neuropathy (AMAN) is another subtype characterised by antibodies targeting different gangliosides such as GM1 and GD1a. This subtype only presents with motor symptoms unlike another subtype called acute motor-sensory axonal neuropathy, having both motor and sensory involvement. Miller Fisher syndrome and acute autonomic neuropathy are the rare subtypes of GBS (Walling & Dickson, 2013).

A study done by Hadden et al, discovered that some infections, particularly caused be Campylobacter jejuni, Cytomegalovirus and Epstein-Barr virus, could be the cause of some developments of GBS (Hadden et al, 2001). In fact the majority of patient present with a history of gastrointestinal symptoms, fever, a cough, sore throat etc. This link is explained by the fact that GBS is an inflammatory neuropathy.

C.jejuni was found to express antigens similar to gangliosides. So due to molecular mimicry and a cross-reactivity, antibodies start targeting the infectious agent as well as the gangliosides. In AIDP, the antibodies target the myelin whereas in AMAN the nodes of Ranvier are damaged (van Doorn et al, 2008). Some have also suggested that following certain vaccinations such as influenza, tetanus and hepatitis, one can also have a higher risk of developing GBS but this is very rare and the benefits outweigh the risks (De Wals, 2012). Recently an upsurge of GBS was linked to the Zika virus epidemic (Wahid et al, 2016).

Treatment of patients with GBS includes plasma exchange to eliminate circulating immune complexes or intravenous immune globulin therapy. Most patients recover however about 3% still die regardless of therapy (Walling & Dickson, 2013).

Case report on Guillain-Barré Syndrome

Presenting complaint:
A 32 year old man presented to casualty with decreased power in both his distal lower limbs after abruptly falling while walking on the pavement. Mr G.B has also decreased sensation on both lower limbs and the weakness is progressing proximally.

History of presenting complaint:
4 weeks previous to the incident he experienced diarrhoea, fever, chills and sweating. The diarrhoea was sometimes with mucus but without blood and brown in colour. He says he was having diarrhoea about 20 times a day. He also complained of dull hypogastric pain before an onset of diarrhoea. The pain did not radiate to anywhere else and stopped when Mr G.B did not have any more episodes of diarrhoea. He did not experience any vomiting. He noticed about 7kg weight loss in the past month with a loss for appetite. 1 week before the incident he noticed his hand cramping and also diminished movement in his legs. He also mentioned that he hobbled a bit before the collapse and complained of different sensation on both his knees. Mr G.B did not have any shortness of breath nor swallowing difficulties. He did not have vision problems, headaches or any other pain.

Previous medical/surgical history:
Mr G.B. had a fracture in his hand and was treated with a metal plate. He does not suffer from diabetes, hypertension, liver or kidney problems, high cholesterol

Drug history:
Mr G.B. does not take any drugs and he does not have any drug or food allergies.

Family history:
His father suffers from Type 1 Diabetes and raised blood pressure which is controlled.

Social history:
Mr G.B. consumes 2 pints of beer a day. He does not smoke nor consumes recreational drugs. He lives with his girlfriend in an apartment. He works as an operations manager in finance.

Systemic enquiry:
Nil to note

Physical examinations and Preliminary investigations:

Examination/Investigation	Result
Blood pressure	109/71 mmHg
Heart rate	84 beats per minute
Respiratory rate	18 breaths per minute
SpO2	100% on RA
Temperature	36.8 °C
Chest	Clear R=L
Cardiovascular	+S1 +S2 +0
Abdomen	SNT
Neurological exam	UL power 5/5 bilaterally LL power GC 4.5 bilaterally, UJ 2/5, AJ 2/5 otherwise power 5/5 bilaterally. Sensation in UL and LL bilaterally intact Plantars downgoing CN grossly intact Decreased ankle DTR jerk and normal knee DTR jerk bilaterally. Gait very unsteady
Chest X-Ray	Lungs are clear. No pneumothorax or pleural effusions. The heart is not enlarged
ECG	NAD
CT brain	The brain, ventricles and sulci are normal. The skull is normal. There is a mucosal polyp within right maxillary sinus
Pulmonary function tests	Unremarkable
MRSA Screen	No MRSA isolated
Blood analysis	Haemoglobin: 15.2 g/dL Na+: 140 mmol/l K+: 4.9 mmol/l Cl-: 99.7 mmol/l Glucose: 5.21 mmol/L

Table 1: examinations and investigations carried out when Mr G.B. was admitted to casualty.

Differential diagnosis:

- Guillain-Barré Syndrome
- Chronic inflammatory demyelinating polyneuropathy

Diagnostic investigations:

- Requested investigation: Lumbar Puncture
- Justification for procedure: To obtain CSF composition
- Result and conclusion: No cells or bacteria seen. The findings are unremarkable
- Requested investigation: Nerve conduction studies and Electromyography
- Justification for procedure: To confirm neuropathy and identify the extent, severity and whether the syndrome is demyelinating or axonal.
- Result and conclusion: This study shows a predominantly demyelinating patchy motor polyneuropathy. The findings in keeping with GBS in the appropriate clinical setting

Diagnosis:

The symptoms were suggestive of GBS. Mr G.B. had distal weakness in his lower limbs with progression to proximal muscle. He also had decreased ankle jerk reflexes. This agreed with the GBS diagnosis. On investigation the cerebrospinal fluid did not have any elevated protein which was not in keeping with GBS, although his white blood cell count was normal. Diagnosis of GBS was finalised with EMG showing a demyelinating patchy motor polyneuropathy.

Management:

- Immunoglobulin therapy: Intravenous immunoglobulin 0.4g/kg body weight per day were given for 5 days
- Physiotherapy: the patient started getting out of bed with assistance and started regaining power in his lower limb muscles. Mr. G.B. is not experiencing any disability now however he has some mild symptoms (1 in the Modified Rankin Scale). He goes about his normal activities without any help.

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Dr. Kimberley Hallett
M.D.

Familial Paroxysmal Hypokalaemic Paralysis (hypoKPP)

External Reviewer
Dr. Christian Zammit
M.D.,M.Sc.

Tutor
Dr. Malcolm Vella
MD, MRCP (UK), FEBN, FRCP (Edin.)

Case Summary:

Demographic Details:
Mr. SF, male, South African was referred by his general practitioner

A 26-year-old South African gentleman was referred to the Neurology Outpatient department due to occasional episodes of bilateral muscle weakness in the lower limbs. The attacks last for approximately 1 hour and may result in complete muscle paralysis. The severe attacks of bilateral lower limb paralysis are uncommon. The most severe attack he had ever experienced lasted for 19 hours when he was 19 years of age.
Mr. SF noticed that stress, carbohydrate-rich meals and exercise triggered recurrent attacks of muscle weakness. The patient's grandfather, father and sister have been diagnosed with 'Familial Paroxysmal Hypokalaemic Paralysis' (hypoKPP). The father had a positive genetic diagnosis from a muscle biopsy. Mr. SF believes that he has inherited the genetic condition, however, he was never tested for the mutation. When the patient suffers an attack of muscle weakness, he takes potassium supplements and rests at home and symptoms resolve.

Presenting Complaint:
Mr. SF presented to the Neurology Outpatient department with recurrent episodes of bilateral lower limb weakness and paralysis. The patient's relatives have been diagnosed with Familial Paroxysmal Hypokalaemic Paralysis.

History of Presenting Complaint:
The patient occasionally suffers episodes of lower limb weakness. He takes potassium supplements during such episodes and symptoms resolve.

Past Medical and Surgical History:

Past Medical History:
- anxiety
- folliculitis
- eczema

Past Surgical History: nil

Drug History and Allergies:

Generic Drug Name	Dosage	Frequency	Formulation	Reason
KCl and $KHCO_3$ (SANDO-K)	54 mmol K^+	6 tablets daily, indefinite	effervescent tablet	control of Familial Paroxysmal Hypokalaemic Paralysis
Alprazolam	0.5 mg	PRN	extended-release tablet	short-term management of anxiety
Methylprednisolone (Advantan)	15 mg	PRN	fatty ointment	topical treatment of eczema
Clonazepam (Rivotril)	0.5 mg	once daily	oral tablet	for anxiety

Allergies:
Patient is allergic to cortisone injections

Family History:
Grandfather, father and sister of patient are known to suffer from hypoKPP
The father tested positive for a known sequence variant in codon 58 of the CACNA1S gene.

Social History:
The patient moved to Malta in 2018. He smokes occasionally, vapes and drinks two beers a week. He is married with no children and has a sedentary job.

Systemic Inquiry:
•General Health: patient looks well in general
•Cardiovascular System: no abnormalities
•Respiratory System: no abnormalities
•Gastrointestinal System: no abnormalities
•Genitourinary System: no lower urinary tract abnormalities
•Nervous System: no abnormalities; bilateral lower limb weakness and paralysis during hypokalaemic episodes only
•Musculoskeletal System: no abnormalities
•Endocrine System: no abnormalities

On Examination:
•Blood Pressure: 105/60 mmHg
•Pulse: 70 bpm
•CVS: S1 + S2
•chest clear
•abdomen: SNT
•LL: NAD
•ECG: NSR @ 72 bpm

Current Therapy for hypoKPP
The patient takes 6 tablets of K^+ effervescent tablets daily to prevent hypokalaemic episodes.

Neurological Examination:
Cranial Nerves: normal. no facial weakness
Inspection: no muscle wasting, scars or fasciculations
Tone: normal
Power: normal
Reflexes: normal
Coordination: normal
Sensation: normal
Gait: normal

Differential Diagnosis:
•Hypokalaemic Periodic Paralysis (hypoKPP)
•Conn's syndrome
•Cushing's syndrome
•Thyrotoxic Periodic Paralysis (TPP)

Diagnostic Procedures:

Laboratory Exams:
Test: Referred for genetic testing for CACNA1S gene mutation
Justification for test: to confirm the presence of the gene mutation

Diagnosis:
Familial Paroxysmal Hypokalaemic Paralysis (hypoKPP)

Final Treatment and Follow Ups:
Continue same treatment.
Follow up with genetic result.

Fact Box

Title: Familial Paroxysmal Hypokalaemic Paralysis (hypoKPP)

Normal Physiology at the Neuromuscular Junction:

When an action potential reaches the axon terminal at the neuromuscular junction, voltage-gated Ca^{2+} channels open, allowing Ca^{2+} ions to diffuse from the synaptic space into the motor axon. The Ca^{2+} ions activate Ca^{2+}-calmodulin dependent protein kinase which phosphorylates synapsin proteins, freeing synaptic vesicles from the cytoskeleton in the process (Hall, 2016). The acetylcholine molecules in the synaptic cleft attach to the muscle fibre membrane via acetylcholine-gated ion channels. In turn, the channel undergoes a conformational change, allowing Na^+ ions to enter the muscle fibre and excite contraction. This action creates an end plate positive potential which gives rise to an action potential. The action potential spreads along the muscle membrane and causes muscle contraction (Hall, 2016).

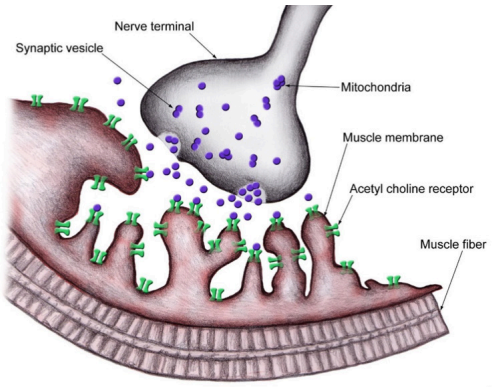

Figure 1: The normal neuromuscular junction showing an axon terminal and a muscle fibre membrane (Abbas Jowkar, MD William D Goldenberg & Aashit K Shah, MD, FAAN, n.d.)

The usual structure and function of Ca^{2+} or Na^{+} channels are altered in hypoKPP. The mutated channels cannot effectively regulate flow of ions into muscle cells, leading to a disruption in ion transport. The ability of skeletal muscles to contract is reduced, giving rise to episodes of weakness and paralysis (Hall, 2016).

Definition and General Overview: Familial Hypokalaemic Paroxysmal Paralysis (hypoKPP) is a relatively rare channelopathy characterised by episodes of flaccid paralysis with concomitant hypokalaemia (serum [K^{+}] <3.5 mmol/L). HypoKPP is correlated with significant morbidity, but rarely becomes life-threatening (Stapleton, 2018).
The frequency of paralytic attacks is highest between age 15 and 35 and eventually decreases as the patient grows older. The duration of these attacks may vary from several hours to days (Statland et al., 2018).

Epidemiology: HypoKPP is an autosomal dominant condition with a prevalence of about 1 per 100,000 individuals. It has 90% penetrance in males and 50% penetrance in females. Indeed, genetic counselling is offered to individuals diagnosed with hypoKPP who are planning to have children (Stapleton, 2018).

Signs and Symptoms: The main features of hypoKPP include reduced muscle tone (flaccidity) proximally, normal to decreased deep tendon reflexes and bilateral muscle weakness during hypokalaemic episodes (Stapleton, 2018).
Causes: HypoKPP is mainly caused by pathogenic variants in the CACNA1S or SCN4A genes. In healthy subjects, these genes code for Ca^{2+} and Na^{+} ion channels respectively. It is estimated, however, that the associated genes are normal in 30% of hypoKPP patients (Statland et al., 2018).

In a study conducted by M. Castañeda et al., a missense mutation in the ATP1A2 gene was noted in a patient diagnosed with hypoKPP who had normal CACNA1A and SCN4A genes. This gene codes for the 2 subunit of the Na^{+}/K^{+}-ATPase pump expressed in skeletal muscle cells and in brain astrocytes (Castañeda et al., 2018).

Precipitating Factors: The consumption of carbohydrate-rich meals and rest after strenuous exercise are the most common triggers of acute flaccid paralysis due to the release of insulin and K^{+} influx into intracellular spaces, respectively. Other triggers include high-Na^{+} meals, cold temperatures, immobility, alcohol intake, anaesthetic procedures, fear and emotional stress (Stapleton, 2018).

Diagnosis: This is based on the patient's clinical history, low serum K^{+} levels and family history of the condition (Stapleton, 2018). The diagnosis of hypoKPP is also based on criteria developed by the European Neuromuscular Centre (ENMC) International Workshop. If all four criteria are met, the individual is diagnosed with the channelopathy. It must be noted, however, that failure to satisfy all criteria does not rule out hypoKPP as a possible diagnosis (Stapleton, 2018).

1. Two or more attacks of muscle weakness with documented serum K <3.5 mEq/L
2. One attack of muscle weakness in the proband, and 1 attack of weakness in 1 relative with document serum K <3.5 mEq/L in at least 1 attack
3. Three of 6 clinical or laboratory features:
   a. Onset in the first or second decade
   b. Attack duration (muscle weakness involving 1 or more limbs) >2 hours
   c. Positive triggers (high carbohydrate-rich meal, rest after exercise, stress)
   d. Improvement with potassium intake
   e. Positive family history or genetically confirmed skeletal calcium or sodium channel mutation
   f. Positive McManis long exercise test
4. Exclusion of other causes of hypokalaemia (renal; adrenal; thyroid dysfunction; renal tubular acidosis; diuretic and laxative abuse)
5. Absence of myotonia (clinically or latent detected by needle EMG), except eye lids

Table 1: Diagnostic Criteria for hypoKPP (Stapleton, 2018)

Preventive Management:
HypoKPP patients are advised to avoid common triggers, such as strenuous exertion. If avoidance is unsuccessful, prophylactic K^+ replacement and/or carbonic anhydrase inhibitors are prescribed (Stapleton, 2018). In patients on life-long K^+ prophylaxis, Mg^{2+} supplements promote renal retention of K^+ ions, thereby enabling a reduction in the K^+ dose (Statland et al., 2018).

K^+-sparing diuretics are often prescribed to patients who have severe, recurrent attacks and remain unresponsive to carbonic anhydrase inhibitors (Stapleton, 2018).

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Gabriella Debono
3rd Year Medical Student at the Faculty of Medicine & Surgery, University of Malta.

An Acute Case of Expressive Aphasia Following Ischaemic Stroke

External Reviewer
Dr. Christian Zammit
M.D.,M.Sc.

Tutor
Dr. Darlene Mercieca Balbi

Mr. D.C. is a 75-year old gentleman brought to casualty after a neighbour found him unable to speak. Since he was severely aphasic, he was unable to give a proper history. The patient was able to understand commands, making this a pure expressive aphasia. He was also noted to have right hemiparesis and right facial weakness. On examination, Mr D.C. was found to have 0/5 power on the right half of his body and 3/5 power on the left side of his body using the MRC muscle power assessment scale. He was noted to have right facial weakness in an upper motor neurone lesion pattern. He was urgently admitted to a medical ward and a CT scan was requested. The scan confirmed a left middle cerebral artery (MCA) ischaemic infarct affecting the basal ganglia and Broca's Area in the inferior frontal lobe.

Fact file on Expressive Aphasia

Expressive aphasia, also known as Broca's aphasia or non-fluent aphasia, is a condition which is characterized by a loss of the ability to produce both spoken and written language. Although patients are unable to communicate properly, their understanding of speech is mostly intact and much better than when compared to their speech.

The most common cause of Broca's aphasia is a left middle cerebral artery thrombus or embolus causing a stroke which affects the third frontal convolution of the frontal lobe, which is also known as Broca's area (Figure 1), and extending into the white matter. However, it may also be caused by any disease or injury which might affect Broca's area. The fact that the area of this lesion is anterior to the inferior part of the precentral gyrus, which is responsible for executing voluntary motor movements, explains why there is also associated weakness in the right upper extremity in this condition ("Stroke Rehabilitation: A Function-Based Approach," 2000).

In contrast to Broca's area, Wernicke's area is important in the understanding of speech not the production of speech. Damage to this area of the brain results in impaired comprehension of speech as well as generation of speech which may contain paraphrase and neologisms, often resulting in a word salad. It is located in the sensory area of the posterior superior temporal lobe in the dominant cerebral hemisphere, close to the lateral sulcus. Infarction of the Middle Cerebral Artery can result in both Broca's aphasia and Wernicke's aphasia. The superior division of the middle cerebral artery supplies Broca's area, therefore decreased perfusion of this vessel or more proximal to it will cause Broca's aphasia. Wernicke's area is supplied by the inferior division of the MCA. Strokes of the inferior MCA hence result in Wernicke's aphasia (''Broca's, Wernicke's and Conduction Aphasias," 2006).

Patients suffering from Broca's aphasia have a dominant feature of agrammatism in their speech and thus find it hard to form full sentences even though content words like verbs and nouns are preserved. Patients therefore end up producing speech which is described as

'telegraphic speech'. Patients' ability to repeat words and sentences is also very poor ("Broca's Aphasia," n.d.). There is currently no treatment for aphasia. The approach to facilitating the patient's quality of life is a multidisciplinary approach involving speech therapy, physiotherapy, neurologists and psychologists. Recovery of language function peaks within two to six months, after which progress decreases, however the patient is still encouraged to keep on working on speech production as improvement can be seen long after the stroke (Acharya and Dulebohn, 2017).

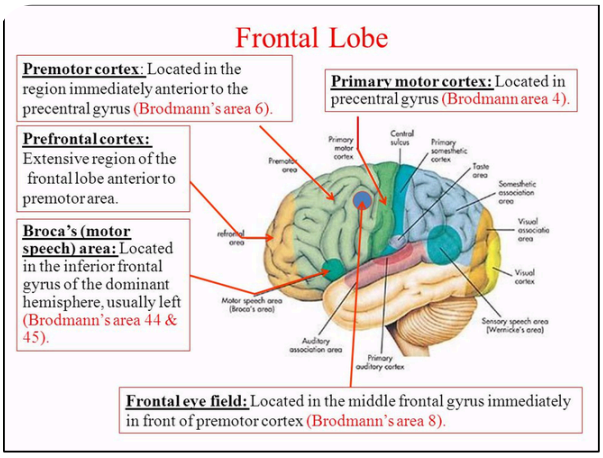


Figure 1 – Diagram illustrating the frontal lobe of the brain and showing Broca's area

This condition is named after Paul Pierre Broca (Figure 2), a French general surgeon who contributed greatly to the field of anatomy. His most important contribution was his discovery of the specific region in the brain that is responsible for speech, Broca's area, in 1861 (Joynt, 1964). Data on the incidence of expressive aphasia is quite limited, however it is estimated that 11,400 people in Britain become aphasic every year following stroke (Wade et al., 1986)

Figure 2 – Portrait of Paul Pierre Broca

Case Report on Acute Expressive Aphasia Following Ischaemic Stroke:

Presenting Complaint:
Mr. DC, a 75-year old male, was found by his neighbour expressively aphasic and suffering from right hemiparesis and right facial weakness. No other symptoms were able to be elicited in the history other than what was clearly visible.

Past Medical/ Surgical History, Family History, Drug History and Social History:
Since the patient was severely aphasic it was not possible to obtain a thorough history from him.

Systemic Inquiry:
Nil of note.

Physical Examination and Preliminary Investigations:
A full neurological examination was carried out.

On examination:
- Right upper limb power: 0/5 (flaccid)
- Right lower limb power: 0/5
- Right facial nerve palsy with upper motor neuron lesion patterns
- Left upper limb power: 3/5
- Left lower limb power: 3/5

Power was assessed using the MRC power scale (Table 1).

Grade	Description
0	No contraction
1	Flicker or trace of contraction
2	Full range of active movement, with gravity eliminated
3	Active movement against gravity
4	Active movement against gravity and resistance
5	Normal power

Table 1: The MRC score of muscle strength

Further general examinations and investigations were also performed. The following are the findings:

- Chest was clear
- Abdomen was soft and non-tender
- Heart sounds S1 and S2 were intact with no added heart sounds
- Tachycardic with a rate of 115 beats per minute
- Blood pressure was found to be 117/77
- Oxygen saturations: 99% SaO2
- Afebrile

Various stroke screening techniques were used. The results are shown in the following figures:

Has there been loss of consciousness or syncope? Y (-1) ☐ N (0) ☐ **UNKNOWN**

Has there been any seizure activity? Y (-1) ☐ N (0) ☐ **UNKNOWN**

Is there a **NEW ACUTE** onset of any of the following symptoms (or on awakening from sleep)?

1. Asymmetrical facial weakness — Y (+1) ☑ No (0) ☐
2. Asymmetrical arm weakness — Y (+1) ☑ No (0) ☐
3. Asymmetrical leg weakness — Y (+1) ☑ No (0) ☐
4. Speech disturbance — Y (+1) ☑ No (0) ☐
5. Visual field defect — Y (+1) ☐ No (0) ☑

* Total Score 4 (-2 to +5)

Stroke is likely if total scores are >0. Scores of </= 0 have a low possibility of stroke but not completely excluded.

Provisional diagnosis ☑ Stroke ☐ None stroke (specify)_____

- If total score > 0 (1-6) a diagnosis of acute stroke is likely, refer to NGH stroke ED guidelines and bleep stroke team on 2939 for transfer to the stroke service at RHH (if under 4½ hours since stroke onset, contact stroke team immediately for consideration for thrombolysis)
- If total scores 0, -1 or -2 stroke unlikely but is not totally excluded, bleep stroke team on 2939 for advice.

Figure 3: Rosier (Recognition of Stroke in the Emergency Room) Score

Category	Score/Description		Date/Time Initials	Date/Time Initials	Date/Time Initials	Date/Time Initials	Date/Time Initials
1a. **Level of Consciousness** (Alert, drowsy, etc.)	0 = Alert 1 = Drowsy 2 = Stuporous 3 = Coma		0				
1b. **LOC Questions** (Month, age)	0 = Answers both correctly 1 = Answers one correctly 2 = Incorrect		/				
1c. **LOC Commands** (Open/close eyes, make fist/let go)	0 = Obeys both correctly 1 = Obeys one correctly 2 = Incorrect		0				
2. **Best Gaze** (Eyes open - patient follows examiner's finger or face)	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation		0				
3. **Visual Fields** (Introduce visual stimulus/threat to pt's visual field quadrants)	0 = No visual loss 1 = Partial Hemianopia 2 = Complete Hemianopia 3 = Bilateral Hemianopia (Blind)		0				
4. **Facial Paresis** (Show teeth, raise eyebrows and squeeze eyes shut)	0 = Normal 1 = Minor 2 = Partial 3 = Complete		1				
5a. **Motor Arm - Left** 5b. **Motor Arm - Right** (Elevate arm to 90° if patient is sitting, 45° if supine)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement X = Untestable (Joint fusion or limb amp)	Left	0				
		Right	4				
6a. **Motor Leg - Left** 6b. **Motor Leg - Right** (Elevate leg 30° with patient supine)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement X = Untestable (Joint fusion or limb amp)	Left	0				
		Right	2				
7. **Limb Ataxia** (Finger-nose, heel down shin)	0 = No ataxia 1 = Present in one limb 2 = Present in two limbs		/				
8. **Sensory** (Pin prick to face, arm, trunk, and leg - compare side to side)	0 = Normal 1 = Partial loss 2 = Severe loss		/				
9. **Best Language** (Name item, describe a picture and read sentences)	0 = No aphasia 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute		2				
10. **Dysarthria** (Evaluate speech clarity by patient repeating listed words)	0 = Normal articulation 1 = Mild to moderate slurring of words 2 = Near to unintelligible or worse X = Intubated or other physical barrier		2				
11. **Extinction and Inattention** (Use information from prior testing to identify neglect or double simultaneous stimuli testing)	0 = No neglect 1 = Partial neglect 2 = Complete neglect		0				
	TOTAL SCORE		11/42				

Figure 4: NIH (National Institutes of Health) Stroke Score

NIHSS SCORE	STROKE SEVERITY	IMPACTED BRAIN DENSITY
0	No Stroke	
0 – 4	Minor Stroke	
5 – 15	Moderate Stroke	
16– 20	Moderate to Severe Stroke	
21 - 42	Severe Stroke	

Figure 5: NIH Stroke Scale Interpretation

Investigations ordered:

1. ECG – To identify any predisposing conditions which may have resulted in the stroke e.g.: Atrial fibrillation/flutter, acute myocardial infarction, infective endocarditis etc. In case any are identified, further prophylactic treatment may be indicated.
2. Routine bloods (Complete Blood Count, ESR, CRP, Urea and Electrolytes, Blood Glucose Levels etc) – to rule out underlying conditions such as sepsis, renal disease and diabetes. Inflammatory markers are often raised in ischaemic stroke. In case any are identified, further treatment may be indicated.
3. CT brain – To determine whether the stroke was ischaemic or haemorrhagic in nature, to properly locate the lesion and to rule out any possible differentials such as space occupying lesions.
4. Echocardiogram – To rule out any underlying structural heart disease which may have caused the stroke e.g.: Valvular heart disease, patent foramen ovale, atrial septal aneurysm etc. In case any are identified further prophylactic treatment may be indicated.
5. Carotid doppler ultrasound – To identify any possible stenosis or plaque build-up in the carotid arteries which may predispose to recurrent strokes. If stenosis is greater than 50%, carotid endarterectomy may be indicated.
6. Geriatric review
7. Stroke rehabilitation including outreach to physiotherapy, occupational therapy and

speech therapy – Stroke management is a multidisciplinary effort.

Findings:

- The CT brain revealed an ischaemic stroke of the middle cerebral artery territory. CT brain results are shown below:

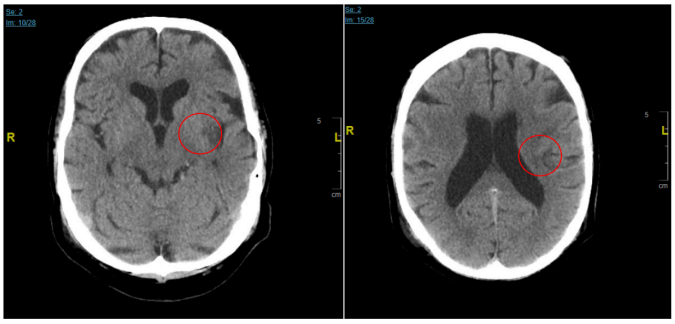


Figure 6: Mr. DC's Brain CT demonstrating areas of ischaemic infarction in the left Middle Cerebral Artery territory

- Mr DC's ECG revealed atrial flutter, a possible source of emboli which may have resulted in the stroke.
- C-Reactive Protein was found to be 51.9 mg/L (normal range <3.0 mg/L). This is common in stroke patients since acute ischaemic stroke may trigger an inflammatory response in the surrounding tissues.
- No abnormalities seen on the echocardiogram.
- Carotid doppler showed no stenosis or atherosclerosis of the carotid arteries.
- Carotid doppler results are shown below:

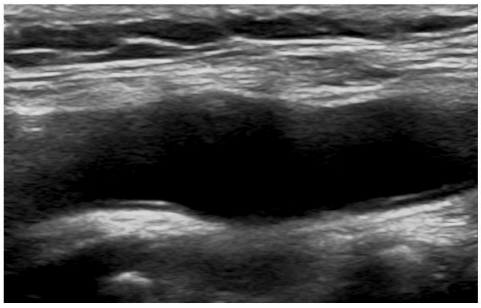
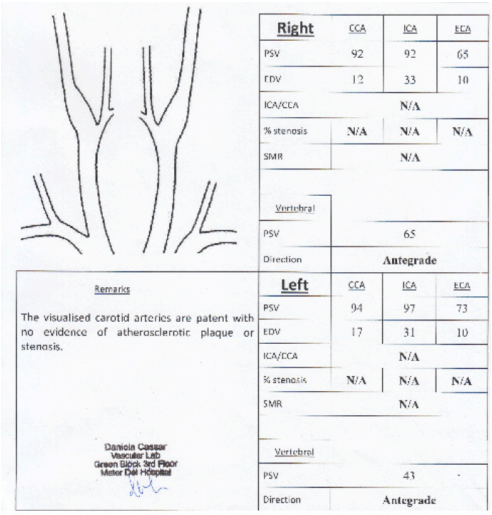


Figure 7: Mr. DC's Carotid Doppler showing a patent carotid artery with no signs of stenosis or atherosclerotic plaque



Right	CCA	ICA	ECA
PSV	92	92	65
EDV	12	33	10
ICA/CCA		N/A	
% stenosis	N/A	N/A	N/A
SMR		N/A	
Vertebral			
PSV		65	
Direction		Antegrade	

Remarks

The visualised carotid arteries are patent with no evidence of atherosclerotic plaque or stenosis.

Daniela Cassar
Vascular Lab
Green Block 3rd Floor
Mater Dei Hospital

Left	CCA	ICA	ECA
PSV	94	97	73
EDV	17	31	10
ICA/ECA		N/A	
% stenosis	N/A	N/A	N/A
SMR		N/A	
Vertebral			
PSV		43	
Direction		Antegrade	

Figure 8: Mr. DC's Carotid Doppler results

Pharmacological Therapy:

Since the CT showed that the stroke was ischaemic rather than haemorrhagic, pharmacological intervention was indicated rather than a surgical approach.

The patient was outside the therapeutic window for administration of Tissue plasminogen activator (tPA) which is 3-4.5 hours, and was therefore started on aspirin 75mg daily, Dipyridamole 100mg tds and Simvastatin 20mg daily. The patient was also started on omeprazole 20mg once daily due to the potential side effect of gastrointestinal bleeding associated with aspirin.

The antiplatelet (Dipyridamole) is to be switched to warfarin after 4-6 weeks. 4 weeks are allowed before switching in order to prevent haemorrhagic conversion i.e. the transformation of an ischaemic stroke into a haemorrhagic stroke. Mr DC was also started on Perindopril 2mg once daily.

Follow Up:

Mr. DC was monitored and followed up closely during the week he spent at Mater Dei Hospital recovering from the stroke. The following is a summary of his recovery:

Day 1 Post Stroke:

- Patient aphasic but able to communicate with hand gestures and by writing on paper
- Patient found to have good gait pattern
- No dyspraxia

Right sided facial weakness persistent but able to swallow.

Day 2 Post Stroke:

- Blood pressure increased to 120/80
- IVI stopped and cannula removed

Day 3 Post Stroke:

- Patient noted to have increased vocabulary – vocalised "thank you"
- Range of movement of the right upper limb noted to have increased substantially
- Able to mobilize with minimal help
- Activities of daily living require help

Day 4 Post Stroke:

- Ambulation and balance good
- Improvement in speech - "I don't like it"
- Hot cold sensation intact
- Communication impairment prevented full interpretation of sensory testing

Day 5 Post Stroke:

- Patient managing to carry out all activities of daily living independently
- Only remaining issue is speech but it is improving, according to wife
- Good gait and balance

Day 6 Post Stroke:

- Upper limb sensory testing repeated - patient noted to have decreased sensation mostly in sharp/dull discrimination. Patient was able to identify light touch
- Able to form sentences but speech intelligibility remains poor
- Written word only contains minor spelling errors which were self-corrected

Day 7 Post Stroke:

- No further physiotherapy or speech therapy needed
- Patient to be discharged home to be supported by wife

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Hannah Xuereb
4th Year Medical Student at the Faculty of Medicine & Surgery, University of Malta.

Adam Al Gededi
4th Year Medical Student at the Faculty of Medicine & Surgery, University of Malta.

NSTEMI in the Context of Cardiovascular Risk Factors and Co-morbidities

External Reviewer

Dr. Alexander Borg
M.D.,M.R.C.P.(Lond.),F.R.C.P.(Edin.),M.D.(Manc.),F.E.S.C.

Tutor

Dr Maryanne Caruana
M.D. (Melit.) Ph.D.(Melit.)FRCP (Edin) FESC

Mr A.N., a 59-year-old male, was referred to casualty by a health centre physician, following the complaint of two episodes of worsening exertional chest pain. He is a known case of hypertension, non-insulin-dependent diabetes mellitus and smokes 1 pack of cigarettes daily.

Following appropriate investigations such as electrocardiogram (ECG), cardiac biomarkers and echocardiography, the patient was diagnosed with non-ST elevation myocardial infarction (NSTEMI). The patient is now stable on treatment; however, his overall cardiovascular risk remains high due to factors such as smoking, uncontrolled type 2 diabetes, hypertension and hypercholesterolaemia. This case highlights the importance of measuring global cardiovascular risk since this has important treatment and follow-up implications; importantly, ischaemic heart disease can be primarily or secondarily prevented through non-pharmacological or pharmacological alteration of the cardiovascular risk factors.

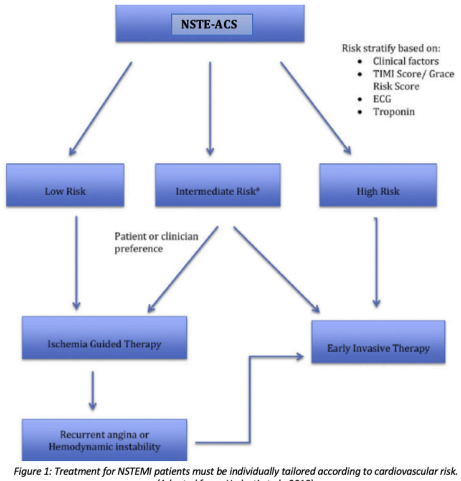

Figure 1: Treatment for NSTEMI patients must be individually tailored according to cardiovascular risk. (Adapted from: Hedyati et al., 2018).

Fact file on NSTE-ACS, Atherosclerosis and Cardiovascular Risk Factors

Acute coronary syndromes (ACS) affect around 1 million patients annually in the USA, and around 75% of these patients are diagnosed with non-ST elevation-ACS: unstable angina or NSTEMI. (Hedayati et al., 2018). These two conditions share a similar pathophysiology but NSTEMI is differentiated from unstable angina since in NSTEMI, the levels of cardiac troponin are higher than the 99th percentile of the upper reference limit for the normal range of the assay. (ESC, Fourth universal definition of myocardial infarction (2018).

This case presents a very important dilemma for a casualty physician: determining the cause of chest pain. The determination of aetiology was complicated by the fact that the patient also suffered from gastro-oesophageal reflux disease (GORD). Due to the fact that visceral pain pathways of the stomach/oesophagus and the heart are shared, the referred pain from these organs can give very similar symptoms.

The pathophysiology of NSTEMI entails mismatch between myocardial oxygen supply and demand: there is subendocardial ischaemia where the atherothrombosis is causing partial blood flow obstruction. As with the other acute coronary syndromes, NSTEMI is the result of the inflammatory process of atherosclerosis and occurs most commonly due to plaque erosion with an intact fibrous cap (Basit et al., 2019; Puymirat et al., 2019).

The other major important clinical point pertaining to this case is the presence of cardiovascular risk factors which determine treatment in the form of early invasive therapy. This patient had a HEART score of 8, indicating high risk and a need for urgent invasive intervention. The HEART score table (Hedayati et al., 2018) shown in figure 2 is a useful tool in stratification and management of patients with ACS.

HEART score		
History	Highly suspicious	2
	Moderately suspicious	1
	Slightly suspicious	0
Electrocardiogram	Significant ST depression	2
	Nonspecific repolarization	1
	Normal	0
Age, y	≥65	2
	45–65	1
	<45	0
Risk factors	≥3 or history of coronary artery disease	2
	1 or 2	1
	None	0
Troponin	≥3x normal limit	2
	1–<3x normal limit	1
	≤ Normal limit	0

Figure 2: Assessment of cardiovascular risk factors is a crucial component of NSTE-ACS management. (From Hedayati et al., 2018).

Presenting Complaint

The patient was referred to A&E after he experienced two episodes of diffuse chest pain of an intermittent nature.

History of Presenting Complaint

The first episode occurred when the patient was at work: he had exerted himself by climbing some stairs and a ladder when he experienced a deep compressive pain in his chest which lasted 10 minutes. The second episode occurred three days later and lasted for around 15 minutes, and was described as centrally compressive chest pain associated with diaphoresis. There was no vomiting or loss of consciousness during either episode, but the patient complained of sensations of nausea. The patient was unable to pinpoint the precise site of the pain: the pain was of a diffuse nature throughout his chest. The patient had been suffering from chest pains of varying nature for 10 years; these have been found to be a mixture of stable angina and pain due to GORD. However, these two particular episodes of chest pain were different from the other chronic episodes since the character of the pain was more compressive, caused more shortness of breath and was of higher severity. The patient denied any radiation of the pain to the left arm, right arm, jaw or neck. This pain was associated with sweating and nausea but not fever. In both episodes, the pain lasted for 15 minutes or less and was intermittent. Cold temperatures and exertion exacerbated the severity of the pain, which the patient grades as 7 out of 10.

Past Medical and Surgical History

The patient is a known case of type II diabetes mellitus and hypercholesterolaemia. During the last year his diabetes has not been well-controlled and the patient admits to not taking medications for his elevated cholesterol levels. Coupled with other non-modifiable risk factors such as genetic predisposition, age and male gender, these modifiable risk factors contributed to this acute coronary syndrome.

The patient also has a 10-year history of GORD which he states was mainly triggered by stress. The patient had a minor operation to remove a benign skin lesion 10 years ago.
Importantly, the patient had experienced a variety of chest pains throughout the last 10 years: these may be of cardiac origin or due to GORD. The patient had never had an acute coronary event, coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) before.

Drug History and Allergies

Patient has no known drug allergies. His drug history is listed in table 1. An important factor, as previously discussed, is that the patient was poorly compliant to prescribed medications.

Drug	Dose	Frequency	Formulation	Reason for Prescription
Amlodipine	10mg	Once daily	Oral tablet	Control of hypertension
Valsartan	160mg	Once daily	Oral tablet	Control of hypertension
Metformin	500mg	Once daily	Oral tablet	Control of T2DM

Table 1 Drug History

Family History
The patient's mother had a history of type II diabetes mellitus and hypertension, but did not die due to a cardiovascular event. His father had a history of heart failure and died aged 82. None of his siblings have experienced an acute cardiovascular event.

Social History
The patient is married and lives at home with his wife and daughter. He is independent and his occupation entails a certain degree of manual labour. His condition might now restrict him from continuing his usual work.

Importantly, given that smoking is an independent risk factor for cardiovascular disease, the patient has smoked 10-15 cigarettes per day since around the age of 20, which equates to 39 pack years.The patient only drinks alcohol socially.

Systemic Enquiry
- General health: overall the patient is healthy, however he has a number of cardiovascular risk factors and is also quite stressed
- Cardiovascular system: hypercholesterolaemia, hypertension, no palpitations
- Respiratory system: no shortness of breath (SOB) at rest, SOB occurred during episodes of chest pain
- Gastrointestinal tract: dyspepsia
- Genitourinary system: pt has no problems passing urine, feels no burning sensation
- Musculoskeletal system: nil to note
- Endocrine system: nil to note

Differential Diagnosis
1. ACS (ECG points towards NSTEMI, diagnosis pending troponin result)
2. Chest pain due to severe GORD (unlikely)
3. Musculoskeletal pain e.g. costochondritis (highly unlikely)
4. Pulmonary embolism due to the presence of right bundle branch block on the ECG. There were no older ECGs to compare with and check whether this is an old or new right bundle branch block. (Nature of the pain meant that pericarditis was very unlikely).

Diagnostic Investigations
1. Investigation: 12-lead ECG
2. Justification: ECG is essential in diagnosis of any ACS since it distinguishes STEMI from NSTEMI, and identifies any arrhythmias which the patient may have developed
3. Result & conclusion: the patient's ECG showed right bundle branch block: QRS complex >120ms and RSR' pattern in the anterior precordial leads V1-V3. In V1-V3, one can observe reciprocal ST segment depressions and T wave inversion, while there was no ST elevation in any of the leads (refer to figure 3). The clinical presentation and the raised troponins combined with these ECG changes led to the diagnosis of NSTEMI.

1. Investigation: bloods: troponins, CBC, U&E, ABGs, lipid profile, glucose levels, liver function tests
2. Justification: CBC is done to rule out any anaemia or infective cause, troponins are used as biomarkers of myocardial injury, ABGs are done in casualty since the patient was short of breath, lipid profile and HGTs aid assessment of cardiovascular risk factors such as hypercholesterolaemia and diabetes mellitus, U&E and liver function tests provide baseline organ function levels which must be considered when choosing pharmacological therapy
3. Result & conclusion: elevated initial troponins and an increase of >20% in the 3-hr repeated troponins together with the typical chest pain and lack of ST elevation on ECG indicated that the patient had NSTEMI, while HGTs and lipid profile confirmed uncontrolled diabetes mellitus and hypercholesterolaemia. The other tests showed no remarkable findings: the patient has adequate liver function and does not have chronic kidney disease.

1. Investigation: transthoracic echocardiography

2. Justification: assessment of any hypokinetic or akinetic areas of myocardium, assessment of LV ejection fraction: it has been found that reduced ejection fraction in NSTEMI patients is associated with greater mortality (Siddiqui and Holzmann, 2019).
3. Result & conclusion: mild concentric LVH indicative of long-standing hypertension, ejection fraction EF>55%, good LV systolic function, reversed mitral inflow pattern in keeping with impaired LV relaxation. Normal RV size and systolic function. The aortic and mitral valves showed no stenosis or regurgitation No specific regional wall motion abnormality was reported.

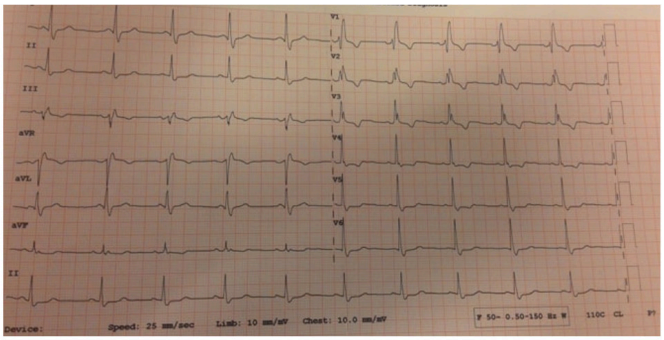

Figure 3: Mr A.N.'s ECG showed inverted T waves as well as ST segment depression in leads V1-V3. There is no ST elevation in any of the leads.

Management

1. Pharmacological Therapy

Following investigations, the patient was started on the following:

Drug	Dose	Frequency	Formulation	Reason for Prescription
Clexane	110mg	Twice Daily	Subcutaneous injection	DVT prophylaxis
Aspirin	75mg	Once Daily	Oral tablet	DVT prophylaxis
Clopidogrel	75mg	Once Daily	Oral tablet	DVT prophylaxis
Atorvastatin	80mg	Nocte	Oral tablet	Control of hypercholesterolaemia
Valsartan	160mg	Twice Daily	Oral tablet	Control of Hypertension
Metformin	500mg	Once Daily	Oral tablet	Control of type II diabetes mellitus: patient is a diabetic
Omeprazole	20mg	Once Daily	Oral tablet	Control of GORD

Table 2 Pharmacological Therapy

2. PCI

The patient's cardiovascular risk factors (stage 2 hypertension, smoking, diabetes mellitus, hypercholesterolaemia) meant that early invasive therapy was chosen as the preferred treatment pathway. (Brown et al., 2018). As shown in figure 4, a very tight stenosis was identified in the proximal LAD, and PCI was done on this lesion. The area was predilated with a 3.5x15mm balloon and stented with a 4x18mm DES (drug-eluting stent).

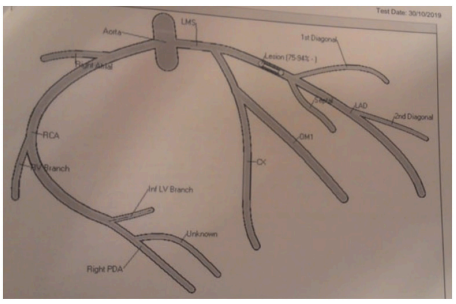

Figure 4: Mr A.N.'s PCI result showing the proximal LAD lesion which was stented succesfully.

3. Follow-up

After NSTEMI, the patient is prescribed one year of dual antiplatelet therapy: aspirin (75mg once daily) and clopidogrel (75mg once daily). Risk factor modification is another important issue: patient is given advice to stop smoking, control his diabetes, hypertension control and keeping LDL below 1.4mmol/L. The patient recovered well following PCI, and was discharged two days later with an outpatients appointment 3 months later.

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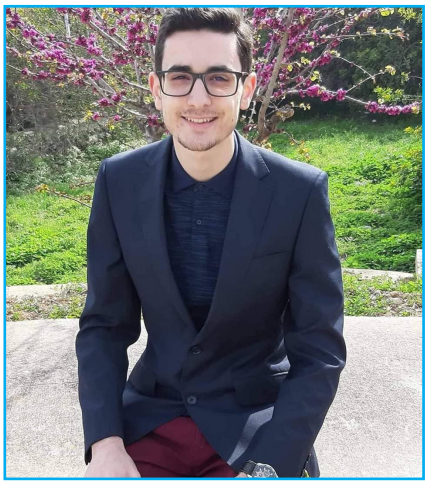

Mark Miruzzi
3rd Year Medical Student at the Faculty of Medicine & Surgery, University of Malta.

Magazine Designers

Jade Borg
Public Relations Officer 2019-2020

Owen Cachia
Public Relations Coordinator 2019-2020
Minima Medica Layout Designer

James Scicluna
Minima Medica Cover Designer

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