The British Student Doctor Journal

BSDJ

VOLUME 5, No.3
Summer 2021
ISSN 2514-3174
bsdj.org.uk

Practical advice for new doctors

bsdj.org.uk


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Journal DOI
10.18573/issn.2514-3174

Issue DOI
10.18573/bsdj.v5i3

The **British Student Doctor** is published by **The Foundation for Medical Publishing**, a charitable incorporated organisation registered in England and Wales (Charity No. 1189006), and a subsidary of **The Academy of Medical Educators.**

Cardiff University Press
Gwasg Prifysgol Caerdydd

The British Student Doctor is an imprint of Cardiff University Press, an innovative open-access publisher of academic research, where 'open-access' means free for both readers and writers.

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No conflicts of interest to declare

Accepted for publication: 02.08.21

Welcome to the Summer Issue of The British Student Doctor Journal!

2021 has already proven to be quite an exciting and busy year for everyone at the journal. A key highlight was the publication of our LGBTQ+ Supplementary Issue in collaboration with GLADD in the Spring. We feel this is one of our most important projects to date as promoting diversity has always been one of our core values. We are thrilled to have been able to share this with you.

Here at The BSDJ, we always try to promote an inclusive environment, incorporate new ideas and implement change. The latest small improvement of this kind has been the re-branding of our regular issues into Summer and Winter issues, replacing the old January and June issues. This gives us more flexibility to create a thought-provoking issue, that can be released at a time when our articles are most relevant to students.

One area we pride ourselves at The BSDJ, is publishing high-quality student research, which is typically underrepresented in medical journals. This Summer Issue starts off with Luke Ottewell's study on the optimal management of recurrent pituitary adenoma, a great example of a well-conducted student project. We are also pleased to share an important study by Emily Pattinson and colleagues, which addresses inequalities in LGBTQ+ mental health provision across the UK. Further, Dr Jennifer Hobbiss and Ms Helen Doran present their audit on general surgical readmissions.

Once again, we will see newly qualified foundation trainees graduate and start work during a pandemic. We appreciate how challenging this must be and are particularly pleased to feature a piece by Dr Pakinee Pooprasert and Dr Ehinomen Inegbedion, who give clinical and practical advice for all newly qualified doctors. We congratulate all junior doctors starting Foundation training in August on passing their final exams under these stressful circumstances and wish them all the best for their first days and weeks as new doctors. Welcome to the NHS family!

Another article that is useful for revision and often overlooked in clinical practice, by Dr Mark Watts and Dr Zarina Shaikh, is the differential diagnosis of intra-oral white lesions and the potentially worrying signs that should prompt referral. Atrial fibrillation and sleep apnoea are also areas that new doctors will come across frequently in clinical practice. However, we know little about the fascinating interplay between the two, which is covered by Vaibhav Mishra. Evolving areas of research may also play an important role in future clinical practice.

Dr James Booker and Dr Rebecca McCarthy, from the University Hospital Southampton, review the role of neuronavigation in current and future neurosurgical practice. We also feature a fascinating review by Jonathan Drake of Oxford University, elucidating the role the gut microbiota plays in metabolic health and disease.

Increasingly, medical schools are reducing the amount of time students spend learning about anatomy. This is addressed by Rami Elias of St George's, who reflects on the use of the cadaver for teaching and learning purposes in medical education today and throughout history. Moving from the anatomy lab to the bedside, we feature an important reflective article by Vishnu Shivanand of Cardiff University highlighting the importance of thanking patients as a medical student. And, is thanking our colleagues as important as thanking patients? Norah O'Sullivan has written a thoughtful response correspondence article in this issue about the power of positive feedback.

As always, we extend our gratitude to our hard-working and dedicated editorial team, peer reviewers, faculty advisory board and our publisher, Cardiff University Press. We look forward to continuing our mission for medical student publishing throughout the coming years and are excited for what the future holds.

We hope you enjoy the Summer 2021 Issue of The British Student Doctor Journal!

The British Student Doctor, 2021;5(3):2-11
doi: 10.18573/bsdj.166
Original Research

What is the optimal management of recurrent non-functioning pituitary adenoma?

ORIGINAL RESEARCH

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Accepted for publication: 18.04.21

ABSTRACT

Recurrent non-functioning pituitary adenomas (NFPAs) pose a difficult challenge to neurosurgeons. NFPAs do not secrete hormones and thus symptoms usually manifest later in the disease process when the adenoma has reached a sufficient size as to cause mass effect on neighbouring bodies. Treatment of pituitary adenoma is commonly surgical with a transnasal, transsphenoidal approach. Growth of the NFPA into adjacent structures can add to the challenge of surgical resection and thus resection of NFPAs is sometimes incomplete. This often leads to recurrence and necessitates further treatment. A variety of treatment strategies may be employed to design an optimal treatment algorithm, and often a combination of these may be used depending on the size and location of the adenoma and age of the patient. This paper aims to present the evidence for each treatment strategy and to guide what the optimal treatment of NFPA may be, faced with the variety of outcomes that may arise from initial treatment.

INTRODUCTION

Recurrent non-functioning pituitary adenomas (RNFPAs) pose a difficult challenge to neurosurgeons. NFPAs do not secrete hormones, although they may be immunohistochemically positive, therefore patients usually manifest symptoms later in the disease process when the adenoma has reached a sufficient size as to cause mass effect on neighbouring bodies. (1, 2) Common presentations include headache, visual disturbance from compression of the optic apparatus, hypopituitarism from disturbance of the pituitary stalk, and more rarely cranial nerve compression from invasion into the cavernous sinus.

Treatment of pituitary adenoma is commonly surgical with a transnasal, transsphenoidal approach. Growth of the NFPA into adjacent structures can add to the challenge of surgical resection. Extension into the cavernous sinus may cause the adenoma to envelope the internal carotid artery – for instance. This would present a serious hazard for the surgeon, and thus resection of NFPAs is sometimes incomplete. A study by Lillehei et al. showed that 14% of resections of NFPA were sub-total, with 6% of the total number recurring at 5 years. (3) Another study by Young et al. reported on 100 NFPAs - 90% of which reported gross total resection – but 42% of which showed residual/recurrent tumour at 5 years follow-up. (4) Furthermore, suprasellar extension often presents a challenge as it leaves a portion of adenoma inaccessible from the transsphenoidal corridor. All of these factors make recurrence of the tumour more likely and thus may necessitate further treatment.

A variety of treatment strategies may be employed to design an optimal treatment algorithm, and often a combination of these – including endoscopic resection and radiotherapeutic means – may be used depending on the size and location of the adenoma and age of the patient. This paper aims to present the evidence for each treatment strategy and to guide the optimal treatment of NFPA on a case-to-case basis, including after disease recurrence. Although definite treatment strategies will be discussed, a "watch-and-wait" approach is often taken due to the relatively asymptomatic nature of the early stages of disease. The author of this paper conducted a literature review of all available data until January 2020. More details on the exact methodology of this search can be found as Appendix 1.

BACKGROUND AND HISTOLOGY

Pituitary adenomas are an important and common type of intracranial neoplasm, representing between 10-20% of all cases in adults. (1, 2) Treatment is commonly surgical for non-functioning and functioning adenomas alike, whilst prolactinomas are commonly treated medically. The advancement of the endoscopic technique has shown a strong emphasis put on this method as the mainstay of surgical treatment, although other techniques remain useful in certain situations. Treatment is sometimes accompanied by radiation therapy and in some occasions radiation therapy is the main treatment of choice.

NFPAs represent a group of tumours that do not manifest with endocrine symptoms due to hypersecretion of hormones. However, evidence has shown that the cells that make up these tumours do express, immunohistochemically, anterior pituitary hormones. (5) This evidence has contributed to recent attempts to rename NFPAs to non-functioning pituitary neuroendocrine tumours (NF-PitNETs). (6)

NFPAs can now be further distinguished by their transcription factor profile and by the pituitary hormone that they immunohistochemically express. The term null-cell adenoma has previously been used to refer to NFPAs but, with the use of this new classification, null-cell adenomas hold only a very small and rare profile. Cell lineages include somatotroph, lactotroph, thyrotroph, corticotroph and gonadotroph lineage, each with distinct hormone straining characteristics and transcription factors. Null cell adenomas, therefore, are exclusively those which show neither hormone staining nor transcription factors. Recent evidence has suggested that among NFPAs, gonadotroph adenomas make up 73% of all cases. (7)

A few papers have been published showing treatment results of groups of patients taking into account their immunohistochemical classification. This is an up-and-coming area of research and may improve treatment for NFPAs. (8, 9)

REPEAT SURGICAL RESECTION

Surgical resection is the first-line modality of treatment for NFPA, however, this does not necessarily dictate that it should be so for recurrent cases. With papers reporting recurrence rates between 44-75% at 10 years follow-up (10) it is of utmost importance to determine whether this modality is effective for recurrent NFPA. Advancement of surgical techniques and technology, such as intraoperative MRI and intraoperative identification of the optic nerve, have been shown to improve surgical outcomes. (11) Analysis of recurrence rates identified various factors that showed to have an impact on treatment outcome. Factors that augured a higher chance of recurrence included large tumour remnant and invasion into the adjacent cavernous sinus. On the other hand, good augurs of tumour control were identified to be small tumour remnant and old age. (10)

A study by Cavallo et al. reported on 59 patients who underwent repeat transsphenoidal surgery (TSS) endoscopically for recurrent NFPA. (12) 62% of the cases showed gross total resection on post-operative imaging. The study identified that patients who had previously undergone microsurgical rather than endoscopic TSS were more likely to achieve gross total resection, whereas patients who had already undergone endoscopic TSS portended to lower rates of total resection post-operatively.

Another larger study by Chang et al. reported lower gross total resection rates of 40% but did not distinguish as clearly between microsurgical and endoscopic approaches. (13) It similarly identified suprasellar extension and cavernous sinus invasion to be

a bad prognostic marker for total resection outcomes. This study did, however, highlight a rigorous breakdown of complication rates, with visual deterioration being experienced in 5% of cases, transient diabetes insipidus (DI) in 4.9%, permanent DI in 1.2%, postoperative hematoma in 2.5%, meningitis in 2.5% and perioperative mortality in 1.2%.

Literature has also been published discussing different surgical approaches, be they microscopic or endoscopic. Some surgeons have described approaches, such as interhemispheric or sub frontal, for accessing NFPA that have invaded into adjacent structures. (12, 14) However, the evidence suggests that endoscopic TSS brings shorter hospital stay, less patient discomfort and reduced perioperative morbidity. (15) A study by the University of Virginia group supported this, finding that 70% of patients undergoing microsurgical resection had intraoperative lumbar drain placement, compared to only 1.7% of patients who underwent endoscopic resection. (15)

ADJUVANT RADIOTHERAPY POST-OPERATIVELY

Adjuvant radiotherapy may be used post-operatively, both in the first surgical instance and in recurring cases. The timing of radiotherapy is a highly debated subject. A study in northern Italy studied tumour recurrence or regrowth in 226 patients who had undergone treatment for NFPA. (16) Each patient was followed-up for a minimum of 5 years. Patients were divided into three categories - A: those who showed no radiological signs of tumour residue post-operatively (n=73); B: those who showed signs of postoperative tumour residue but did not undergo radiotherapy (n=77); C: those who showed signs of postoperative tumour residue and underwent radiotherapy. In group A, recurrence occurred in 14/73 patients (19.2%), after a mean period of 7.5 years; group B showed tumour regrowth in 45/77 patients (58.4%) after a mean period of 5.3 years; group C showed tumour regrowth in 14/76 patients (18.4%) after a mean period of 8.1 years. The choice of radiotherapy in this study was stereotactic radiotherapy.

STEREOTACTIC RADIOSURGERY FOR RECURRING NFPA

Stereotactic radiosurgery (SRS) has been abundantly discussed in pituitary literature. The mechanism by which it works is delivering a very high dose of ionising radiation to a highly accurate point. This is highly beneficial as it spares the surrounding structures of radiation. Furthermore, it is usually delivered in a single dose. Notwithstanding this, it can also be delivered in different sessions, called fractionated radiotherapy (XRT). Stereotactic radiosurgery and stereotactic radiotherapy differ in that stereotactic radiosurgery is a single, high dose of radiation, as opposed to stereotactic radiotherapy which uses lower fractionated doses of radiation over several sessions. The term stereotactic refers to the frame and technique used to administer these therapies, wherein the patient's head is clamped into a frame, which in turn is used to standardise coordinates of the patient's brain to be able to map the therapeutic area.

Various factors may lead the clinician and patient towards deciding which type of radiotherapy to undergo. Convenience is a strong factor leading to choose SRS. Location of the adenoma is also a factor which must be strongly considered in making this decision. If the target is between 3-5mm from the optic pathway, SRS may be contraindicated due to the risk of damaging the optic apparatus. Large size of adenoma is also a contraindication for SRS, as it may be too large to irradiate with a single dose. Therefore, appropriate and detailed contouring of the adenoma is of utmost importance. This can adopt the form of stereotactic MRI and/or CT.

There are various mechanisms of delivery of SRS. Gamma-knife (GKS) is a frequently used mechanism that employs radioactive isotope Cobalt-60. Linear accelerators are also widely used to deliver SRS. These accelerate electrons and convert this energy to high-energy X-rays, also called photons. Cyberknife is another mechanism but can deliver both stereotactic and fractionated radiotherapy. It also is a linear accelerator but is much smaller and is mounted on a movable arm. This allows for higher patient comfort, with greater mobility and flexibility of positioning. Finally, there is proton-therapy, which employs high energy protons from a cyclotron or synchrotron. The main benefit of this technique is that it greatly reduces exposure of surrounding tissues to treatment, therefore may be associated with fewer complications and side-effects. Radiosurgery is image-guided and affords sub-millimetre accuracy.

A case-control study by Picozzi et al. divided two sets of patients with recurrent NFPA into: G1 - observation (n=68) and G2 - receive GKS (n=51). (17) This showed that progression-free survival was achieved in 51.1% of patients who were observed for an average of 41.6 months, compared to progression-free survival of 89.8% of those who received GKS and were followed-up for an average of 40.6 months. In a larger study by Sheehan et al. in 2013, 512 patients who had undergone Gamma-knife surgery for recurrent NFPA were studied. (18) They were followed up for 36 months and showed a tumour control rate of 93.4%. Progressive-free survival was 98% (3 years), 95% (5 years), 91% (8 years) and 85% (10 years). It identified that patients with a smaller adenoma volume had a favourable outcome, and conversely suprasellar extension was found to be an unfavourable factor. 21% of patients suffered from hypopituitarism post-operatively, and 9% showed new cranial nerve deficits.

A study by Wilson et al. observed patients who had undergone treatment for recurrent NFPA in the form of SRS, fractioned stereotactic radiation therapy (FSRT) and conformal radiotherapy (CRT). (19) Those who underwent SRS (n=51) showed 100% progressive-free survival at 5 years, compared to those who underwent FRST (n=67) and CRT (n=53), with 93% and 87% progression-free survival respectively. A review by the Congress of Neurological Surgeons (CNS) reviewed all available studies on SRS for NFPA, in which it identified 24 independent studies which showed tumour control from 83% to 100%. (10)

FRACTIONATED RADIATION THERAPY

Conventional radiation therapy (RT) has been used for decades in the treatment of recurrent NFPA and has been the subject of much scientific research. Earlier models of RT used four-field techniques, whereas in the past ten years the emergence of more advanced, three-dimensional conformal RT, as well as intensity-modulated techniques, have predominated. Radiation therapy for NFPA is fractionated, delivering 45-54 Gy in total over 5-6 weeks, five days a week. Each fraction, therefore, approximates to around 1.8-2 Gy per day. Fractionated radiation therapy itself has several subtypes which include conventional fractionated radiation therapy (XRT), intensity-modulated radiation therapy (IMRT) and stereotactic radiation therapy (SRT).

A study by Chang et al. described 663 patients treated with RT for recurrent NFPA. (20) Each one was followed-up for 101 months. Tumour control was achieved in 90.3%, and progression-free survival was achieved in 93%, 87%, 81% at 5, 10 and 15 years respectively. This study also found cavernous sinus invasion and subtotal previous resection to be unfavourable factors. Another study by Losa et al. grouped patients into 3 groups: G1 – showed no tumour on postoperative imaging (n=279), G2 – showed residual tumour on postoperative imaging but did not undergo RT (n=76) and G3 – showed residual tumour and underwent RT (n=81). The study found that progression-free survival was achieved in 87.1% of G1, 39.2% of G2 and 100% of G3. (21)

Figure 1:

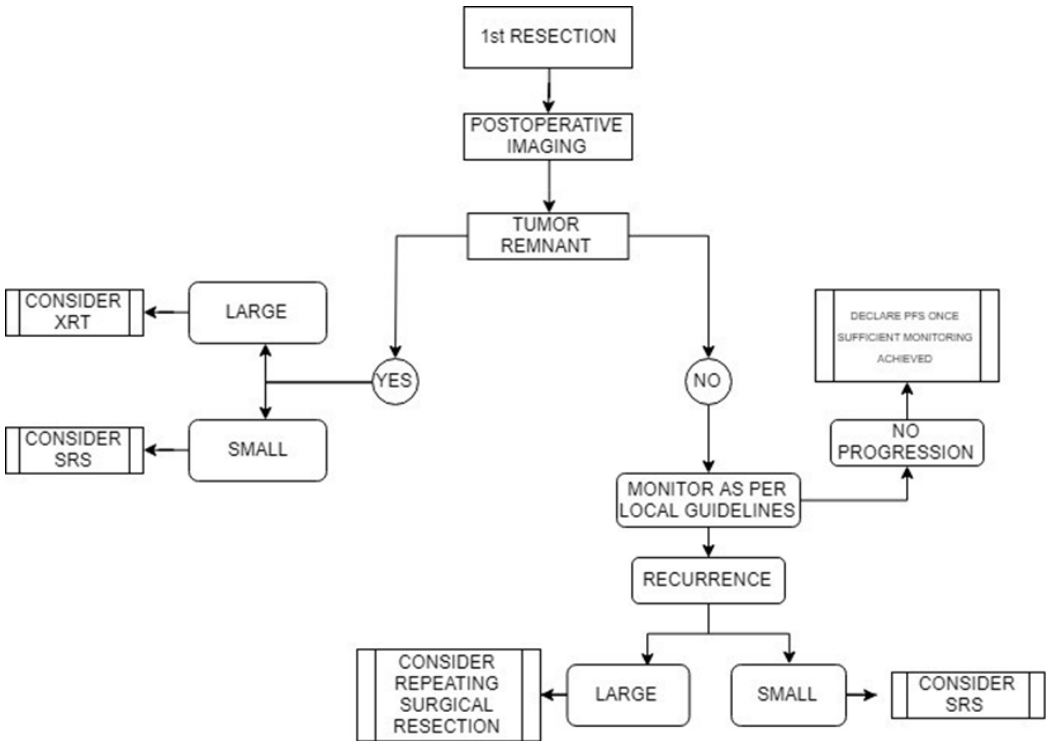
Proposed algorithm for the management of recurrent non-functioning pituitary adenomas.

Breen et al. reported on a cohort of 120 patients who had undergone XRT for recurrent NFPA, and progression-free survival was reported to be 87.5%, 77.6% and 64.7% at 10, 20 and 30 years after XRT, accordingly. (22) This large study also described the complications of the procedure and announced 0.8% developed optic and oculomotor neuropathy, whilst 1.7% developed radiation-induced neoplasms. Complications following radiation therapy often manifested as post-operative side-effects, namely nausea and vomiting, which were found to last between 1-2 months. However, the most common side effect of RT was hypopituitarism, described as highly as in 88% of cases in one study by Langsenlehner. (23) On average, tumour control following XRT or SRT was between 74% to 100% in 20 studies available.

SUMMARY AND CONCLUSION

Each treatment modality discussed has a role in the treatment of RNFPA. The indications for each modality are varied and often made on a case-by-case basis, dictated often by the anatomy of the patient and the nature of the tumour. However, a summary of the possible scenarios has been designed to summarise the above points.

Analysis of all available data has been useful to highlight that recurrent NFPA responds to different treatment strategies. Large remaining tumour size and invasion into adjacent structures, such as the cavernous sinus, have been shown to increase the chance of recurrence of NFPA. On the other hand, small tumour remnant size and old age have both been associated with a smaller chance of recurrence. As highlighted before, studies have highlighted that 40-60% of patients undergoing repeat resection for recurrent NFPA achieve Progression-free Survival (PFS). (10-14)
Evidence suggests there is a higher chance of achieving PFS via



endoscopic transsphenoidal surgery if the first attempted resection was microsurgical. (12) Conversely, repeating endoscopic transsphenoidal surgery is associated with a lower chance of total resection. Endoscopic transsphenoidal resection for NFPA, however, has lower associated complications and perioperative morbidity. It is also important to highlight the importance of adjuvant perioperative radiation therapy. Adjuvant RT in patients with clear postoperative tumour remnant was shown to decrease tumour recurrence by 40% in one study. (16)

Stereotactic radiosurgery has also been shown to be effective in the treatment of recurrent NFPA. One study saw PFS achieved in almost 90% of patients treated, compared to 50% of the controlled, observed group. (17) It has been shown to be particularly effective in small tumour remnants. Larger tumour size and invasion into the cavernous sinus have been shown to diminish the effectiveness of SRS, on the other hand. Although the risks of radiation to the body in SRS are lesser, they are not non-existent: due to its high intensity of radiation in a specific spot, it is contraindicated if the irradiation aim is close to the optic apparatus. Hypopituitarism has also been described in frequencies of 0-40%. Cranial nerve deficits are rare but must be considered, described in 0-13% of patients in different studies. (10, 17-19)

Finally, conventional radiation therapy has been shown to be highly effective in treating NFPA. In one study, it achieved almost 60% more PFS when given RT after post-operative imaging revealed tumour remnant, compared to those in whom tumour remnant was also detected but were not administered RT. (21) However, as many as 88% of patients have been described to develop postoperative hypopituitarism. It has also been associated with radiation-associated neoplasms, described in 1-2% of all cases. (22) As a closing statement: although above has discussed what is the best treatment method to employ, very often the "watch-and-wait" method is the method elected. The indications for employing this option are varied and non-specific; often it is simply the clinician's clinical judgement which makes this decision. Evidence of tumour remnant in a very elderly patient would not necessarily require action, which would often bring much more morbidity and worry to the patient than the small tumour remnant could do in the next ten years. Therefore, a case-by-case approach, based on strong dialogue between patient and surgeon is often the most effective treatment algorithm.

Acknowledgements

I would like to sincerely thank Mr Adam Williams for supervising this project, for his input and invaluable teaching on this topic. I would also like to extend a warm thanks to this surgical team, registrar and juniors for their time. A special thanks to the Medical School Education Centre for facilitating their expertise on the topic of literature searches, without whom this paper would have been the lesser.

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PMID: 17497095

APPENDIX

The author collaborated with a librarian at the University Hospital Bristol Education Centre to conduct the literature search. The author and librarian searched PubMed using previously published search strategies to concrete the relevant literature. Below is the employed search strategy:

1. Pituitary Neoplasms [Mesh] OR Adenoma [Mesh] OR Adenoma, Chromophobe [Mesh

2. Microadenoma*[Title/Abstract] OR adenoma*[Title/Abstract] OR macroadenoma*[Title/Abstract] OR incidentaloma*[Title/Abstract] OR chromophobe*[Title/Abstract] OR transsphenoidal*[Title/Abstract])

3. Ppituitary[Title/Abstract] OR hypophyse*[Title/Abstract] OR sellar[Title/Abstract] OR transsphenoidal[Title/Abstract])

4. #1 OR (#2 AND #3)

5. Residual[Title/Abstract] OR recurr*[Title/Abstract])

6. #4 AND #5

7. NOT Comment[pt] NOT Letter[pt] Limit to English, Humans, publication date to 01/01/2020

The British Student Doctor, 2021;5(3):12-19
doi: 10.18573/bsdj.213
Original research

An audit on general surgical readmissions

ORIGINAL RESEARCH

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No conflicts of interest to declare

Accepted for publication: 18.04.21

ABSTRACT

Introduction: The objective of this study was to investigate general surgical readmissions at Salford Royal Foundation Trust (SRFT) and to assess the patterns of readmission in pathology and patient group characteristics.

Methods: We performed a retrospective audit of patients re-admitted as an emergency within 30 days of being discharged by the general surgery team at SRFT over seven months from April 2018 to October 2018. Patient NHS numbers were provided by Hospital Episode Statistics via the Information Business Team at SRFT. Data was input into Microsoft Excel and statistical analysis was performed using StatsDirect 2018.

Results: During this period, 171 patients were coded as general surgery emergency readmissions. Subsequent exclusion left 91 patients in our readmissions group. We compared this with 3261 patients who had been admitted to the general surgical team over the same time period. Gallstone pathology made up 26.4% of the readmission patients, but only 9.26% of all general surgical patients. 58.5% of the surgery on the readmission group was non-elective, compared to 29.7% of all patients. In the readmission group, patients who had a previous operation cancelled had higher rates of early post-operative complications per operation (0.6 complications per operation) from their subsequent operation, than patients who had no previous cancellations (0.229). Four patients (4.4%) had no discharge summary; another seven (7.7%) did not get any patient advice. For 16.5% of patients, the written discharge advice to them, or lack of such advice, was involved in their readmission.

Conclusions: Gallstone pathology was over-represented in the readmissions group. Of the patients who had surgery on index admission, the readmission group had a higher proportion of non-elective surgery than all surgery patients. Written discharge advice was varied and inconsistent, and was not present for 12.1% of patients. Clearer discharge advice with more available written advice could reduce avoidable readmissions.

INTRODUCTION

Emergency readmissions into hospital are disruptive and costly for both the patients and hospitals and are associated with worse outcomes. An emergency readmission is any readmission that is unplanned and occurs up to 30 days after discharge from initial admission. (1)

On both sides of the Atlantic, emergency readmission rates have been used as a quality indicator and have been the basis for 'pay-for-performance metrics, making them a target area for both clinicians and hospital management. (2, 3) In the UK, the National Tariff Payment System (NTPS) has 'incentivised' British hospitals by withholding funding for a patient's readmission since 2011. (1) The withheld money was to be spent on the key areas that may have been implicated in readmissions: 'better discharge planning, more collaborative working and better co-ordination of clinical intervention with community and social care providers'. (1)

It is therefore not surprising that there has been a huge amount of research into emergency readmissions. However, there are two main reasons for further analysis of surgical readmission rates. Firstly, despite financial incentives and large amounts of research, emergency readmission rates are on the rise in the UK. Figures from the Nuffield Trust show that between 2010/2011 and 2016/2017 the number of emergency readmissions increased by 19.2%. (4) Healthwatch England reported in November 2018 that rates are 'growing faster than before'. (5)

Secondly, the vast majority of the readmission research has focused on medical patients. As Wiseman et al. state in their systematic review of surgical readmissions, 'readmissions have received less attention in the surgical specialties', a fact which they describe as 'remarkable given the frequency of surgery'. (6)

Post-operative complications are often the leading cause for the readmission, with McSweeney et al. showing a significant correlation between the number of post-operative complications and an increasing readmissions rate. (7) In addition, they found that intra-abdominal operations were more likely to lead to post-operative complications than other general surgical procedures such as mastectomy, parathyroidectomy and thyroidectomy. (7) Dehydration was the cause of up to 20% of emergency readmissions after surgery in some studies, followed by post-operative infection. (8, 9)

The relationship between length of stay for the index admission and readmission rates is not clear at present. There are worrying trends though, as Manilich et al. report, with the length of stay in hospital going down for colectomies for colon cancer while readmission rates are going up. (8) There is an ongoing debate on whether open or laparoscopic surgery delivers better outcomes and higher readmission rates. (9) Finally, some of the literature highlights that surgical readmissions tend to be readmitted for a surgical problem, rather than a medical problem, which is perhaps explained by the 'medical optimisation' of surgical patients before elective surgery. (2)

There is an underlying question throughout much of the current literature on emergency readmissions: what proportion of readmissions are avoidable? The figures vary wildly from 75% to less than 20%. (8, 10) This lack of clarity raises the question as to whether 30 day emergency readmission rates are reliable quality indicators. As Jotny and Jha put convincingly, 'much of what drives hospital readmission rates are patient- and community-level factors that are well outside the hospital's control'. (10) They cite socio-economic status and co-morbidities, such as mental illness, as the key factors in readmission rates within the 30 day timeframe rather than hospital care. They argue that if readmission rates are to play their part as a quality indicator, then they must be limited to only seven, or even three days post-discharge. (10)

Hospital trusts look at local rates of readmission and, if necessary, local solutions to reduce them. At Salford Royal Foundation Trust (SRFT) an audit was undertaken in the general surgery department by Dr Matthew Davenport to explore the proportion of general surgical readmissions that reflected 'true emergency readmissions' according to the NTPS definition. (1, 11) This audit found that readmission rates of general surgical patients varied between 5-10% from April to October 2018. (12) Of these readmissions, there were only 5 patients who were incorrectly coded as general surgical emergency readmission errors, accounting for only 2.9% of the total patients classed as readmission. (12) As this was lower than expected and therefore unlikely to reveal much scope for improvement, focus turned to the 'true readmissions'. It was felt that a greater understanding of this group was needed and further investigation was required.

The aims of this study were to investigate general surgical readmissions within 30 days at Salford Royal Foundation Trust between April 2018 and October 2018. Our objectives were to further assess patterns of pathology in patient groups identified by the previous audit and to identify trends in patient characteristics in patients who have an emergency readmission to a general surgical ward.

MATERIALS AND METHODS

Study setting

Salford Royal Foundation Trust (SRFT) is a large hospital trust in the city of Salford in the Northwest of England. It is responsible for local health services to the people of Salford with a population of over one million people, whilst also providing many specialist services to Greater Manchester and its surrounding area. (13)

Study design

We performed a retrospective audit of patients admitted under the general surgery team at SRFT from April 2018 to October 2018 inclusive. We then further reported on the patients from this group who, following discharge by the general surgery team, were subsequently readmitted as an emergency within 30 days.

Participants
In the initial audit, 171 patients were received as emergency readmissions. Nine patients were then excluded after being decided they were 'not true' readmissions. This was due to either being incorrectly coded as general surgery (n=5), their second admission was a planned day case procedure (n=3) or due to a patient self-discharging and later reattending (n=1).
This left 162 'true' admissions. These were subsequently divided into further subgroups depending on the reason for their readmission (Figure 1).

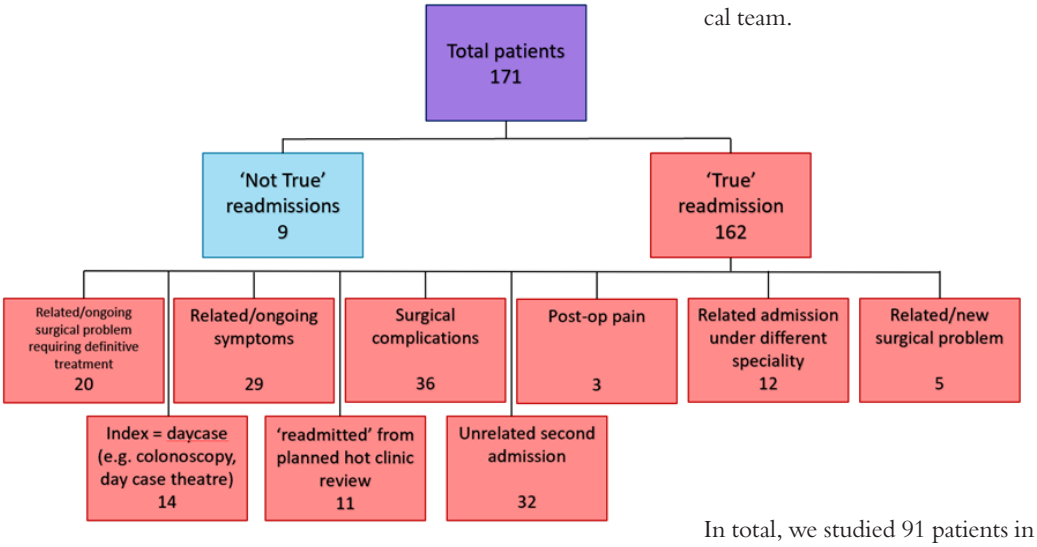

Figure 1: *'True Readmissions' Taken from initial study by Dr M. Davenport. Flow chart showing the division of the patients into 'True' and 'Not True' Readmissions and the further division of the subgroups within 'true readmission.'*

Following the initial study, we decided to further explore these subgroups. As we wanted to focus on the general surgical team and their role within readmissions in our study, we decided to exclude a number of the 'true' subgroups. See Table 1 for the reasons behind which subgroups were excluded.

'True' readmission subgroup	Reason for exclusion
Post op pain	The improvement to their management was clear- better pain relief.
Related/new surgical problem	New yet unrelated problems cannot be seen as a failure of the discharge process as they are unpredictable. For example, a patient presenting to A&E with a supraventricular tachycardia fifteen days after having an elective colonoscopy.
Unrelated second admission	
Index = day case	Although these technically should be included, it was found that actually all patients were readmitted with an unrelated problem.
Readmitted from HOT clinic (acute ambulatory surgical review)	Includes patients who were seen in A&E, sent home with a HOT clinic appointment and were subsequently admitted from the HOT clinic. It was acknowledged that the HOT clinic appointment is a sign that the risk of deterioration and potential further hospitalisation was appreciated at the discharge and therefore the patient was placed on an appropriate pathway.

Table 1: *Reasons for the exclusion of patients in the subgroups of 'true' readmissions.*

This left four subgroups to further investigate:

- Related/ongoing surgical problem requiring definitive treatment (n=20)
- Related/ongoing symptoms (n=29)
- Surgical complications (n=36)
- Related admission under different specialty (n=12).

During the data collection process, I further excluded one patient from the 'Related/ongoing surgical problem requiring definitive treatment' group and five patients from the 'Related/ongoing symptoms' as they were not actually accepted by the general surgical team.

In total, we studied 91 patients in the readmission group:

- Related/ongoing surgical problem requiring definitive treatment (n=19)
- Related/ongoing symptoms (n=24)
- Surgical complications (n=36)
- Related admission under different specialty (n=12).

The NHS numbers were provided by Hospital Episode Statistics via the Information Business Team at SRFT and the subsequent data collection was performed by the author. Data was input into Microsoft Excel and statistical analysis was performed using StatsDirect.

RESULTS

There were 91 patients in the readmission group. We received data on 3529 general surgical (GS) patients from the Salford Royal Information Business Team who were coded as 'general surgical' patients. We excluded 268 as they were not general surgical patients (diagnosis was an orthopaedic, obstetric and gynaecological, medical or neurosurgical problem) and were coding errors. This left 3261 GS patients.

Gallstone Pathology

Gallstone pathology made up 9.26% (n=302) of all GS patients. They accounted for 26.6% (n=24) of the readmission group. Over half of all GS patients with gallstone pathology had surgery during their admission 53.3% (n=161). In contrast, of the gallstone

patients who would be readmitted, only 29.2% (n=7) had surgery during their first admission. Of those patients who did not have surgery on index but were subsequently readmitted, 37.5% (n=9) had 'definitive' treatment (either cholecystectomy or endoscopic retrograde cholangiopancreatography) during their second admission.

Surgery on index admission

In the readmission group, 45 % (n=41) of the group had surgery on their index admission, while 37% (n=1206) of all GS patients did. Of those 41 patients in the readmission group who had surgical procedures on index, there were 15 open and 11 laparoscopic abdominal surgeries. A further 14 patients had either superficial (for example abscess incision and drainage) or non-abdominal operations (such as total thyroidectomy). One patient had a cholecystectomy but due to lost notes, it was not clear if it was open or laparoscopic. Whilst 29.7% (n=358) of the surgeries on index of the all GS patients were non-elective, 58.5% (n=24) of surgeries of the readmission group were (Figure 2).

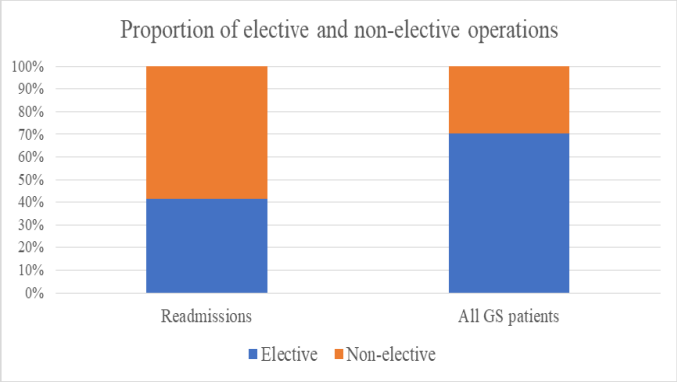

Figure 2: *Clustered bar chart showing proportions in percent of Elective and Non-elective surgery of those patients who had surgery at index, comparing all the GS patients and the readmissions group*

Post-operative complications

All 41 patients who had surgery at index were readmitted due to complications of their surgery, either returning as a general surgical patient or admitted under another specialty. Of those 41 patients, 78.0% (n=32) did not have an early post-operative complication which was noted during their index admission. Of the 9 patients who had post-operative complications while admitted, 5 (12.2%) had one complication and 4 (9.8%) had two complications.
We found no association between intra-abdominal surgery and early post-operative complications which occurred during index admission (p=0.5307) [Chi Square X2 (2, N=41) =1.267, p=0.5307].

Cancellations

Out of the 40 patients who had surgery at index in the readmissions group, 12.5% (n=5) had had their operation previously cancelled (Table 2). As one patient's pre-operative medical notes could not be found, it was unknown whether they had been cancelled previously or not, hence n=40 in this case.

Number of post-operative complications	0	1	2	Total	% of n
Previous cancellations	3	1	1	5	12.5%
No previous cancellations	29	4	2	35	87.5%
Total	32	5	3	40	
% of n	80%	12.5%	7.5%		

Table 2: *Number of post-operative complications during first admission for those who were previously cancelled and those who were not*

In the group which had been previously cancelled, 40% had a complication, compared to 17.1% of those with no previous cancellations. The patients who had had previous cancellations also experienced a complication per operation rate of 0.6 while those who had not been previously cancelled had a complication per operation rate of 0.229.

Discharge

A discharge summary was not present on the Electronic Patient Record (EPR) for 4.4% (n=4), while 7 discharge summaries did not contain any information for the patient. In total, 12.1% (n=11) did not receive any specific advice on discharge. In addition, only 28.6% (n=26) of patients were given safety-net advice. This is basic, non-specific advice to seek medical attention if the patient becomes unwell or symptoms recur (Table 3).

	N=
No discharge summary	4
No patient information	7
Safety netted	26
Specific patient information	54

Table 3: *Table showing the number of patients in the readmissions group receiving varying degrees of written information on the discharge summary following their index admission*

Readmission timeline

Over half of the readmissions (54.9%, n=50) were in the first week after discharge, with numbers declining over the next three weeks (n=18, n= 15 and n=8).

DISCUSSION

Emergency readmissions are multifactorial and, to some extent, are inevitable. However, there are some key themes to be drawn from our study.

There is a discrepancy between the percentages of gallstone pathology patients who made up only 9.26% of all of the GS patients, but 26.4% of the readmitted patients. Gallstone disease and the timing of intervention has long been a matter of debate. (14, 15) NICE guidance (updated in 2014) advocates prompt laparoscopic cholecystectomy for patients presenting with acute cholecystitis (within one week of diagnosis). (16) We found that only 29.2% (n=7) of the gallstone patients in the readmissions group had surgery on index admission, while a further 37.5% (n=9), who did not have an operation on index, had 'definitive' emergency treatment on their readmission. SRFT does have a surgical HOT clinic for patients to be seen the next day for biliary tree symptoms, however it seems not all patients who require prompt management are being seen in a timely fashion. In line with some of the literature, our research points to early intervention in gallstone disease, which could help reduce emergency readmissions resulting in emergency or urgent procedures. (14, 15)

It is worrying for clinicians and managers alike that patients with previously cancelled operations had higher rates of early post-operative complications after their subsequent surgery. On the first admission, the 5 patients with at least one cancellation suffered from a 40% post-operative complication rate compared to only a 17.1% complication rate in patients with no cancellations. Patients who had been previously cancelled also had a greater complications per operation rate of 0.6, compared to 0.229 complications per operation in the group who had not been cancelled.

While there is a known relationship between post-operative complications and readmission rates, there is little in the literature on whether previously cancelled operations are related to post-operative complications. (7, 17) In an example from our study, a patient was readmitted as an emergency due to gallbladder pathology two days after their elective laparoscopic cholecystectomy should have taken place. More investigation is needed into the reasons for cancellations and if the cancellations made the subsequent surgery more dangerous for the patients.

Several previous studies reported a higher rate of post-operative complications after intra-abdominal surgery compared to extra-abdominal. (7) No such association was found in this study.
The discharge summary informs the patient's GP about their current admission, informs the patient about their admission, gives post-discharge advice and is the written document of verbal advice given in line with NICE Guidance. (16, 18) We found that 4.4% of the readmission patients did not have an initial discharge summary on the EPR system. When there was a discharge summary, the 'Patient Information' section was left blank in 7 of them, leaving 12.1% of patients without written discharge information.

When information is given, it could be clearer and more consistent. Examples included a patient who was readmitted with shortness of breath 21 days after an inguinal hernia repair. Despite clear advice from The Royal College of Surgeons to 'keep moving', this patient was only given safety net advice on the discharge summary. (19) On readmission, the patient said he had lain on the sofa for three weeks after being advised to rest following his operation and was diagnosed with a pulmonary embolism and community-acquired pneumonia. In addition, the advice to gallbladder patients was variable. In particular, this concerned advice on a low-fat diet or other dietary triggers following admission and before the elective cholecystectomy, both of which are specifically named in NICE guidance. (16) One of the readmitted patients experienced an attack of acute cholecystitis after eating chips following her first discharge; there was no record that she had received advice about keeping a low-fat diet.

A noticeable absence from the patient information leaflet search engine on the SRFT website is information on gallbladder disease. (19) We have no doubt that the vast majority of the ward team do give advice on discharge to their patients, however there is a lack of written advice in known channels of information and documentation. Given the volume of patients who are readmitted as an emergency with an exacerbation of gallbladder pathology, we advise an accessible information document on the SRFT website.
In total, 15 patients (16.5%) received no advice on discharge, or had inadequate advice which could have been implicated in their readmission. This is a target area of improvement. (19)
Non-elective surgical procedures during index admission are over-represented in the readmission group compared to the number of non-elective operations on all GS patients. This is in line with other studies in the literature. (17) While it is reasonable to argue that non-elective surgery results in more complications, a longer length of stay and perhaps a worse outcome, the readmission rate is more of an indicator of the discharge process and post-discharge care, rather than the severity of the presenting complaint. (1) Salford has well-established post-discharge care following upper gastro-intestinal, colorectal and anal surgeries, including input from specialist nurses, information leaflets on discharge and regular follow-up. Many of these structures are in place for elective procedures, but the same cannot be said for non-elective.

Limitations

This is a small study over one period, at only one centre. In addition, as the data collection required in-depth review of clinical notes with limited time available, there is less clinical information regarding the GS patient group (n=3261) who were discharged but not readmitted. In addition, due to coding restraints, we were unable to remove the readmissions group from the GS patient group. Therefore, there are clear limitations in analytical comparisons between the two groups. Being an audit, this study has been observational and therefore further analysis is needed to draw any stronger conclusions. Finally, addressing some of the key areas with the general surgical department and then completing the audit cycle

would be the most satisfactory next steps.

CONCLUSION

Our study has further added to the awareness that emergency readmissions of general surgical patients is varied, but that there are key areas in which patient care can be optimised. Further research is needed in the post-discharge care in place for patients who have undergone non-elective operations, in the causes and outcomes of patients who have operations cancelled and if there could be an improvement in the management of gallstone patients. Action is needed in ensuring every patient receives a discharge summary with personal advice.

Acknowledgements

I would like to acknowledge and thank the people who have vastly contributed to this project. Firstly, Dr Matt Davenport who conducted the initial study and who guided me through the process of data collection. Ruth Swindells from the Information Business Team provided me with all the patient information that I requested. For statistical advice, I thank Dr Matthew Gittins from the University of Manchester Centre for Biostatistics. Finally, Ms Helen Doran who has given me invaluable advice and support throughout the project.

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The British Student Doctor, 2021;5(3):20-29
doi: 10.18573/bsdj.289
Original Research

Tackling LGBTQ+ youth mental health inequality: Mapping mental health support across the UK

ORIGINAL RESEARCH

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No conflicts of interest to declare.

Accepted for publication: 06.07.21

ABSTRACT

Young people who identify as lesbian, gay, bisexual, transgender and queer/questioning (LGBTQ+) experience higher rates of mental health distress than reported in the general population, yet are far less likely to seek support services. Factors such as homophobia, biphobia and transphobia, cis-heteronormativity, fear of judgement and lack of staff awareness of LGBTQ+ identities are barriers to help seeking. This paper reports on the first stage of a study that investigated and mapped current LGBTQ+ youth specific mental health service provision across the UK. An online and offline service mapping exercise was undertaken to locate services. 111 services were identified across the search strategies, the majority in urban settings in England. There were three significant characteristics of LGBTQ+ child and adolescent mental health UK provision. Firstly, there was an absence of mainstream NHS support that specifically addressed the needs of LGBTQ+ young people. Secondly, the majority of LGBTQ+ youth mental health support was provided by voluntary/community organisations. Thirdly, there was a rare model of service based on collaborative working between NHS trusts and community/voluntary organisations. The results of this mapping exercise suggest that there is a reliance on the voluntary/community sector to provide mental health provision for LGBTQ+ young people. Furthermore, there was a distinct divergence in the approaches of the support provided by the voluntary/community sector and those from within the NHS. The affirmation of LGBTQ+ identities that is pivotal to the support provided by voluntary/community services contrasted with the 'treating everyone the same' approach prevalent in mainstream service provision. NHS mental health services must recognise that to tackle LGBTQ+ youth mental health inequality, statutory mental health support must address specifically the mental health needs of LGBTQ+ young people.

BACKGROUND

Lesbian, gay, bisexual, transgender and queer/questioning (we use LGBTQ+ to refer collectively to sexual minority and gender diverse identities) young people face significant mental health inequalities, experiencing higher rates of poor mental health and worse mental health outcomes than their heterosexual counterparts. (1-5) In a pooled analysis of twelve population surveys, LGB identified people under 35 years old were twice as likely to report symptoms of poor mental health compared to heterosexual people of the same age. (3) Trans and non-binary people were also found to have higher rates of poor mental health, suicidality and experiences of victimisation than the levels found in the general population. (6) Moreover, there is evidence to suggest LGBTQ+ mental health disparities start as young as age 10. (5) The prevailing model that offers an explanation of this disparity is 'minority stress'. (7) The experience of stigma, prejudice, and discrimination create a hostile and stressful social environment that leads to mental health problems. Development of the minority stress model posits that being LGBTQ+ locates young people outside the social norms of cis-heteronormativity i.e. the assumption that being heterosexual and cisgender (non-transgender) are the norm. These norms marginalise young people with LGBTQ+ identities through silence and a lack of mainstream visibility, in addition to the discrimination, (micro)aggression, bullying, and victimisation they experience. (8, 9) More recently, this inequality has been exacerbated by the COVID-19 pandemic and the impact of national and regional lockdowns. There is emerging evidence that lockdowns have led to the high levels of stress and depressive symptoms reported by LGBTQ+ people; especially those in the youngest age category examined by this study (18 – 24 years), and trans and gender non-conforming people. (10)

Despite the disparities in mental health outcomes for LGBTQ+ young people, this population also have elevated unmet mental health needs compared to their cis-heterosexual peers and underuse mental health services. (11-15) Findings from a UK study, indicated that in a sample of 789 LGBTQ+ young people, only one fifth of participants had sought help for their mental health difficulties. (14) Through interviews and survey data, the study found that LGBTQ+ young people were reluctant to access statutory or third sector mental health services because of experiences of homophobia, biphobia and transphobia; cis-heteronormativity (fear their sexual orientation or gender identity would be scrutinised or blamed for their mental health problems); difficulties disclosing their sexual and/or gender identity; fears of being misunderstood or judged by adults because they were young; and stigma related to having mental health problems. (14-18) Importantly, studies show that LGBTQ+ youth tend to seek mental health help online and from peers (13, 15) and prefer accessing LGBTQ+ organisations for mental health support. (14, 19)

In addition to the hesitancy to seek help, research suggests LGBTQ+ youth have a poor overall experience of mental health services and support. (6, 8, 11, 12, 16, 20) Problems highlighted are the limited staff understanding of LGBTQ+ issues and minority stresses, fear of being 'outed', and exclusion from the decisions made about their care. (11, 13, 21) Research suggests the competence of health care staff to provide appropriate care to LGBTQ+ young people is a vital factor in ensuring access. For example, an EU study found that the barriers to healthcare for LGBTQ+ people are exacerbated by two related assumptions held by healthcare professionals. Firstly, the assumption that patients are heterosexual and cisgender and, second, the assumption that LGBTQ+ people do not experience significant problems due to their LGBTQ+ identity, and therefore, LGBTQ+ identity is mainly extraneous to the delivery of appropriate healthcare. (22)

Despite the recognition that LGBTQ+ youth are less likely to access mainstream mental health services, and often do not find those services helpful, the evidence base examining LGBTQ+ youth's mental health support needs and service preferences is very limited. A recent systematic review of international qualitative evidence found that existing research is more likely to focus on barriers to access rather than factors that enable and facilitate engagement with services. (23) The current study (www.queerfutures2.co.uk) aims to address this knowledge gap by examining 'what works best?' for supporting the mental health of LGBTQ+ young people with common mental health problems at an early stage. We report here on the first stage of the study that sought to map existing LGBTQ+ youth mental health support in the UK. The aim of this stage was to both identify the type of service provision available and to generate a critical appreciation of the current landscape of service provision available for LGBTQ+ young people seeking early intervention mental health support. This stage of the study specifically addressed the research question: What type of service models for mental health early intervention and supported self-care to LGBT young people are currently provided?

MATERIALS AND METHODS

This stage of the study drew on the successful mapping methods used in Pryjmachuk et al.'s children and young people mental health self-care research. (24) Between February 2019 and February 2020, we employed systematic online and offline search strategies to identify services of various types e.g. self-care, peer-support, digital support, clinical; in a range of service settings e.g. health, local authority, third sector. The services identified were tested against inclusion criteria in the information extraction phase and a final typology was generated to describe service provision across the UK.

Search strategy

Online and offline searching was performed by two independent reviewers (members of the research team; RE, EP) to identify services in the UK where youth, sexuality or gender identity, and mental health were a focus. All services located were recorded on a single spreadsheet for comparison. During online searching, Google (the internationally most used search engine) and Bing (the default search engine for the respective organisation's I.T systems) were used to locate websites of interest using the following search phrases:

- LGBTQ+ Young People Mental Health Services [ADD GEOGRAPHICAL AREA]
- LGBTQ+ CAMHS [ADD GEOGRAPHICAL AREA]

• LGBTQ+ Youth Group [ADD GEOGRAPHICAL AREA]

These search phrases were selected and piloted with LGBTQ+ young people and service providers, to ensure they reflected the type of search term used when looking for mental health support for themselves or a service user. The rationale for this search strategy was that current active services would need to be discoverable to potential service users in a basic web search and therefore these phrases should illuminate most of the available service options. The first ten sites yielded through these search terms were checked for available services. Information about the service and provision offered was also gathered through specific websites, forums, and blogs; and relevant social networking sites. Online searches were also conducted for local Children and Adolescent Mental Health Services (CAMHS) transformation plans, which were likely to detail current and planned services for LGBTQ+ young people. In addition, searching for LGBTQ+-associated charter marks (e.g. Stonewall Champions, The Rainbow Flag Award to identify potential school services) was undertaken. The online search was supplemented by standard systematic search strategies including expert informants (academics and service providers) and subject-specific hand searching of print media (March 2019 issues of DIVA, Attitude, and Gay Times). (25)

In addition, we undertook a Freedom of Information (FOI) request directly to all NHS trusts delivering CAMHS in the UK (n=79) to enquire about any LGBTQ+ youth specific mental health service provision as CAMHS have a minimal online presence, and we were unable to obtain service information. FOI request contained the following questions:

1. Does your trust provide a specific mental health service for LGBTQ+ young people?

2. Are your staff offered LGBTQ+ awareness training?

3. Do you deliver the training in house or is it provided by an external partner?

4. Do you have a specific policy for working with LGBTQ+ people?

Trusts were asked to provide contact details for a staff member who would be able to provide more information about any services identified.

Inclusion/exclusion of services

The identified services were considered against inclusion and exclusion criteria. Determining whether services meet the inclusion criteria was an iterative process, dependent on the information available through the website and informal conversations with expert informants and the services directly. The inclusion/exclusion criteria are detailed in Table 1.

Table 1: *Mapping inclusion and exclusion criteria*

Domain	Inclusion Criteria	Exclusion Criteria
Mental health	Provide support for common mental health condition e.g. depression, anxiety, self-harm	Crisis services No mental health provision
Age	Targeted to 12 – 25 year olds	Services for exclusively under 12 years old Services exclusively for over 25 years old
Sexuality gender	Targeted to LGBTQ+ young people Youth mental health support within gender identity services	No LBGTQ+ youth provision Gender identity services (physical health services)
Service operation	Moderated by an agent e.g. service staff member Active during Feb 2019 – Feb 2020 Delivered in the UK (England, Scotland, Wales, Northern Island)	Services where no agent/staff were involved e.g. self-help apps Not active between 1st Feb 2019 – 31st Dec 2019 Delivered exclusively outside the UK

Information extraction

Detailed information about the operation of the eligible mental health services was collected using the service website, online resources, key contacts, and direct contact with the service via telephone or email. The following information was extracted:

• Service name
• Service provider
• Target group
• Sexual orientation target group
• Gender identity target group
• Mental health conditions addressed
• Theoretical approach
• Mode of deliver
• Tools/techniques used
• Duration service has been running
• Specific commissioning information
• Self-care element
• Support element
• Setting
• Rural/urban
• Average length of contact
• Average frequency of contact
• LGBTQ+ training offered
• LGBTQ+ policy available
• Facility adaptions
• Country/County

Typology generation

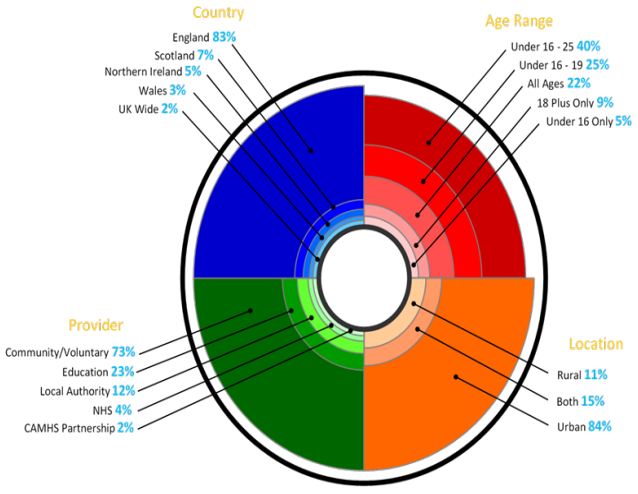
The typology of early intervention mental health service/support for LGBTQ+ young people was developed by five members of the research team. After reviewing the services located in the mapping exercise that met the inclusion criteria, the research team identified a simple typology that identified the type of service provision available in the UK.

RESULTS

The service mapping identified 111 services in the UK that offer early intervention mental health support for LGBTQ+ young people with common mental health problems (see Figure 1). The majority (82%) of the services operated in England (n=92), followed by Scotland (n=7), Northern Ireland (n=5) and Wales (n=4), and a small number of services operated UK-wide (n=3). Services were predominantly based in urban settings (n=84), focused around cities or towns, with only 13.5% providing for both urban and rural areas (n=15), and 11% providing services in an exclusively rural area (n=12).

The main service provider of early intervention mental health services for LGBTQ+ young people were the community/ voluntary sector (n=81), followed by Local Authority services (n=13), education/school-based services (n=10), and a small number of services being provided directly by the NHS (n=4). Three services were provided by a voluntary sector service in partnership with the local CAMHS. There was a variety of age ranges targeted by the services, with the largest number (n=40) aimed at young people ranging from under 16 years up to 25 years, 22.5% of services were aimed at under 16 years to 19 years (n=25) and 19.8% were aimed at all ages (n=22). A smaller number of services had more specific age ranges such as under 16 years only (n=5) and over 18 years only (n=10).

Figure 1: *Service Mapping by Descriptive Categories*



Service Typology

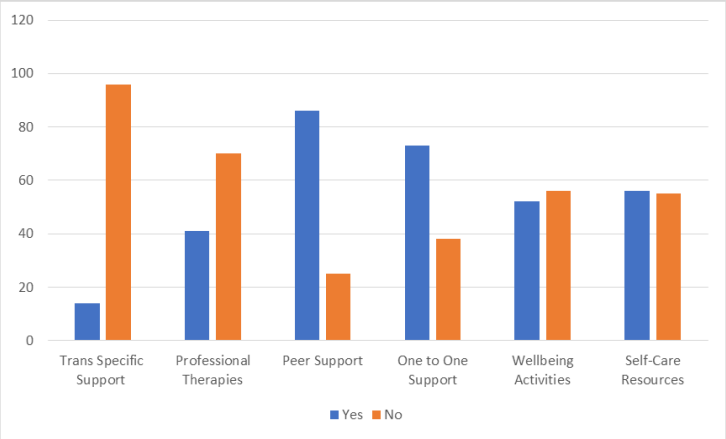
The aim of developing a typology was to define groups of service models with a similar set of characteristics. The typologies identified will then be used to inform the sampling of case studies in the Queer Futures 2 project to ensure that these represent the range of services across the UK. A simple typology of service provision was generated as there was very little LGBTQ+ youth mental health provision identified within the NHS, and services appeared to be located mainly in the community and voluntary sector in response to a demand for mental health support for LGBTQ+ young people. Thirdly, although some of these services offered an online service component, we identified no exclusively online mental health support for LGBTQ+ young people . Finally, obtaining detailed information about LGBTQ+ mental health services within an educational setting proved especially difficult. The typology overview categories are presented in Table 2.

	Typology category	Definition	Number (n=)
1	LGBTQ+ youth specific	Mental health provision provided by LGBTQ+ youth specific organisations (all service type providers).	51
2	LGBTQ+ specific youth inclusive	Mental health provision for all young people provided by LGBTQ+ organisations (all service type providers)	31
3	Integrated youth	Mental health provision provided for all young people with an LGBTQ+ specific component (all service type providers)	14
4	NHS	Any Mental health service provided by NHS e.g. CAMHS, sexual health providers.	5
5	Education	Mental health service provided by schools, further & higher education	10

Table 2: *Typology of LGBTQ+ young people's early intervention mental health and self-care support services*

Only 12.6% (n=14) of the services identified in the mapping process were specifically targeted to give early intervention and prevention mental health support services for trans and gender-diverse young people. Overall, 98% of the services offered primarily face-to-face services with two services offering a telephone only service. A high number of the services offered one to one support (66%, n=73) where a young person could talk in private to a staff member or youth worker, and peer support (77%, n=86) which was primarily in the form of youth group activities. A smaller number of services focused on professional therapies (37%, n=41) such as counselling or Cognitive Behavioural Therapy; wellbeing activity sessions (47%, n=52) which were usually one-off sessions rather than regular activities; and self-care resources (50%, n=56) such as leaflets or online resources were offered by half of the services.

Figure 2: *Service Mapping By Support Type*



DISCUSSION

This mapping stage of the study suggests three significant characteristics of current LGBTQ+ child and adolescent early intervention mental health provision in the UK. Firstly, there is an absence of mainstream NHS support that specifically addresses the needs of LGBTQ+ young people. Secondly, the majority of LGBTQ+ youth mental health support in the UK is provided by voluntary/community organisations reliant on charity and non-statutory funding that is often precarious. Thirdly, there is a rare model of service that is based on collaborative working between NHS trusts and community/voluntary organisations.

The dearth of mainstream NHS-specific mental health support for LGBTQ+ young people in the UK is a significant concern. Our view is that this is due, in part, to the lack of recognition of the necessity for adolescent mental health services to specifically address LGBTQ+ needs to tackle LGBTQ+ mental health inequality. Some NHS Trusts explicitly stated in their FOI responses that it was not necessary to offer LGBTQ+ specific mental health support, and this may even exclude young people. There were also examples of NHS Trusts conflating providing the 'same' service to everyone, as equitable service provision. This indicates a misunderstanding of i) the heightened risk of poor mental health in this population group; ii) the reasons for this elevated psychiatric morbidity; iii) the underutilisation of mental health services by LGBTQ+ youth; iv) LGBTQ+ youth poor experiences of mental health support. However, some NHS Trusts, despite not currently having a LGBTQ+ specific mental health service, reported their efforts towards developing inclusive support for LGBTQ+ young people. These service developments included, for example, funding and support for community/voluntary sector organisations to provide LGBTQ+ youth mental health support, collaborating with key stakeholders and LGBTQ+ young people to improve services, and LGBTQ+ visibility and staff training.

These developments in mainstream statutory services are to be welcomed but the majority of LGBTQ+ youth mental health support remains located within the charity and voluntary sector. These services were often developed in response to the absence of mainstream mental health services as attempts at meeting the demand from LGBTQ+ young people who often had poor experiences of NHS mental health support. (14) Our concern here is that the services in this sector are reliant on non-statutory and charity funding, which means the services are vulnerable to the instability of funding availability from a range of external sources. During the mapping exercise, there were instances where charity-provided services had to dramatically reduce their service provision or even close all together due to loss of funding. However, within the voluntary and community organisations was the expertise to provide appropriate and effective mental health support to LGBTQ+ young people. This was clearly orientated upon an understanding for services to generate an environment that affirmed marginalised sexual and gender identities (LGBTQ+) and were cognisant of the ways LGBTQ+ young people can encounter hostility, discrimination and victimisation, and feel like they do not 'fit in' within wider societal cis-heteronorms and how this may impact on adolescent mental health.

The examples of collaborative working between mainstream statutory health services and voluntary organisations was an encouraging initiative. Three services highlighted a potential model for bridging the gap between the knowledge of the voluntary/community sector and the stability of the statutory sector, through a CAMHS partnership model. These services offered a collaborative approach that involved, for example, funding support and CAMHS practitioner support within charity/voluntary LGBTQ+ youth settings. This type of service encouraged knowledge sharing, facilitated safe and inclusive environments for LGBTQ+ young people, and began developing a 'one stop shop' approach advocated by Future in Mind guidance, (26) and addresses some of the barriers LGBTQ+ young people face when seeking mental health support. (12, 13, 15)

Enhanced understanding of the needs of the LGBTQ+ community within a multi-level health equity framework could provide a platform for further development of new and existing LGBTQ+ mental health services. (27, 28) The results of the mapping stage of this study highlighted promising pockets of service provision development in healthcare and education settings across the UK. This included expanding staff LGBTQ+ knowledge, addressing practical issues such as monitoring forms and gendered toilets, as well as including LGBTQ+ youth in the design and evaluation of new and existing service provision. However, provision remains limited mainly to non-statutory LGBTQ+ specific mental health services in urban settings which presents a clear barrier to access, suggesting those living in rural areas may have to travel sizable distances to reach appropriate services. Similarly, the small number (12.6%) of services that offered a trans or gender diverse-specific mental health support illustrates the increased difficulty for trans and gender-diverse young people in accessing mental health services with appropriate training and knowledge.

Limitations

There were certain limitations to the use of online search strategies as it restricted the search to services with an established online presence, potentially missing smaller services with less informative or developed websites, or statutory services provided by the NHS, local authorities or schools, that were less likely have their own online presence. It is also worth noting that although the search

strategy was detailed it was time restricted, meaning the findings do not necessarily illustrate provision in development or provision adaptions due to the COVID-19 pandemic. Additionally, there was a range of views on what constituted mental health support as a service might employ a youth work lead approach and/or interpreted mental health as meaning formal medical interventions. Further clarification was often necessary to ensure that self-care, peer support and less medicalised approaches were considered early intervention and prevention mental health support.

Conclusions

Children and young people's mental health is a national priority that has intensified because of COVID-19 restrictions, (29) and LGBTQ+ young people have been recognised as a particularly high-risk group. (26, 30-32) NHS England have identified the importance of providing access to high-quality mental health services to LGBTQ+ youth who have a greater vulnerability to mental health problems but find it more difficult to access help. (26) The results of the analysis and classification of LGBTQ+-specific mental health services in UK reported in this paper demonstrate that we are a long way from fulfilling the ambition of national policy statements and NHS guidance. The importance of developing services that are appropriate for LGBTQ+ young people is even more crucial given the detrimental impact of COVID-19 on adolescent mental health. There exists, in urban setting particularly, supportive LGBTQ+ youth specific mental health services but these are under-resourced and exist on precarious funding from the charity sector. While mainstream services such as CAMHS have started to recognise LGBTQ+ youth mental health needs, the mapping exercise found few NHS specific examples. The results of this mapping exercise are the first stage in the Queer Futures 2 study (www.queerfutures2.co.uk) that aims to examine appropriate mental health early intervention provision for this vulnerable group and tackle LGBTQ+ young people's mental health inequality.

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doi: 10.18573/bsdj.217
Education article

Atrial fibrillation and sleep apnoea - a review of the mechanical interplay

EDUCATION

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No conflicts of interest to declare.

Accepted for publication: 21.07.21

ABSTRACT

Summary
Atrial fibrillation, a chaotic and irregular arrhythmia, is occasionally encountered in clinical practice alongside sleep apnoea, a form of sleep-disordered breathing. The pathophysiological mechanisms underlying the link remain ambiguous. Together, these two conditions seem to be mutually reinforcing and significantly interfere with an individual's quality of life.

Relevance
Atrial fibrillation is the most common cardiac arrhythmia faced by clinicians worldwide, whilst sleep apnoea is becoming increasingly prevalent. It is important for medical students to be clinically aware of the relationship between the two as therapeutic rehabilitation of one may reduce the severity of the other and improve overall prognosis in patients who suffer from both.

Take Home Messages
Further research is needed to explore the synergistic relationship between atrial fibrillation and sleep apnoea and the likelihood of one complicating into the other. However, it is important to be aware of this link as it is often missed in practice, leading to deterioration of symptoms and patient anxiety.

BACKGROUND

Atrial fibrillation is a widespread supraventricular arrhythmia characterised by irregular atrial activity as a result of abnormal conduction. (1) Sleep apnoea is a form of sleep-disordered breathing delineated as repeated cessation of breathing and/or periods of overly shallow breathing during sleep, co-existing with physiological stressors that include hypercapnia and autonomic nervous system fluctuations. (2) Atrial fibrillation and sleep apnoea are occasionally seen together in clinical practice, but the causal relationship and pathophysiological mechanisms implicated between the two remain unclear. As well as understanding the relationship between atrial fibrillation and sleep apnoea, the objective of this review is to determine whether the maintenance of normal sinus rhythm in patients with atrial fibrillation can reduce the severity of sleep apnoea, and vice versa. This is a topic of high relevance to medical students as the interplay between atrial fibrillation and sleep apnoea is often missed in university lectures that outline these conditions. This may be due to a lack of awareness of this link amongst medical professionals or perhaps due to the poor understanding of the complex mechanisms underpinning the two. Cardiology and respiratory medicine are two important specialities to which medical students are continuously exposed to through teaching and ward-based work. Understanding and recognising the relationship between atrial fibrillation and sleep apnoea will allow students to extend their studies beyond the curriculum to explore how they can improve outcomes in these patients further.

Atrial Fibrillation

The prevalence of atrial fibrillation increases with age, affecting roughly 4% of the Western population over the age of 60. (3) Several mechanisms have been suggested for the pathogenesis of atrial fibrillation, the most popular theory being a single electrical focus or multiple foci which orchestrate irregular electrical activity throughout the atria, leading to the formation of unstable circuits and multiple wavelets that maintain each other by generating areas of slow conduction. (1) Most of such focal activity originates in the pulmonary vein where cardiomyocytes evolve pacemaker-like properties, directing abnormal calcium release and triggering automaticity which leads to increasing atrial ectopy, spontaneous depolarisation and re-entry of circuits. (4)

Sleep Apnoea

The severity of sleep apnoea is measured using the apnoea-hypopnoea index. Apnoea is defined as the "cessation of airflow for at least ten seconds" and hypopnoea can be defined as any one of "substantial reduction in airflow (>50%)", "moderate reduction in airflow (<50%) with desaturation (>3%)", or "moderate reduction in airflow (<50%) with electroencephalographic evidence of arousal". (2, 5) Sleep apnoea is subdivided into obstructive and central.

Obstructive Sleep Apnoea

Obstructive sleep apnoea is a highly prevalent sleep-disorder characterised by repetitive interruption of ventilation during sleep, due to collapse of the upper airway resulting in an apnoea-hypopnoea index of '≥5 per hour with more than 50% obstructive in nature'. (2) This leads to oxygen desaturations and frequent night-time wakening with ramifications such as daytime somnolence and elevated sympathetic output. Irregularities in the anatomy of the pharynx, the physiology of upper airway muscle dilators and the stability of ventilatory control are principal causes of repetitive pharyngeal obstruction during sleep. (2) Regular arousal from sleep occurs to remedy the collapse by activating the sympathetic nervous system and hence causing fractured sleeping patterns, reduced cognitive function and quality of life. (2)

Central Sleep Apnoea

Central sleep apnoea is characterised by an unsteady ventilatory drive leading to weakened gas exchange. It is primarily diagnosed when the apnoea-hypopnoea index is five or more per hour with more than 50% of episodes being classed as central in subset. (5) Ventilation is managed through chemoreceptors at the carotid body peripherally and through neurones in the medulla centrally. They answer to CO2 via alterations in H+ concentration and chemosensitivity fluctuates between healthy and unhealthy individuals. Individuals with a high chemosensitivity respond to minute changes in chemical stimuli which in turn creates unstable breathing patterns. (5)

The Causal Relationship Between Atrial Fibrillation and Sleep Apnoea

It is approximated that 50% of patients with atrial fibrillation also have obstructive sleep apnoea. However, it is difficult to establish whether the two are mutually perpetuating due to the existence of several other risk factors such as increasing age, high BMI, hypertension, diabetes mellitus and congestive heart failure. (1) Central sleep apnoea has been shown to increase the risk of incident atrial fibrillation by 2.58-fold, especially in older men. (6) It is not well understood as to whether sleep-disordered breathing leads to the initiation and perpetuation of arrhythmogenicity or vice versa; understanding the causal relationship between the two may aid to identify therapeutic interventions and whether treatment of one can rehabilitate the other.

Atrial Fibrillation and Obstructive Sleep Apnoea

Existing respiratory effort during pharyngeal collapse stipulates considerable decreases in intrathoracic pressure. Negative intrathoracic pressure increases cardiac preload and left ventricular afterload. (2) After the discontinuation of apnoea, an increased stroke volume alongside a vasoconstricted circulation causes repetitive increases in systemic blood pressure during night-time. Chronically, obstructive sleep apnoea consequently leads to sustained periods of increased blood pressure and ultimately hypertension. Hypertension is associ-

ated with left ventricular hypertrophy, impaired ventricular filling, left atrial enlargement and slowing of atrial conduction velocity, all of which can initiate and maintain atrial fibrillation. (7)

One interventional cross-over study found that simulating obstructive apnoea and hypopnoea in patients produced premature atrial contractions, an important trigger for atrial fibrillation. (8) The forced inspiratory effort in resistance to a congested airway seen in patients with obstructive sleep apnoea during sleep, causes substantial sub-atmospheric drops in intrathoracic pressure. Repetition of this throughout the night misshapes the left atrial wall and induces an electrical trigger along with atrial conduction deformation. The combination of this leads to premature atrial contractions during obstructive apnoeic episodes, eliciting atrial fibrillation. A limitation of this study, however, was that sympathetic activity was not precisely measured and elucidated through observation of changes in heart rate.

Deformation and slowing of conduction was also observed in a separate study which found that obstructive sleep apnoea was related to bi-atrial structural remodelling through speckled areas of low voltage and non-typical electrograms mediated by mechanical stretch of the atrial wall and spontaneous atrial premature beats. (9) A key strength of this study was that individuals with confounding risk factors such as hypertension, obesity, diabetes mellitus and structural heart disease were excluded. Although the sample size was relatively small and there was lack of real randomisation in the trial, the results are useful as an indicator for a bigger study design.

Atrial Fibrillation and Central Sleep Apnoea

There are strong associations between central sleep apnoea and atrial fibrillation in patients with congestive heart failure. (10) However, the relationship between central sleep apnoea and atrial fibrillation in the absence of congestive heart failure is unclear and there is limited literature analysing this. One study evaluated 60 patients with central sleep apnoea, 60 patients with obstructive sleep apnoea and 60 healthy controls, with aims to identify the prevalence of atrial fibrillation in central sleep apnoea in the absence of other cardiovascular disease. (11) The prevalence of atrial fibrillation in patients with central sleep apnoea was 16-fold higher than in the obstructive sleep apnoea group and 8-fold higher than in the control group. This demonstrates that the well-founded relation between central sleep apnoea and atrial fibrillation is not restricted to patients with congestive heart failure and can happen in its non-existence. The study hypothesised that the mechanism triggering central sleep apnoea in patients with atrial fibrillation involves irritation of pulmonary vagal irritant receptors leading to respiratory system unsteadiness, similar to the underlying link between central sleep apnoea and congestive heart failure. It is also speculated that central sleep apnoea may trigger atrial fibrillation due to chronic hyperventilation, prompting hypocapnia and ultimately impairing cardiac electrical stability. (10)

Due to the closely related confounding variables mentioned, it is difficult to pick apart the exact mechanisms associated between sleep apnoea and atrial fibrillation and whether one encourages the other. One population study aimed to differentiate the connections of obstructive sleep apnoea from central sleep apnoea with atrial fibrillation. (12) After adjusting for confounding variables, individuals with central sleep apnoea showed a 2-3-fold increase in odds of progression to atrial fibrillation. These results were homogenous in minimally adjusted models, as well as models modified for atrial fibrillation risk factors and obstructive apnoea-hypopnoea index. However, it was observed that atrial fibrillation was underrepresented in their evaluation due to its paroxysmal nature and so it may be plausible that some individuals may have been missed in the follow up. It is interesting to note that the study did not find any significant connection between obstructive sleep apnoea and atrial fibrillation based on obstructive apnoea-hypopnoea index, after adjusting the model for covariates. This is in contrast to previous studies which were able to determine a relationship between obstructive sleep apnoea and atrial fibrillation in the absence of other risk factors. (8, 9) It can be concluded that the population study above may be more reliable due to the larger sample size and the meticulously systematised collection of sleep data. (12)

Therapeutic Interventions

Obstructive sleep apnoea, as a modifiable risk factor for atrial fibrillation, can be a suitable target for intervention in conjunction with catheter ablation, a highly effective method of rehabilitating sinus rhythm in patients with atrial fibrillation. Catheter ablation involves the passing of a thin tube via the femoral vein to the heart. The catheter is able to detect unusual electrical activity and destroy the arrhythmogenic cardiac myocytes using radiofrequency ablation. The commonest site of ablation is at the ostia (openings) of the pulmonary vein where radiofrequency lesions leave scar tissue that is unable to conduct electricity, hence eliminating the source of the arrhythmia. (13) In a prospective observational study, 251 patients with a mean age of 57.6 years and continuous atrial fibrillation were assessed to determine the link between obstructive sleep apnoea and sinus rhythm preservation, following pulmonary vein isolation. (14) 114 of these patients had obstructive sleep apnoea. The study found that the presence of obstructive sleep apnoea reduced chances of effective ablation therapy and it was suggested that screening and treatment for obstructive sleep apnoea could ameliorate the success rates of atrial fibrillation ablation. However, obstructive sleep apnoea patients were also older, had greater BMI and larger neck and waist circumferences than patients without obstructive sleep apnoea, all of which are individual risk factors for atrial fibrillation. Therefore it is difficult to establish a direct causal relationship.

The first line of treatment in both central sleep apnoea and obstructive sleep apnoea is continuous positive airway pressure (CPAP) therapy. CPAP is a form of non-invasive ventilation that works by delivering continuous pressure through a face mask to stent and stabilise the upper airway. This helps to maintain functional residual lung capacity and reduce the work of breathing. (15) CPAP therapy is used overnight in patients with sleep apnoea to ensure that the airways remain fully patent and good airflow is achieved. A 2013 study examined the role of CPAP on atrial fibrillation recurrence in obstructive sleep apnoea patients receiving pulmonary vein isolation. (16) Amongst 426 atrial

fibrillation patients sustaining pulmonary vein isolation, 62 had a polysomnography-confirmed diagnosis of obstructive sleep apnoea and 32 of these were using CPAP. The study found that 71.9% of the CPAP users remained in sinus rhythm after the first pulmonary vein isolation as opposed to 36.7% of non-CPAP users. Although there was limited collection of data displaying obstructive sleep apnoea severity, patients with obstructive sleep apnoea undergoing CPAP as well as ablation were shown to have a remarkably improved prognosis and an overall reduced arrhythmia recurrence rate. It was also suggested that patients not using CPAP may be less compliant to treatment and this may have overstated the effects of CPAP. The results of another study of 153 patients demonstrated that patients with obstructive sleep apnoea are less likely to persist in sinus rhythm following radiofrequency catheter ablation. (17) 116 of these patients were confirmed to have obstructive sleep apnoea and 82 were administered CPAP, alongside 34 without CPAP and 37 controls. CPAP treatment of obstructive sleep apnoea was related to lower recurrence rates following radiofrequency catheter ablation. Although this study further reaffirms a conclusive role of CPAP reducing atrial fibrillation recurrence following ablation, it is important to identify the limitations of this study which include the small sample size and lack of randomisation of use of CPAP. Patients with obstructive sleep apnoea were also found to have a higher prevalence of hypertension and a higher BMI.

The effective role of CPAP in patients with both atrial fibrillation and obstructive sleep apnoea was further supported in another prospective observational study which aimed to address the impact of CPAP therapy on reverse atrial remodelling by monitoring total atrial conduction time. (18) This was measured using tissue Doppler imaging intervals (PA-TDI) in patients without atrial fibrillation. Total atrial conduction time indicates atrial substrate by delay in conduction across the atria which is a reliable signal of atrial fibrillation. 55 patients were analysed and, of these, 35 had obstructive sleep apnoea and 20 were controls. Patients with obstructive sleep apnoea were found to have longer total atrial conduction time compared to healthy individuals. After CPAP therapy, the PA-TDI interval in obstructive sleep apnoea patients reduced, indicating reverse atrial remodelling and an improvement in total atrial conduction time. Despite the observed effects not being displayed in the different severities of obstructive sleep apnoea, the investigation still conveyed significant atrial remodelling reversal via CPAP treatment. There is very little research investigating the effects of CPAP in treating central sleep apnoea in atrial fibrillation, however, since the first-line treatment is the same in both obstructive and central sleep apnoea, it can be theorised that the results attained above may be transferrable to central sleep apnoea as well.

CONCLUSION

It is difficult to establish an immediate link between atrial fibrillation and sleep apnoea due to the presence of several other common risk factors which may also contribute to atrial wall stress. The literature that has been reviewed has identified certain mechanisms implicated between sleep apnoea and atrial fibrillation. Simulation of obstructive sleep apnoea in patients without obstructive sleep apnoea has been shown to further deteriorate the arrhythmia in patients with atrial fibrillation. Alongside study models which excluded confounders, a correlation between obstructive sleep apnoea and atrial fibrillation can be inferred. However, it is difficult to reliably confirm this due to the conflicting results proposed by separate studies, which claim there is a greater link between central sleep apnoea and atrial fibrillation when compared to obstructive sleep apnoea and atrial fibrillation. There is scope for ongoing research and conduction of investigations with larger sample sizes in order to validate the current findings. The evidence showing that CPAP therapy in conjunction with catheter ablation significantly reduces risk of atrial fibrillation recurrence, in patients who exhibit both, is particularly noteworthy as it provides a foundation for amplifying the effectiveness of treatment in these patients. Continuing to develop knowledge of the apparent interdependence between these two conditions is of clinical relevance as the fabrication of further therapeutic strategies can improve the prognosis in these patients.

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The British Student Doctor, 2021;5(3):36-47
doi: 10.18573/bsdj.163
Education

The impact of the gut microbiota on human metabolism

EDUCATION

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No conflicts of interest to declare.

Accepted for publication: 25.07.21

ABSTRACT

The increasing prevalence of obesity is a global health problem due to the associations of obesity with co-morbidities such as diabetes, cancer and stroke. Current obesity management strategies and public health measures are doing little to fight the ever-growing burden of obesity in today's obesogenic environment, therefore new approaches are clearly required. The gut microbiota has long been implicated in the pathophysiology of a number of diseases and is emerging as an important player in the pathogenesis of obesity, diabetes and metabolic syndrome, however the exact nature and mechanism behind how gut bacteria can influence host metabolism is an area of intense debate. This article explores how the gut bacteria can influence energy metabolism and whether our knowledge of this can be converted into useful clinical interventions at a time when better care for obese and metabolically unhealthy patients is fast becoming an urgent necessity.

INTRODUCTION

In 2016, there were over 650 million obese adults worldwide, with global obesity burden doubling from 1980. (1) Obesity is a strong risk factor for type 2 diabetes, cardiovascular disease and cancer, with the burden of these diseases following the same trend as obesity. (2) The increasing burden of obesity therefore represents a huge global challenge, so it is of critical importance that the prevention and management of the condition is improved.

The gastrointestinal tract contains a vast number of bacteria, with an estimated 10 trillion to 100 trillion microorganisms populating the adult intestines. (3) The genome of these bacteria (the microbiome) is around 150 times the size of our own with around 500 times the coding potential. (4) Hippocrates, often referred to as the 'father of medicine', stated that 'all disease starts in the gut' following his observations of the influence of the diet and gut health on human pathology. Furthermore, along with the gut influencing our physiology, we in turn influence the composition of our gut, primarily through our diet. Diet-induced changes to gut microbiota were first observed almost 100 years ago, when Herter and Kendall found increases in Bifidobacterium and 'proteolytic bacteria' in response to high-fat and high-protein based diets in dogs. (5) We have only recently begun to understand the powerful impact that the microbiota has on our physiology, with alterations to the microbiota being implicated in a host of conditions from depression, sleep apnoea, abnormal social interactions, cognitive flexibility and schizophrenia, (6–10) to autoimmune diseases, (11) inflammatory disorders, (12) and obesity (13). However, the mechanisms behind these interactions, and whether they can be manipulated with any significant clinical benefit, remains a highly controversial subject.

Recent technological advances such as the advent of bacteria rRNA shotgun sequencing have revolutionised the study of the microbiota, resulting in a surge of interest in the field. With this in mind, this review will address some of the many known changes implicated in host metabolism and the impact these have on obesity, diabetes and metabolic syndrome. It will argue that this is a field not to be overlooked and that it may provide therapeutic benefits in our management of obesity. Throughout, there will be references to bacterial populations at all taxonomic levels. Accordingly, the reader is referred to the taxonomy diagram in Supplementary Figure 1 to aid understanding of the relevant bacterial ecology.

How does the microbiota influence metabolism?

Short chain fatty acids

The gut microbiota ferments dietary fibres into short chain fatty acids (SCFAs) and is therefore responsible for extracting energy from the approximately 30g of complex carbs and 13g of undigested protein the gut receives each day. (14) The importance that colonic fibre fermentation has on energy consumption is shown in gnotobiotic (germ-free) mice. These mice are much leaner than their normal counterparts and are protected from obesity when fed a Western (high fat) diet. (15) This highlights the principle that gut microbiota are involved in energy extraction from food, as these animals are unable to extract energy from these food products, preventing the uptake of around 10% of the energy from a standard diet. (16) As obesity is the long-term consequence of an energy imbalance, changes to this energy extraction process through gut microbiota alterations are an important factor to consider in the management of obesity. (17)

The major products of fibre fermentation are the SCFAs acetate, propionate and butyrate which constitute nearly 95% of the SCFAs in the gut at a ratio of around 60:20:20. (18,19) As well as being absorbed, these bind to free fatty acid receptors (FFARs), modulating L-cell incretin secretion and communicating with the brain via the vagus nerve; this gut-brain axis is essential to how the microbiota impacts our physiology and is excellently reviewed elsewhere. (20) For example, the binding of FFAR1 by dietary-derived fatty acids leads to GLP-1 release from L-cells, which positively modulates insulin secretion. (21) The knock-out of FFAR2 in rats significantly reduced GLP-1 secretion both in vitro and in vivo, further highlighting the key role that SCFAs play in host metabolism. (22) Figure 1 shows a schematic representation of some of the effects of FFAR binding and thus the effects that SCFAs have on our metabolism.

Each of the major three SCFAs have specific metabolic roles, with butyrate and propionate appearing to be mainly anti-obesogenic. Butyrate is the major metabolic substrate for the colonic epithelium and stimulates the growth of this layer, as well as stimulating peripheral tissue mitochondria. (23, 24) Butyrate supplementation in mice improved insulin sensitivity and increased energy expenditure through increasing fatty acid oxidation and stimulating mitochondrial function and biosynthesis. Although butyrate supplementation at 5% of a high fat diet is far from physiological, and thus may not demonstrate the normal function of butyrate, this indicates a beneficial role for butyrate in the diet. (25,26) Butyrate also has known anti-inflammatory effects through downregulation of NF- kB, a key transcription regulator of cellular stress responses. (27) Inflammation leads to the development of insulin resistance, metabolic syndrome and diabetes, so increasing butyrate absorption from the gut may help to prevent the aberrant inflammation that contributes to these diseases. (28,29)

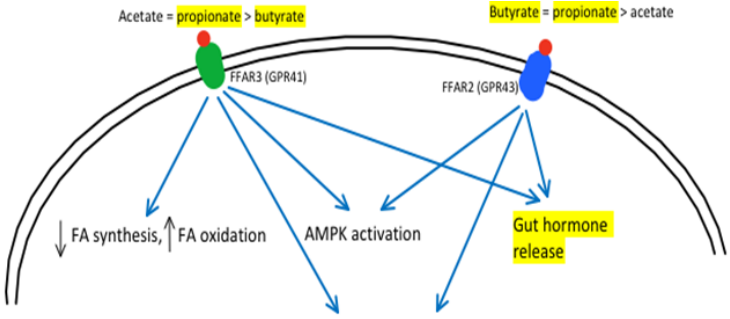

Figure 1: *A diagram representing some of the known responses to FFAR binding, with the binding affinities of FFAR3 and FFAR2 shown (74) and those actions restricted to butyrate and propionate highlighted in yellow (19,75–77)*

Propionate is another SCFA with apparent anti-obesogenic benefits. This was first suggested by Chen et al., who found a reduction in liver and serum cholesterol levels in cholesterol-fed rats supplemented with 0.5% sodium-propionate supplementation, vs control. (14) They suggested that propionate may (in part) be responsible for the hypocholesterolaemic effects of certain soluble plant fibres, which was supported by a study finding the same reduction in liver cholesterol pool, as well as reduced fasting plasma glucose and urinary glucose excretion, in obese hyperinsulinemic (fa/fa) fats on propionate supplementation. (15) Propionate, along with butyrate, is a strong stimulator of FFAR2 (see Figure 1). Binding to this receptor leads to release of gut incretins such as GIP from K cells and GLP-1 from L cells, in addition to release of other satiety signals such as CCK-1 and PYY. (16,17)

Acetate is absorbed into the peripheral circulation where it is the basis for cholesterol synthesis, however whether or not acetate is beneficial or detrimental to host metabolic health is still unclear. Many labs have reported positive health outcomes associated with acetate; dietary acetic acid reduces serum cholesterol and triglycerides in rats on a high cholesterol diet, and the acetic acid in vinegar reduces body weight, body fat mass and serum triglyceride levels in obese Japanese men. (18,19) Recently, Prof Frost's lab followed the uptake of dietary 11C-acetate into hypothalamus with PET-CT, and found that it stimulated parasympathetic nerve fibres and decreased appetite. (20) However, some labs have suggested that acetate may negatively affect host metabolism. In 1993, it was shown that plasma acetate levels are higher in diabetic subjects than obese normoglycaemic and healthy controls, with significant correlations seen between glycosylated haemoglobin (HbA1C), plasma glucose and acetate levels. It was not reported whether or not these changes in acetate matched changes in the other SCFA levels (i.e. whether total SCFA level was increased or just acetate level), which somewhat limits the strength of conculsions drawn from the study. (21) However, subsequent work has shown that acetate supplementation via addition of an acetate-producing prebiotic leads to an increase in plasma LDL and cholesterol vs control. (22) Finally, Perry et al. have shown that acetate stimulates ghrelin secretion, leading to hyperphagia and thus predisposing to obesity, further suggesting that acetate has detrimental effects on host metabolism. (23)

Bacterial metabolites

As well as fermenting fibres, the gut microbiota produces metabolites that can influence host metabolism. Trimethylamine (TMA) is metabolised from cheese, seafood and red meat by gut bacteria and is enzymatically oxidised by flavin-containing monooxygenase-3 in the liver to TMA N-oxide, or TMAO. (24) Serum levels of TMAO correlate with obesity, atherosclerosis and poor cardiovascular health, suggesting that these TMA-producing bacteria have a negative impact on host metabolic health. (25) TMA-producing bacteria are distributed over Firmicutes, Actinobacteria, Proteobacteria and Gammobacteria, and are particularly highly expressed in Escherichia and Shigella, as found by detection of TMA-synthesis gene expression. (26) Whilst it may be early to draw conclusions, the pathogenicity of the changes in microbiota with obesity described in the next section may in part be played by the increase in production of TMA by these bacteria. Drugs such as 3,3-dimethyl-1-butanol that reduce TMAO levels by inhibition of TMA production or conversion to TMAO are under development, and can reduce cardiac dysfunction in Western diet-fed mice. (27) It is hoped that as our understanding of TMA and other microbiota metabolites increases, we can use this knowledge to improve obesity care.

Changes to gut microbiota seen in obesity and diabetes

Changes at the phylum level

The major change seen in the obese patient's microbiota is a relative increase in the *Firmicutes* phyla relative to the Bacteriodes (see Supplementary Figure 1), along with an increase in abundance of Proteobacteria. (3,28–32) For example, ob/ob mice - which develop obesity through hyperphagia - have almost 50% lower Bacteriodetes compared to *Firmicutes*. (33) Whilst it is unclear whether obesity causes the change in bacteria or the bacteria change results in obesity, it is thought that the diet can alter the bacteria which then predisposes people to obesity due to a higher efficiency of energy extraction by the unhealthy microbiota. This is supported by Hildebrandt and colleagues, who studied the effects of high fat diets (HFD) on wildtype and the obesity-resistant RELM-b mouse strain. Switching from standard chow to HFD caused obesity in wildtype mice but not in the RELM-b mice, however the *Firmicutes*: *Bacteriodes* ratio was altered in both independently of any gain in weight. (4,28)

The relative composition of these phyla appears to impact on the ability of the gut to harvest energy from food. Jeffrey Gordon's lab found that colonising genetically identical gnotobiotic mice with the microbiota of a diet-induced obese mouse results in more total body fat gain than colonising the mouse with lean mice microbiota. This 'obese microbiota' appears to be adapted to ferment fibres more efficiently, as seen by higher expression of fermentation enzymes in the obese microbiome. The faeces of the obese microbiota mice had less energy remaining when measured with bomb calorimetry vs control, further supporting this theory. (31) The gut concentration of butyrate and acetate is higher in patients with this altered microbiota, (34) so it is unclear how these 'obese microbiota' appear to be detrimental to host health despite increasing the production of butyrate which is known to be beneficial to host health. It is possible that the increase in butyrate is simply a change that was measured in these experiments which indicates an increase in whole energy harvesting, or that in these patients and animals, there is a different source of butyrate (such as undigested protein vs carbohydrates) which somehow confers the obesity phenotype. Or perhaps the satiety signals and other SCFA responses are aberrant in these patients, thus predisposing to obesity? This apparent contradiction is a source of debate and needs to be understood to elucidate the interactions between diet, health and gut bacteria.

Changes to specific bacteria

Certain bacteria have specific effects on host metabolism. *Akkermansia muciniphila* appears to have a protective effect on metabolic profiles, with orally-administered muciniphila protecting against obesity and enhancing glucose tolerance in mice. (50) This protective effect is also seen in humans, with the abundance of the bacteria inversely correlated to fasting plasma glucose level, waist:hip ratio and subcutaneous fat diameter. Furthermore, amongst obese patients, those with a higher *A. muciniphila* abundance had the best metabolic profiles (as determined by parameters such as plasma triglycerides and fasting glucose) and displayed the greatest improvement in insulin sensitivity in response to a 6-week calorie restriction. (51) Interestingly, diabetic patients treated with metformin have changes in the gut microbiota which include an increase in *A. muciniphila* compared to untreated diabetics, potentially suggesting that some of the benefits of metformin may be mediated through the drug's impact on gut bacterial populations. (52) A number of other changes to bacterial populations are shown in Supplementary Table 1, which describes a number of different bacteria of nearly all major phyla and their apparent roles in altering host metabolism.

Therapeutic modulation of the gut microbiota

Prebiotics

The dietary supplementation of propionate as a weight control therapy is currently being investigated by the Frost lab, who have developed an inulin-propionate ester that can be added to food. The conjugation to inulin (a fibre) ensures targeted delivery of propionate to the colon, as the propionate is only released upon fermentation of inulin resulting in a gram-level delivery of the SCFA to the colon that wouldn't be feasible through diet alone. As discussed above, propionate stimulates GLP-1 and PYY secretion and seems to prevent hepatic lipidosis. In a 24-week study, overweight adults were given the inulin-propionate ester, which significantly reduced weight gain and reduced gain of intra-abdominal adipose tissue vs an inulin control. Interestingly, whilst acutely the propionate-inulin ester stimulated an increase in GLP-1 and PYY secretion, by the end of the 24-week study, no significant difference in the release of these gut hormones was found, even though subjective rankings of postprandial appetite were lower in the propionate group. Clearly, the gut microbiota's influence of satiety and therefore obesity is complex, however this study indicates that dietary interventions targeting the microbiota could emerge as a novel management of obesity. (53)

Although the exact benefits or problems associated with acetate aren't clear, the role of fibre in improving metabolic health is vastly understated. The average Western diet is deficient in fibre, with the UK guidance on consumption of fibre being (inadequately so) to 'eat lots', which fails to stress how beneficial dietary fibre is. (54) Howarth et al demonstrated that when subjects were left to eat as they pleased, the addition of fibre to this diet resulted in a 10% average decrease in energy intake, resulting in nearly 2kg weight loss over 4 months vs control. (55) Clearly, fibre has overall benefits to host health, so improving public education of benefits of dietary fibre could help reduce the burden of obesity.

Faecal microbial transplantation

Faecal transplant is an established treatment in recurrent C. difficile and has an excellent safety profile. Numerous animal studies have shown that a metabolic profile can be transferred through faecal microbiota transplant (FMT) as discussed above, (56) with a limited number of studies now beginning to show some efficacy in humans. Max Nieuwdorp's group have shown that FMT from lean donors resulted in a significant improvement in insulin sensitivity at 6 weeks in insulin-resistant obese males with metabolic syndrome. In this 2012 study, they found that the improvement in insulin sensitivity correlated with an increase in butyrate-producing bacteria. (57) This is thought to improve host health through the mechanisms described above, although the contradiction between the benefits of butyrate production and the increase in energy extraction through this SCFA need to be examined. However, the group's most recent trial showed that whilst they could replicate this positive change in phenotype at week 6, by week 18 after FMT the effects on insulin sensitivity had worn off, which was associated with a return to baseline faecal microbiota composition. (58) This raises the idea of a 'personal core faecal microbiome', suggesting perhaps that host immune system interactions resulted in this return to baseline microbiome from the foreign gut flora. If FMT is to become a successful future intervention for metabolic syndrome and/or obese patients, this issue needs to be further understood to allow us to cause lasting change in the patient flora. On top of this, we need to better understand what makes a good faecal donor and what predicts the level of patient response, with lower initial bacterial diversity in the patient and higher levels of butyrate-producing bacteria in the donor appearing to be good markers of success. (56,57) Other bacteria implicated in degrees of FMT success can be found in Supplementary Table 1, and as such development of more sophisticated algorithms to better select patients and donors to maximise responses is required if this treatment is to become mainstream.

Clinical outlook/concluding remarks

The role that the gut microbiota plays in a number of different disease states is an area of extensive research and intense debate. It is clear that there is a significant relationship between changes in the gut microbiota and obesity, diabetes and metabolic syndrome, and that this is often overlooked in weight and diabetes management strategies. The extent to which potential microbiota-focused interventions such as FMT and pro- and prebiotics may play in our management of obesity and diabetes remains to be seen. In an age where fad diets commonly direct patients' weight loss strategies in an unscientific manner, greater appreciation and understanding of the importance of gut bacteria and how our diet can influence these will assist patients in making more informed lifestyle choices. Overall, obesity along with its associated co-morbidities is a complex disease and there is not a single approach which will offset the rise in obesity. This paper does not aim to present the gut microbiota as the answer to obesity care, however it is an important factor to consider when addressing the global problem of obesity.

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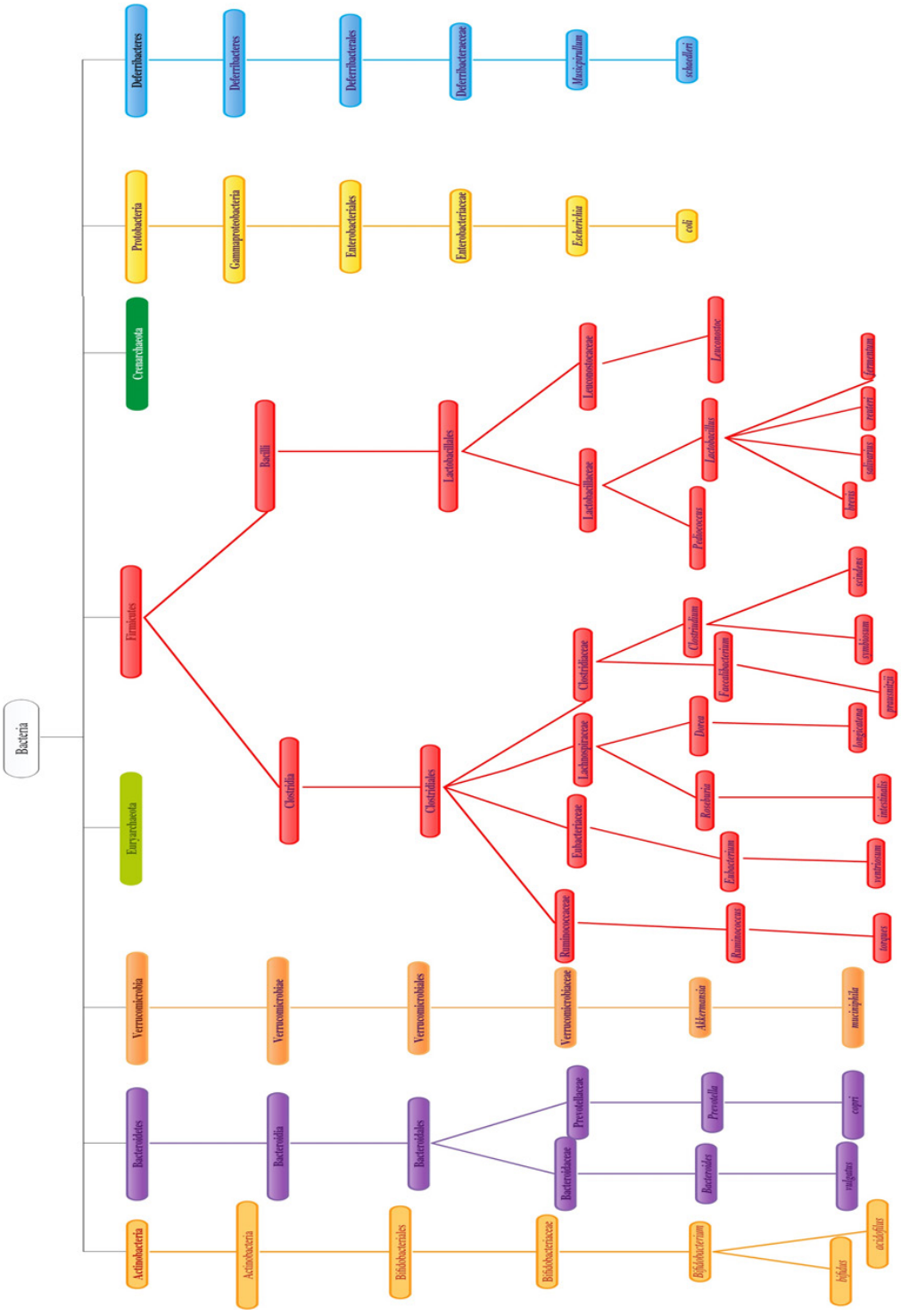
APPENDIX



Supplementary Figure 1: *A diagram showing the taxonomic relationships of the bacteria referred to throughout this paper*

APPENDIX

Bacteria/bacterial metabolite	Metabolic indication
Akkermansia (Cerrucomicrobia)	Increased after Roux-en-Y gastric bypass surgery. [35]
Akkermansia muciniphila	Appears to have beneficial metabolic effects. Found to increase in FMT responders [36] and inversely correlated fasting glucose and body fat mass in mice and fasting glucose, waist:hip ratio, plasma triglycerides subcutaneous adipocyte diameter in humans. [37] Increased by metformin treatment. [38]
Bacteriodes vulgatus	BCAA producing species found in higher abundance in insulin-resistant patients vs control. [39]
Clostridium scindens	Found to be strongly negatively correlated with body weight in mice. [40]
Dorea longicatena	Correlated with better FMT response. [36]
Enterobacteriales	Increased after Roux-en-Y gastric bypass surgery. [35]
Escherichia coli	A G- bacterium that produces LPS. E. coli and LPS are both elevated in diabetes patients and LPS is able to induce inflammation of fat tissue and reduce insulin sensitivity in mice. [41–43]
Eubacterium sp.	Produce butyrate. Administration of live E. halii to obese and diabetic mice improved insulin sensitivity and increased energy expenditure. [44]
Eubacterium ventriosum	Inversely correlated with better FMT response. [36]
Euryachaeota and Crenarchaota	Increase the efficiency of bacterial fermentation by removing H_2, found in higher abundance in ob/ob mice vs normal. [33]
F. prausnitzii	Suggested to be involved in strengthening the gut barrier whereby reducing inflammation and diabetes progress.[38] Found in lower abundance in patients with type 2 diabetes.[45]
Lactobacillus fermentum	Found to lower cholesterol and triglycerides when given as a microencapsulated probiotic to hypercholesteraemic hamsters. [46]
Lactobacillus reuteri	Found to be strongly positively correlated with body weight and obesity in mice; elevated in obese humans. [40,47–49]
Lactobacilus brevis	Produces GABA. L. brevis supplementation improves glucose homeostasis in insulin-resistant rats, [50] correlating with direct GABA supplementation improving insulin resistance through reducing inflammation. [51]
Leuconostoc	Found in a higher abundance in patients who regained more weight in a 6-week diet followed by 6-week restabilisation study. [33]
Mucispirillum schaedleri	Found to be strongly positively correlated with body weight in mice. [40]
Pediococcus	Found in a higher abundance in patients who regained more weight in a 6-week diet followed by 6-week restabalisation study. [33]
Prevotella	Enrichment of Pr. linked to improved tolerance to glucose on whole-grain diets. [52]
Prevotella copri	BCAA producing species, found in higher abundance in insulin-resistance patients vs control. Administration of P. copri induced insulin resistance in mice. [39]
Roseburia intestinalis	Produces butyrate. Negatively correlated with subcutaneous adiposity, body weight, liver weight and serum insulin in mice, [40] negatively correlated with human plasma glucose [47] and less abundant in T2DM patients. [41]
Ruminococcus torques	Inversely correlated with better FMT response. [36]
Subdoligranulum variabile	Correlated with better FMT response. [36]
Verrucomicrobiales	Significantly increased after Roux-en-Y gastric bypass surgery. [35]

Supplementary Table 1: *Bacteria implicated in host metabolism*

The British Student Doctor, 2021;5(3):48-53
doi: 10.18573/bsdj.179
Education

Practical advice for newly qualified doctors in the UK

EDUCATION

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No conflicts of interest to declare

Accepted for publication: 19.08.20

ABSTRACT

Summary: Foundation year 1 doctors beginning their medical career may experience apprehension and uncertainty prior to undertaking their new role. The transition between being a medical student and becoming a doctor can be daunting. It is a pivotal and natural progression in the medical graduate's career.

Relevance: The tips in this article provide a practical guide to starting life as a doctor, based on experience from current foundation doctors in the UK.

Take-home messages: Starting foundation year 1 can be a challenging experience, however this article aims to ease the transition by offering the following tips:

1. Understanding the contract
2. Being familiar with the new surrounding
3. Staying organised
4. Know your limits
5. Take regular breaks
6. Be proactive
7. Teamwork
8. Continuous learning
9. Learning from mistakes
10. Maintain confidentiality
11. Preparing for night shifts or long on-calls
12. Career planning

INTRODUCTION

Although medical school equips new doctors with the appropriate clinical knowledge required to begin working in the hospital setting, many new doctors still enter with a feeling of anxiety and unpreparedness. (1) This has often been deemed as a major cause of psychosocial distress amongst medical school graduates. (2) Based on personal experience and discussions amongst clinical colleagues, we have highlighted tips specifically aimed to enlighten UK medical graduates transitioning to foundation year one and provide them with essential information which may not have been a core focus within the medical school curriculum. By understanding this information, medical graduates will feel less apprehensive about the prospect of beginning life as a fully-fledged doctor and therefore improve patient safety.

Understanding the contract

It is essential to be familiar with the contract, especially in the context of maximum or minimum working hours, eligible sick leave, less than full-time training options and trainee support and supervision at work. This is particularly relevant as the recruitment process has been constantly changing due to the impact of COVID-19. It is particularly important to verify that trainees are well-supported and working within the stated number of hours according to the guideline to ensure fairness at work and patient safety.

Being familiar with the new surrounding

Entering an entirely new system can dampen productivity and hinder confidence, especially as a junior in the profession. Being familiar involves two aspects: physical familiarity with the work environment, and familiarity with work colleagues and styles of consultation which may vary between the consultants. Firstly, physical familiarity can be achieved by orientating yourself amongst bay and bed layouts, doctor and nursing stations, treatment rooms and document shelves. This could be particularly vital during an emergency on the ward. Additionally, building a good and professional rapport with colleagues in all levels of seniority is especially important in promoting both teamwork and support at work.

Staying organised

The list of tasks throughout the day will be in a variety of forms, including documentation, referrals, as well as clinical skills - many of which can be time pressing. Having a system of prioritisation will ensure that the most important tasks are completed thoroughly and safely. The time management matrix formulated by Stephen Covey suggests dividing tasks into both levels of urgency and importance. (3) The most urgent and important task should be dealt with first while the non-urgent and non-important task can either be delegated to another colleague or completed last on the list. For example, one should prioritise reviewing an acutely deteriorating patient before attempting to complete a discharge summary. Similarly, when pressed with two equally important and time-consuming tasks, a decision to delegate one of the tasks to a colleague might be necessary, or can be planned to be undertaken simultaneously, if deemed appropriate. For example, two urgent referrals or advice to the same speciality can be done at the same time.

Know your limits

Arguably, one of the most important skills you may possess as a doctor is the ability to work only within your capability and ask for help when needed. Patient safety remains of utmost importance. It is far better to seek help when unsure rather than take chances and possibly risk causing harm. This becomes particularly apparent during on-calls and out of hours as there is often a smaller group of seniors to assist. Therefore, it would be useful to familiarise yourself with your direct seniors and anyone else who may be available for you to escalate to. Your colleagues will appreciate you calling them for advice on a matter you are unsure of, or even just to update them on important changes with regards to your patients. This is a good way to ensure that a strong flow of communication is maintained throughout the multidisciplinary team and ultimately enhances patient care.

Take regular breaks

As a doctor, you will inevitably be exposed to high levels of stress. It is important to learn how to manage this to avoid burnout. Although moderate amounts of stress may be harmless to some, and sometimes beneficial, increasing prolonged stress levels can lead to a decrease in morale and job satisfaction. (4) Doctors who experience burnout are more likely to make poor decisions, display hostile attitudes towards patients and colleagues and make more medical errors. (5) Thus, it is important to work within your scheduled hours and if you find yourself working beyond these limits repeatedly, it is important to identify the reasons for this and escalate to your seniors. Make efforts to take regular breaks during the working day to rehydrate. Facilities such as the doctors' mess are often available and beneficial for providing snacks and a safe space to socialise at work. Maintain a healthy work/life balance by continuing or starting hobbies outside of the workplace. Some ways to implement this include joining or organising group activities, unrelated to work, with fellow colleagues. Often, particularly during the first few weeks or months, foundation doctors partake in social activities together (e.g. climbing, running clubs). Creating a weekly schedule which is flexible for all to join ensures that activities can continue on a consistent basis throughout the year.

Be proactive

As a junior doctor, it is important to be proactive as there will be various practical procedures and administrative skills to become familiar with daily. Furthermore, there will be a constant list of tasks to act upon proficiently and with an increase in pressure to finish jobs within a limited amount of time. One method of being

proactive is listing out practical procedures that might need further practice. It is also useful to ask colleagues about tips and tricks of how to get certain jobs done. An example could be advice on getting efficient referrals done, such as what certain information specialists might require, or what kind of investigations need to be performed before a referral is sent to aid in management. Another way to remain proactive is being aware of learning opportunities, which can constitute both internal departmental teaching and those in other specialities. Additionally, being familiar with the updated trust guidelines can aid in management and efficiency of working.

Teamwork

As a doctor, it is important to build a good rapport with both the immediate and multi-disciplinary team as no single task is usually completed alone and the need to engage with others is increasing due to increasing co-morbidities and complexity of care. An effective teamwork can positively affect patient safety and outcome while promoting well-being at work (6). The incorporation of shared responsibilities will increase the accountability between team members and prevent 'near misses' as members of the team can communicate and formulate management plans before actioning. In order to be a good team member, it is important to introduce yourself to the team, clarifying your roles and level of expertise. It is also helpful to be assertive when required, but also be helpful when needed especially during a busy day or when dealing with an acutely ill patient. Further, when in conflict, it is important to concentrate on what is right for the patient, rather than who to blame or who is right. During a particularly difficult day, it can also be useful to perform a team briefing before the tasks are delegated and a debrief afterwards as a reflection on what is performed well and what could be further improved.

Continuous learning

The importance of lifelong learning and maintaining clinical skills throughout one's medical career is widely recognised. (7) The completion of a medical degree only opens the door to life as a doctor; active learning, practice and experience is what truly prepares doctors for the challenges that the job can bring. Medical science is rapidly evolving and as a doctor, you will be expected to keep up to date with current affairs. (8) Making efforts to read about pathology you come across in hospital will accumulate episodic memory to better retain semantic information. (9) Furthermore, it is worthwhile learning from senior colleagues; making the effort to be proactive about attending teaching sessions not only further clinical knowledge but is paramount as portfolio evidence of professional development. Lastly, take every opportunity to teach colleagues and medical students; this will help to enhance your own understanding and development as a clinical teacher.

Learning from mistakes

Oftentimes, medical errors are attributed to laziness, inattention or incompetence of an individual. One of the first principles you are taught in medical school is to "do no harm". This stigma creates an environment focused on blame and guilt. (10) Although few errors are caused by physician negligence, the majority are the result of poorly designed processes and systems of care. (11) As a foundation doctor at the beginning of your career, the lack of knowledge and experience can potentially lead to errors in the workplace. It is also important to note that not all errors lead to patient harm. Learning from your mistakes enables you to build confidence, strengthen your knowledge and ultimately provide better patient care. Support systems in the form of senior colleagues, nursing staff and the wider multidisciplinary team are in place to assist you during this transitional period.

Maintain confidentiality

Maintaining patient confidentiality is a widely recognised topic of importance in the medical profession. (12) The GMC states that "doctors are under both ethical and legal duties to protect patients' personal information from improper disclosure." (13) Therefore, respecting confidentiality is legal and ethical duty of healthcare professionals which is essential to safeguard the wellbeing of patients and maintain the doctor-patient relationship. Although the fact may seem obvious, most occasions where patient confidentiality is breached are unintentional. (14) For example, discussing cases in hospital corridors, canteen, or other public areas. Additionally, breaches may occur when using technology which is not adequately encrypted to communicate with colleagues. Uphold good practice from the beginning of your career by anonymising patient information wherever possible, not allowing others to use your hospital login information and not viewing the information of any patient to whom you are not involved with.

Preparing for night shifts or long on-calls

The demand to work long hours while aiming to maintain patient safety and high-quality care can be physically and mentally straining. Thus, it is important to be prepared for a long day of on-call or a night shift, especially when working during unfamiliar hours. Before the start of the shift it is wise to get adequate rest, stay hydrated and have a nourishing meal. It is also vital to attend handovers as this will keep you updated on the patients to be aware of, and how busy the shift can potentially be. Handovers are also a good opportunity to fully meet the team and delegate tasks if needed. During the shift, it is important to take timely breaks as this will maintain alertness and stamina. Preparing for a nightshift can involve building a sleep routine such as getting extra sleep before working the first night shift, and a pre-shift two-hour sleep can reduce the build-up of fatigue. After a nightshift, it is important to gauge the level of fatigue as driving while tired is effectively no different to driving while over the legal limit for blood alcohol content. (15) An alternative could be taking public transport or using sleeping accommodation to recover.

Career planning

In the beginning, you may or may not have an idea of which specialty you would like to pursue after foundation training. As many

specialty applications open during the beginning of foundation year 2, it is worthwhile taking time to evaluate your interests and beginning planning for your future. Completing online medical specialty aptitude tests, such as the 'specialty explorer' available from the BMA, (16) may help you to identify specialties most compatible with your interests and priorities. Maximise your chances to obtain specialty posts by undertaking audits, attending conferences and publishing research. Some specialities are more competitive than others and therefore early preparation will greatly increase your chances of securing a place in your chosen job. Reach out to registrars and consultants within your specialty of interest and enquire about the pros and cons that they have experienced throughout their career. Furthermore, researching into the specific requirements for your chosen specialty will enable you to actively work towards strengthening your application. Points are often awarded per portfolio requirement; research relevant courses to attend as well as specialty exams which can often be undertaken during foundation years e.g. MRCP/MRCS/FRCOphth. It is also worth reflecting on projects, presentations and awards you may have completed during medical school, as such achievements may contribute to your application. Focus on 'low hanging fruit' i.e. be strategic; 'easy' points can be gained by organising taster weeks or teaching sessions in comparison to points gained by completing a master's degree or publications.

CONCLUSION

The tips outlined in this article can help shed insights for new foundation doctors in the UK on how to effectively start their career - ensuring patient safety while fostering an interest in lifelong learning and training progression.

Note on contributors

Ehinomen Inegbedion and Pakinee Pooprasert are currently foundation doctors working in ophthalmology and acute medicine. They have a special interest in medical education and ophthalmology.

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The British Student Doctor, 2021;5(3):54-62
doi: 10.18573/bsdj.224
Education

Neuronavigation: How it continues to revolutionise neurosurgical practice

EDUCATION

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No conflicts of interest to declare.

Accepted for publication: 14.06.21

ABSTRACT

Summary
Neuronavigation is a surgical technology that gives real time image-guidance to neurosurgeons as they operate within the boundaries of the skull and spinal column. Prior to its development, the success of neurosurgery was highly variable as it was determined by the anatomical knowledge, experience and surgical aptitude of each neurosurgeon. However, operations were notoriously difficult, given lesions can be found deep within the brain or spinal cord. To accommodate for this, a large area of exposure was made, which increased the risk of damaging surrounding functional brain tissue. Neuronavigation revolutionised the neurosurgical practice of multiple subspecialites by providing intraoperative image guidance enabling neurosurgeons to precisely locate surgical targets and resect lesions with a minimally invasive technique.

Relevance
In neuro-oncology, neuronavigation has increased the proportion of a brain lesion that can resected safely, which has lengthened the duration of survival and reduced post-operative complication rates. In neurovascular surgery, neuronavigation has optimised surgical approaches to difficult to reach cerebral aneurysms and reduced the risk of losing surgical orientation intraoperatively if a haemorrhage is present. In epilepsy surgery, neuronavigation has increased the accurate localisation of epileptogenic zones, which once resected can dramatically reduce the frequency of seizures for epilepsy resistant to medical management. Ultimately, such improvements have transformed patient outcomes worldwide.

Take home messages
Neuronavigation has revolutionised the practice of neurosurgery by facilitating minimally invasive surgical technique in a range of neurosurgical subspecialties. It is not a static technology but continues to develop as new technologies continue to be integrated into it, and it presents further exciting prospects for the future of neurosurgery.

Keywords: Neuroimaging; brain shift; iMRI.

INTRODUCTION

The human brain has a complex structure, consisting of 86 billion neurons intricately connected together. (1) Injured neurons demonstrate limited capacity for regeneration and therefore neurosurgical procedures must be minimally invasive. This prevents surgical margins extending into surrounding brain tissue and causing neurological deficits. The ability for neurosurgery to innovate and overcome these inherent challenges has been inextricably linked to the creation and development of neuronavigation. This article discusses how neuronavigation has revolutionised neurosurgery and how it continues to pave the way for future neurosurgical innovations.

THE DEVELOPMENT OF NEURONAVIGATION

Neuronavigation or image-guided neurosurgery are computer-assisted technologies that allow neurosurgeons to navigate the confines of the skull and spinal column during an operation. (2) Prior to the development of neuronavigation, the success of neurosurgery relied heavily on neurosurgeons' visuospatial knowledge of neuroanatomy and manual dexterity. A neurosurgeon would have to orientate and identify surgical targets purely by utilising anatomical landmarks and clinical experience. This was notoriously difficult, given lesions can be found deep within the brain or spinal cord. To accommodate for these limitations, a large area of exposure was made, which increased the risk of damaging surrounding functional brain tissue. An early attempt to reduce surgical exposure was the introduction of a framed stereotactic tool by E. Spiegel et al. (1947), an Austrian-born neurologist and Professor at Temple School of Medicine, USA. (3) The frame attached to the patient's head and in conjunction with an anatomy atlas was used to identify internal brain anatomy. (4) Despite these measures, neurosurgery still lacked the precision that it required. Anatomical variation and space-occupying lesions would distort the anatomy leading to wildly inaccurate measurements on the location of deep brain structures. It was not until technological advances of medical imaging that neurosurgery was revolutionised with the subsequent development of neuronavigation.

HOW NEURONAVIGATION WORKS

Neuronavigation provides image guidance by rendering preoperative images into a three-dimensional computer model and calibrating them with the three-dimensional space of an operation. It can be split into four separate steps:

1. **Preoperative Imaging**: the patient is scanned as close to the time of surgery as possible. Scanning modalities include Computerised Tomography (CT), Magnetic Resonance Imaging (MRI), functional MRI (fMRI) and diffusion tensor imaging (DTI). (5)

2. **Surgical Planning:** the images are uploaded to a neuronavigation system and converted to a three-dimensional model where the neurosurgeon can identify the optimal approach to a lesion. If fMRI imaging was used in the previous step, 'surgical corridors' comprised of non-critical brain tissue can be dissected to reach a surgical target. (6) This reduces disruption of surrounding white matter tracts.

3. **Registration**: this is the accurate calibration of preoperative imaging with the intraoperative patient. To achieve this, anatomical landmarks such as the sagittal suture and/or fiducial markers are used. Fiducial markers are objects affixed to the head immediately prior to preoperative imaging that are visible on scans and provide a point of reference. (6) At the start of surgery, the surgeon individually touches these anatomical landmarks and/or fiducial markers with a tracked probe to pair the preoperative imaging with the points. (7)

4. **Intraoperative Navigation:** the navigation system allows the accurate visualisation of surgical targets during the operation. (5)

CLINICAL IMPORTANCE – NEURO-ONCOLOGY

In neuro-oncology, neuronavigation guidance has increased the percentage of tumour resected during surgery. (8) In a retrospective cohort study, 52 patients with primary glioblastomas who were operated on using neuronavigation were matched to patients who had resection of primary glioblastomas without use of neuronavigation. Gross Total Resection (GTR) defined as no visible tumour on post-operation MRI scans (9) was achieved in 31% using neuronavigation vs 18% without. (10) Due to low patient numbers in the study this result failed to reach statistical significance ($p = 0.167$). However, the rate of GTR had a downstream effect on patient survival – with a median survival of 18 months compared to 10 months without neuronavigation ($p < 0.0001$). (10) In another retrospective cohort study, 100 patients who received meningioma resections using neuronavigation were compared to 170 patients who received meningioma resections using without neuronavigation. The complication rate after meningioma surgery sharply decreased from 14% to 6% ($p = 0.019$) and hospital stay from 13.5 days to 8.5 days ($p = 0.017$). This resulted in a reduction of the overall cost of surgery, admission and follow-up by 20%. (11) Neuro-oncology has further benefitted from the integration of modern imaging modalities for functional mapping of eloquent brain tissue such as the cortical language area and corticospinal tract. (12,13) Among these imaging modalities include fMRI, repetitive Transcranial Magnetic Stimulation (rTMS) and DTI. rTMS is a non-invasive neurophysiologic technique that works by directing a strong magnetic field which causes neuronal activation in the brain. (14) This cortical reactivity can be assessed and used to map out functional brain tissue prior to an operation to plan the optimal surgical approach. (14,15) A meta-analysis comprising 1009 patients in 7 studies investigated the role of rTMS integrated into neuronavigation. It found that the integration rTMS into neuronavigation systems further reduced the risk of postoperative motor deficits (odds ratio = 0.54, $p = 0.001$) and increased the rate of Gross Total Resection (GTR) (odds ratio = 2.32, $p < 0.001$), when compared patients operated using neuronavigation without rTMS. (16)

CLINICAL IMPORTANCE – NEUROVASCULAR SURGERY

In neurovascular surgery, neuronavigation has optimised the surgical approach and intraoperative localisation of neurovascular pathologies. Dorsal anterior cerebral artery (DACA) aneurysms are particularly difficult to identify because, unlike other aneurysms, they lack an anatomical landmark. (17) Also, the surgical approach to clip a DACA aneurysm is via the interhemispheric fissure, which is difficult to dissect and has close relation to important arteries and brain structures. (17) Following subarachnoid haemorrhage even experienced surgeons could lose orientation within the surgical field. This resulted in increased length of procedure and even unexpected premature rupture of aneurysms intraoperatively. (17) Using neuronavigation, surgeons are able to precisely locate DACA aneurysms and increase operator confidence in clipping. This has resulted in a dramatic improvement in surgical success. A case series presented a single centre experience of consecutively clipping 12 DACA aneurysms under the direct guidance of neuronavigation. Patients had a mean age of 55 years and had CT proven DACA aneurysms ranging from 3-10mm. The clipping of DACA aneurysms with neuronavigation guidance had no technical or surgical complications, and all patients made a good recovery. (17) Arteriovenous malformations (AVMs) are abnormal connections between the venous and arterial system in the brain leading to large venous dilatations, which are prone to bleeding. Previously, the resection of small AVMs posed was problematic – they are difficult to locate intraoperatively by direct visualisation and can be located adjacent to eloquent brain tissue. However, with the assistance of neuronavigation, AVMs can be localised and resected with high precision. A cohort study of 25 patients with small AVMs found the accuracy of neuronavigation was 1.1mm and resulted in the complete removal of the AVM in 96% of cases. (18)

CLINICAL IMPORTANCE – EPILEPSY SURGERY

In epilepsy surgery, neuronavigation has a particularly important application because accurate localisation of epileptogenic zone, which once resected can dramatically reduce the frequency of seizures. (19) As previously mentioned, in cases where there is an obvious structure lesion such as a brain tumour, neuronavigation significantly increases GTR. (10) However, lesions may not be visible macroscopically as they may have only subtle subcortical dysplasia or may not be associated with an anatomical lesion at all. In these cases, neuronavigation can be invaluable because the epileptogenic zone may only be visible to specialised imaging modalities such as magnetoencephalography, single photon emission computed tomography and positron emission tomography. (20–22) These imaging modalities can then be fused with MRI images used for neuronavigation. This enables the accurate placement of subdural electrodes to diagnose epileptogenic brain tissue, and the resection of these areas to treat epilepsy resistant to medical management. (23) In a large, single-centre cohort study 415 patients underwent resection of epileptogenic zones using neuronavigation with integration of specialised imaging modalities. Despite the seizures being previously refractory to medical treatment, 72.7% of patients were completely seizure free at a mean follow-up of 36 months. (24) However, there have been no high-quality studies comparing neuronavigation with standard surgical resection. (25) This does not rule-out neuronavigation showing benefit in epilepsy surgery, but instead indicates an urgent need for well-designed studies.

CLINICAL IMPORTANCE – SPINAL SURGERY

In spine surgery, the precise placement of pedicle screws is paramount in the treatment of thoracic and lumbar degenerative disease. (26) Insertion of a pedicle screws poses a unique challenge to surgeons as imprecise screw placement not only increase the risk of neurological and neurovascular injury but also reduces the biomechanical strength of the screw. (26) Introduction of neuronavigation increased the accuracy of screw placement and reduced cases of misplacement. In a meta-analysis comparing pedicle screws inserted using a freehand technique compared to a technique utilising neuronavigation, insertion using neuronavigation was more accurate (odds ratio 2.46, 95% confidence interval, 1.92-3.16) $p = 0.021$ and operations had significantly less blood loss $p < 0.001$. (27) Inaccurate pedicle screw placement not only reduces the biomechanical strength of the screw, but also increases the risk of iatrogenic injury to the nearby spinal cord and spinal vasculature. (28)

CLINICAL IMPORTANCE – FUNCTIONAL NEUROSURGERY

Finally, in functional neurosurgery, neuronavigation has been used to improve the optimise the efficacy of deep brain stimulation in treatment of advanced Parkinson's disease. In this treatment, electrodes are inserted into the subthalamic nucleus, a deep brain structure. The electrodes act by applying high-frequency electrical stimulation to surrounding structures, causing a dissociation of input and output signals. (29) Cerebral vasculature is at risk of intersection during this procedure causing haemorrhagic complications. Using neuronavigation, a study made planned trajectories for the electrodes which intersected significantly finer vasculature than before, thus reducing post-operative bleeding. (30)

LIMITATIONS OF NEURONAVIGATION

Brain shift is a complex spatio-temporal phenomenon with a wide range of causes that neuronavigation systems using preoperative imaging do not account for. The removal of pathological brain tissue in tumour resection causes adjacent remaining brain tissue to sag into the space under gravity. Simultaneously, neurosurgery produces swelling of surrounding brain tissue and loss of cerebrospinal fluid. Over the course of an operation this can distort the position of the brain by up to 50mm relative to preoperative images. (31) Consequently, neurosurgeons depended on the neuronavigation guidance to identify a surgical target, but once it is reached rely on their own judgement. However, this has led to inaccurate assumptions over the extent of tumour resection resulting in residual tumour being left after surgery. In cases where there is residual high-grade tumour, patients are at over six-times higher risk of death in comparison to GTR. (32) To overcome this limitation, neuronavigation has seen the integration intraoperative MRI (iMRI) to accommodate for brain shift and aid the identification of residual tumour that would otherwise remain. iMRI continually updates the neuronavigation and image accuracy, resulting in precise tumour margins, high rates of GTR and improved monitoring capabilities for complications. (33) In a single-centre, randomised control trial of 58 patients with glioma cell tumours, rates of GTR were 96% when using iMRI compared to 68% when using

standard neuronavigation (p = 0.023). Whilst this is only a surrogate marker of clinical benefit, previous studies have shown a considerable extended overall survival when GTR is achieved.(10) Unfortunately, iMRI has considerable installation costs of $3-8 million and prolongs surgery times by one hour on average. (34) Therefore, despite some compelling early data, currently there is limited evidence for its use because as it is restricted to a select group of well-funded neurosurgical centres.

THE FUTURE OF NEURONAVIGATION

Neuronavigation is not a static technology but continues to develop. Thus far, neuronavigation has required surgeons to continually refer to an external monitor. However, the emergence of augmented reality neuronavigation (ARN) would eliminate the need for this. In ARN a three-dimensional image would be overlayed intraoperatively onto the surgical field highlighting anatomy and disease. Currently, there is a lack of high-quality evidence for the use of ARN over existing neuronavigation but this may change. (35) Additionally, advancements in technology may entirely eliminate an operating surgeon completely with the integration of semi-independent robots into neuronavigation. For example, a neuronavigation system would provide intraoperative navigation to an operating robot, controlled remotely by an overseeing surgeon. The movements of the robotic arms would be controlled by voice commands or a handheld control device providing haptic feedback to the surgeon. (36) These predictions may seem speculative, but neuronavigation continues to be a rapidly evolving field and it is unclear what future directions it will take.

CONCLUSION

Previously, the outcomes of a neurosurgical procedure were entirely dependent of the skill and experience of the surgeon. Since then, neuronavigation has optimised surgical approaches and the intraoperative localisation of brain lesions. Subsequently, minimally invasive neurosurgery has developed – maximising the resection of brain lesions, whilst minimising damage to surrounding brain tissue. Neuronavigation has improved outcomes across multiple sectors of neurosurgery, including neuro-oncology, neurovascular surgery, epilepsy surgery, spinal surgery and functional neurosurgery. Neuronavigation will incrementally advance in years to come as new technologies continue to be integrated into it, and it presents further exciting prospects for the future of neurosurgery.

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The British Student Doctor, 2021;5(3):63-73
doi: 10.18573/bsdj.227
Education

Unravelling white patches of the mouth

EDUCATION

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No conflicts of interest to declare.

Accepted for publication: 25.07.21

ABSTRACT

Summary
This article aims to provide a guide for medical students and junior doctors on how to carry out a focused clerking of patients that present with intra-oral white lesions. In addition, it summarises the most common diagnoses as well as their management. Advice is given on how to quickly identify which lesions are likely to be malignant and how to manage such patients safely. 'Best of five' multiple-choice questions are provided to help with application and consolidation of knowledge.

Relevance and Take-Home Messages
Doctors and medical students need not panic when presented with a patient that has intra-oral white patches. This step-by-step guide will allow them to clerk these patients with more precision and confidence. It provides a deeper insight into which lesions are more likely to be dysplastic or in-situ carcinomas as well as how to safely manage and make onward referrals to the relevant specialty.

INTRODUCTION

White patches of the oral cavity are common and diverse, and although the majority represent benign disease, some are malignant. Establishing the correct diagnosis early on is key. Clinicians have a responsibility to be aware of them and minimise the potentially detrimental consequences of delayed diagnosis and treatment. This article aims to provide a simple way of systematically examining these lesions. Examination of the mouth can be overlooked when a patient is admitted into hospital for other problems, however, it is important for this to be done as part of a primary clerking so that the appropriate action, such as a specialist referral if indicated, can be taken.

It is not uncommon for white patches in the mouth to be asymptomatic and these cases are often picked up as a result of the diligence of dental or medical practitioners who have noticed the lesions as part of a thorough examination. (1-3)

Presenting Complaint & History

A patient may be referred by a doctor, dentist or present acutely in the emergency department. A structured history is essential for establishing a differential diagnosis.

Important questions to ask the patient are:

- Where is the white patch and how long has it been there?
- Is there one isolated lesion or are there multiple?
- If multiple, are they unilateral or bilateral?
- Is it soft or firm?
- Is it changing?
- Did it suddenly appear?
- Is it growing or shrinking?
- Does it come and go?
- Does it change location in the mouth?
- Does it change in colour?
- Are there any associated or relieving factors?
- Do hot & spicy foods, or toothpaste make it worse?
- Are any sharp teeth or dentures rubbing against the lesion?
- Pain? – Site, onset, character, radiation, relieving or exacerbating factors, severity (scale of 1 to 10)
- Does it bleed?
- Is it ulcerated? (1)

Relevant medical and social history

The oral cavity is bathed in saliva. Saliva has an immunological and protective role to maintain a healthy oral flora and dentition and further assists in healing and cellular turnover.

Reduction in the volume or quality of saliva can have significant repercussions for the balance of this dynamic environment. In addition, the mucosal lining of the mouth has a rapid turnover in response to the repeated trauma of daily use. Some medical conditions and medication can upset this balance giving rise to intra-oral white patches. These include:

- Dermatological disease (e.g. lichen planus or lupus erythematous)
- Haematological disease (e.g. associated with anaemia)
- Immunosuppressed states (uncontrolled diabetes, HIV), immunosuppressant medication including corticosteroids (systemic and inhaled), immunomodulators and chemotherapy (2,3)
- Iatrogenic (e.g. through the use of broad-spectrum antibiotics giving rise to opportunistic infections and steroid inhalers giving rise to candida infections which often present at the junction of the hard and soft palate)

Tobacco and alcohol habits are strongly related to many pre-malignant intra-oral white patches and their synergistic effect compounds their malignant potential. (4) Other recreational drugs such as betal nut and paan are implicated, specifically in sub-mucous fibrosis. Patients with psychological illness may inflict artefactual trauma to their mouths resulting in the formation of characteristic marks or patterns. (2,3)

See Table 1. for detail relating to specific white patches.

Examination

An extra-oral examination should be carried out first to check for signs of systemic disease, such as nail bed changes, pigmented or scaly lesions, rashes and papules on the arms, legs and genitals and palpable cervical lymph nodes (see Table 1. for relevance). The mouth should be examined in a systematic manner so as to avoid missing a lesion. Start at the front and work backwards.

A. Soft tissues:
Lips (including commissures) →labial mucosa (including sulci) →buccal mucosa (including sulci) → gingiva around all teeth, labial, buccal, lingual surfaces and behind the last standing molar teeth, including the retromolar trigone region → floor of the mouth (anterior, posterior, lingual gutter) → tongue (ventral, lateral and dorsal surfaces, you can use gauze to gently hold and pull the tongue out to gain a proper view), posterior tongue and oropharynx →hard, soft palate, uvula and tonsils.

B. Hard tissues:
Palpation of teeth and bone. Gentle tapping of teeth to check if any teeth are tender to tap, which would raise your suspicion of an associated dental infection. If patients are wearing dentures, check the

soft and hard tissues under the dentures. Check for poorly fitting dentures, sharp teeth or cheek biting trauma.

The clinical photographs in Figure 1. can be used as a guide.

A good torch and a dental mirror will aid your assessment. If a dental mirror isn't available, a tongue depressor will suffice. Be aware that lesions located in the depths of the patients' sulci and under the tongue and retro-molar area are often missed.

Describe any lesions found as follows:

- site
- size (in mm or cm)
- shape
- outline (regular or irregular)
- colour (it may be a mixed red and white lesion which is more concerning)
- texture (e.g. smooth, speckled, striated)

Asking the patient to take their own photographs at home can help with monitoring or diagnosis of lesions if they wax and wane. Clinical photography with appropriate patient consent is also good practice.

Red Flags

- Does the lesion look ulcerated with raised/rolled margins?
- Is the lesion rapidly growing?
- Is it a mixed red and white patch? (erythroleukoplakia)
- Is the lesion rough, tender & friable?
- Is the base granular? (i.e. does it feel rough and appear bumpy, 'cobblestone' like, rather than smooth and homogeneous)
- Any evidence of induration? (Fixed to underlying tissues)
- Any unexplained looseness of teeth specifically associated to the lesion?
- Does the lesion bleed to the touch?
- Is there any facial numbness or weakness? e.g. lips, cheeks
- Is there any unexplained loss of weight?
- Is there any ear pain? (otalgia) - ask in particular for unilateral otalgia
- Pain on swallowing? (odynophagia)
- Difficulty swallowing? (dysphagia)
- Change in voice? (dysphonia)

These signs should raise your suspicion of malignancy, particularly if it is an isolated, ulcerated lesion that has been present for more than three weeks. The position of the lesion can also be a prognostic indicator: White patches that are found to be squamous cell carcinomas are generally more likely to metastasise to regional lymph nodes if found in the posterior part of the oral cavity. (5) The floor of the mouth is also high risk as chemicals collect there and it is often missed. (5)

Investigations

These may include blood tests (e.g. full blood count, haematinics), viral, bacterial, fungal swabs and concentrated oral rinse cultures (CRCs) for fungae.
An incisional or excisional biopsy may be required. If an intra-oral white patch requires a biopsy, for the vast majority of cases an incisional biopsy is preferred. This involves taking a sample of tissue at the margin of the abnormal site including a margin of adjacent normal tissue. An excisional biopsy or an excision is usually only taken when the clinician is more certain of the diagnosis. If the lesion is highly suspicious, additional imaging may also be required following discussion and assessment by the maxillofacial team. See Table 1. for special investigations required for the diagnosis you are suspecting.

Diagnosis

Using all the information you have gathered so far, a working diagnosis for the intra-oral white patch, or patches, can be made (see Table 1.).

Management

The specific management of white patches can vary considerably depending on the patient history, clinical appearance, changes in appearance and the differential or definitive diagnosis. Generally, the precipitating causes are corrected first. Treatment may include:

- Counselling or referral for cessation of smoking and reduction of alcohol consumption (especially for malignant and pre-malignant lesions)
- Management of associated comorbidities and correction of associated haematological abnormalities (such as deficiencies of vitamin B12, iron and folate)
- Trauma reduction - consider referral to a dentist to smooth sharp teeth or denture edges. Address any self-inflicted harm. Many of these lesions will resolve spontaneously after removal of the cause. Protective bite guards can also be helpful.
- Symptomatic relief such as use of chlorhexidine mouthwash, steroid mouthwashes and sprays. Systemic medication may be required in refractory cases.

White patches may be super-infected with fungus such as candida which should be treated if detected. The same goes for any virus or potentially causal non-commensal or pathogenic bacteria which may be isolated on an oral swab or rinse. Using a spacer cone for steroid inhaler use and rinsing the mouth with water after use can reduce opportunistic fungal infections. Topical anti-fungal medication can be used, progressing to systemic if unresponsive. Where

possible, avoid prescribing multiple courses of broad-spectrum antimicrobials, instruct patients on maintaining good oral and denture hygiene and manage xerostomia with continuous hydration and saliva substitutes (pastilles, drops or gels). This will help to better manage and reduce the risk of oral candidiasis.

Monitoring of white patches is essential and is more frequent for dysplastic lesions, diagrams can be drawn, patients can be educated and clinical photographs can be a helpful adjuvant. (2,3)

When to Biopsy

If the intra-oral white patch is associated with any of the red flags, consider an urgent incisional biopsy within two weeks to rule out a malignancy (see Table 1). If the white patch does not appear to be associated with any of the aforementioned red flags and is clearly associated with a reversible cause only, the cause should be addressed and the patient should be reviewed after a few weeks to assess the effects of your measures and to see if they have adhered to advice such as smoking and alcohol cessation. If there is no improvement or worsening in the symptoms or appearance of the lesion, consideration should then be given for an incisional biopsy.

Biopsy-proven mildly dysplastic white patches can be reviewed by the patient's dentist on a three- to six-monthly basis with continued efforts for smoking and alcohol cessation and a healthier diet plan as appropriate. Re-referral to Oral & Maxillofacial Surgery (OMFS) can be made if the lesion changes. White patches with moderate or severe dysplasia are usually excised before they can develop into carcinomas. (2,3)

How do I make sure I am safe and how do I refer a patient with a white patch*?*

There are two arms on the pathway for these referrals, one is to the patient's dentist and the other is to the Oral & Maxillofacial Surgery (OMFS) Department.

Some white patches are pre-malignant and therefore if there is any uncertainty regarding the diagnosis of malignancy, or degree of dysplasia, an urgent two-week wait referral should be made to the OMFS team. The national guidance below can be used. A referral can be done by letter or via an electronic referral system if one is available. If a lesion is found not to be malignant but needs symptomatic relief or monitoring, it can be referred to, or reviewed by a dentist. Ensure the patient is registered with a dentist. If access to dental care is poor, referrals with clinical photographs including patients' own mobile phone photographs attached to referrals can help streamline referrals. Ensure any photographs used are managed in line with information governance policy for the region that you work in.

What are the national guidelines for referral?

The most recognised referral guideline is the Head and Neck Cancer Guideline published by the National Institute for Health and Care Excellence (NICE).
Regarding white patches, it states: "Consider an urgent referral (for an appointment within two weeks) for assessment for possible oral cancer by a dentist in people who have a red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia." (6)

The guidance states that if the above lesion is detected by a dentist, that an onward "cancer pathway" referral should be considered by that dentist i.e. to be seen by the OMFS team within two weeks. However, if you are highly suspicious that the oral lesion is cancer, please refer to OMFS, not the patient's dentist, as a delay such as this can result in a delay to the patient's diagnosis and a worse prognosis.

The NICE guidance also states that if the white patch is associated with an ulcer lasting more than three weeks or a persistent and unexplained lump in the neck, an urgent cancer pathway referral (to be seen in two weeks by OMFS) should be considered. (6)

How to document and pass the information to the next team

Documentation, even if it is brief, should be in the format of a history as described above, including relevant findings of an examination and previous treatment given. If the patient is systemically unwell with the lesion, contact the on-call clinician in OMFS via bleep or hospital switchboard. Otherwise, the patient can be referred to the OMFS team via the pathway described above.

What's new on this topic?

Research is being conducted into aiding early detection and diagnosis of dysplastic intra-oral white patches. For example, use of chemiluminescence which involves the use of incandescent light and toluidine blue dye to identify the lesions. A recent study has suggested a high specificity and sensitivity for diagnosis with this technique. Although it does not replace the gold standard of histopathological diagnosis, it can help to identify the extent of the lesions on examination. (7)

DISCUSSION

Oral white lesions are varied and at times complex to diagnose. Using a systematic and thorough approach to history-taking and examination, makes establishing the correct diagnosis and instigation of successful management more likely. The integration of multidisciplinary care both in the community and through hospital referral is something that every doctor should be aware of and use where indicated to optimise the care delivered. Although often inadequately covered in medical training, the hope is that students and doctors will use this guide and further reading to ensure that all patients being admitted into hospital have an assessment of their mouth to screen for concerning lesions as part of their initial clerking. With experience, the clinician can diagnose many systemic conditions from lesions in the mouth. To further knowledge and experience in oral medicine, the authors recommend that junior doctors and medical students consider organising a period of observation with their local oral medicine or OMFS department.

Table 1.INTRA-ORAL WHITE PATCHES – SPOT DIAGNOSIS		
BENIGN	Key clinical features	Relevant special investigations
Linea alba	Distinct white line (not always straight) in the cheeks, usually next to where the teeth meet	Nil
Fordyce spots	Represent ectopic sebaceous glands – small, usually multiple spots measuring 1-2mm in the mouth; commonly buccal mucosae; yellow/white	Nil
Chemical burns	White friable slough, often easily removed to leave a bed of redness and ulceration (commonly due to incorrect use of aspirin as topical pain relief)	Nil
Leukoedema	Whitish-grey filmy appearance of mucosa, common in buccal mucosae – disappears on stretching of the mucosa.	Nil
White sponge naevus	Asymptomatic white lesions in several mucosal sites – particularly buccal mucosa, also affects mucosa of vagina, vulva, anus and oesophagus. Commonly affects other family members, developmental but often only noticed in second decade of life. Mutations in gene coding for keratin.	Nil
Coated tongue	Whiteness or other discolouration of the tongue when there is a failure of exfoliation of surface epithelial cells – often occurs in patients with febrile illnesses who are not eating much or who are on a soft diet – can also be orange or brown depending on external factors such as tea/coffee and smoking.	Oral fungal swab or rinse
Frictional keratosis	Corrugated or thickened white patch, commonly lips, lateral tongue and buccal mucosa along the line of teeth biting	Nil – sometimes requires fungal swab /biopsy
Geographic tongue	Irregular de-papillated red areas on the tongue surrounded by pale white well demarcated margins – mostly occurs on the dorsum and lateral borders of the tongue, appear and disappear over a period of a few days (sometimes longer) and move around different areas of the tongue/mouth – some people complain of discomfort on eating, especially hot and spicy foods.	Full blood count, haematinics (Zinc if no other cause identified)
Pseudomembranous candidiasis	Common in the immunocompromised, elderly and infants. Soft creamy-yellow white patches, can affect large areas, can be wiped off. Local causes: courses of antibiotics, steroids (systemic and inhalers), smoking, under un-clean dentures/wearing dentures at night. Systemic causes: HIV, Blood dyscrasias, uncontrolled diabetes, transplant patients.	Oral fungal swab or rinse
Nicotinic stomatitis (Smoker's keratosis)	Heat and chemicals from tobacco produces whiteness with "punctate" red dots marking out minor salivary glands, most commonly on the hard palate, although can affect other areas. If a denture is worn, it will form around it. If on the palate, very low risk of malignant transformation.	Nil, incisional biopsy if looks sinister
Hairy leukoplakia	Asymptomatic, corrugated white lesion along lateral tongue border only, commonly associated with Epstein-Barr virus (EBV) – common in the immunocompromised e.g. HIV, immunosuppression after organ transplantation	Full blood count, fungal swab, HIV test
Lupus erythematosus (discoid vs systemic)	Can look like lichen planus in the mouth (striated keratotic, can be red) discoid version often has raised, red scaly patches on sun exposed skin. Systemic version has multi-system organ involvement resulting in kidney, pulmonary, cardiac & joint disease. May have a butterfly rash on the skin of the face (commonly zygomatic processes of the maxilla). May have dry mouth and eyes with Sjogren's syndrome.	Incisional biopsy Anti-nuclear anti-bodies Rheumatoid factor, SSA & SSB antigen
Pyostomatitis vegetans	Common in patients with inflammatory bowel disease (e.g. Crohn's, ulcerative colitis) – redness anywhere in the mouth leading to 2-3mm yellow pustules which can progress to larger vegetating lesions of the oral mucosa.	May require biopsy if unsure, full blood count, C-reactive protein (CRP)
Graft-versus-host disease (GVHD)	Usually in the chronic form i.e. more than 100 days after a bone marrow transplant – mimics forms of auto-immune disease. In the mouth there may be white reticular lesions that resemble erosive lichen planus. Patients may complain of burning secondary to candidiasis or dry mouth	Nil – biopsy if looks sinister

Table 1: *This has been created by the authors to summarise features of intra-oral white patches to help with differential diagnosis. (1) (2) (3) (8)*

Please note that this is not an exhaustive list and in particular does not include some rare hereditary conditions. It is also important to note that other lesions in the mouth may present as white patches at some stage if they have been traumatised.

Table 1: INTRA-ORAL WHITE PATCHES – SPOT DIAGNOSIS		
MALIGNANT & PRE-MALIGNANT	Key Clinical Features	Relevant special investigations
Squamous cell carcinoma (SCC)	Alcohol, tobacco and paan chewing are common contributing factors, sun exposure common for lip. Can take many forms, however as a white patch it is often painless to palpation in the early stages with irregular margins and induration. Often associated with local soft tissue trauma (e.g. sharp tooth). Can arise anywhere in the mouth, although most common under the tongue and behind the lower molar teeth.	Incisional biopsy; staging scans as necessary (MRI, CT)
Lichen planus	Variable appearance – reticular "fisherman's net" appearance or papular, plaque-like, atrophic or erosive types. Patients experience oral soreness or burning over the lesions, often to hot, spicy or acidic foods. It can affect all oral mucosa, commonly the buccal mucosa and gingiva. Initially patients may also have purple pruritic papules on flexor surfaces of their arms, legs and genitals. Low risk of malignant transformation.	Incisional biopsy May require a full blood count and anti-nuclear antibodies
Lichenoid reaction	Similar appearance to Lichen planus but often presents next to metal fillings (e.g. amalgam), metal tooth crowns, and rarely white fillings. Some contributory medication e.g. hypoglycaemics, antihypertensives and NSAIDS. Low risk of malignant transformation.	Incisional biopsy
Chronic hyperplastic candidiasis (CHC)	Similar causes to pseudomembranous candidiasis – commonly associated with heavy smoking and alcohol habit. White patch in the buccal mucosa (corner of the mouth close to the lip commissure) or tongue. Can vary from a faint white patch to an indurated ulcer with a white/yellow slough. Does not rub off. High risk of malignant transformation.	Incisional biopsy Oral fungal swab and rinse
Leukoplakia	A white patch or plaque on the oral mucosa that cannot be rubbed off or characterised clinically as any specific disease i.e. diagnosis of exclusion. Can be mixed red and white "speckled" and thickened leathery appearances which are the most concerning, tongue and floor of mouth are higher risk sites for malignancy. Other appearances include flat white patches and wart-like lesions. Tobacco and alcohol habit common. Low to moderate risk of malignant transformation.	Incisional biopsy May require haematinics and full blood count Fungal swab if suspected overlying candida
Submucous fibrosis	Most commonly present as fibrous bands that can be palpated in the buccal mucosae or palate – chewing betal nut (areca) is the primary cause, patients will often deny usage or be chewing a product with betal nut in with a different brand name. Chillies in the diet and haematinic deficiencies can worsen the condition. Moderate to high risk of malignant transformation.	Incisional biopsy May require haematinics

Table 1 continued: *This has been created by the authors to summarise features of intra-oral white patches to help with differential diagnosis. (1) (2) (3) (8)*

Please note that this is not an exhaustive list and in particular does not include some rare hereditary conditions. It is also important to note that other lesions in the mouth may present as white patches at some stage if they have been traumatised.

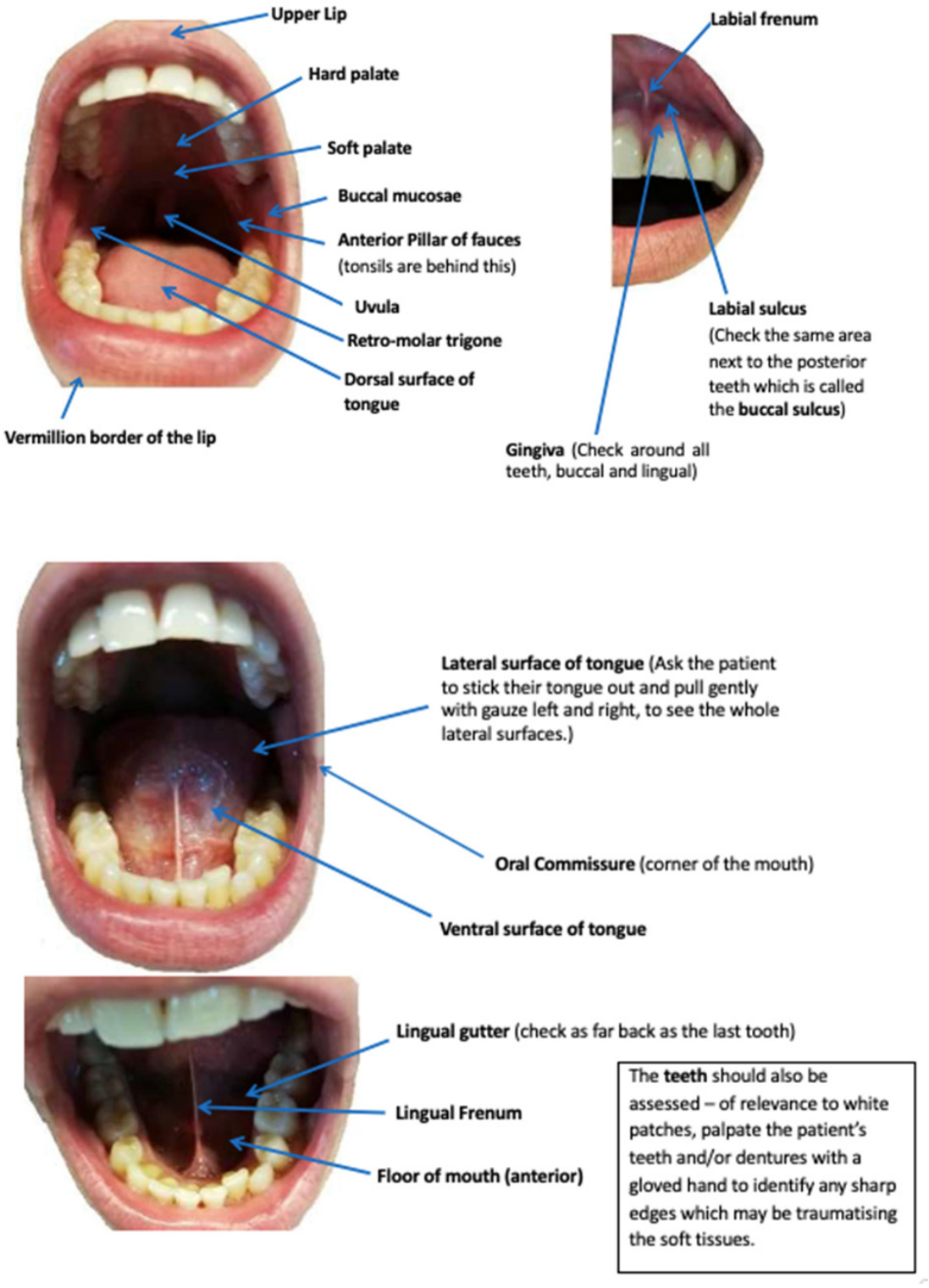

Figure 1: *Clinical photographs of normal clinical anatomy. Photographs owned by the authors.*

Multiple-Choice Questions (MCQs)

Best of five – select the single best answer.

1.) A white patch occurring in which area of the mouth has the highest malignant potential out of the following options?

a. lip
b. palate
c. buccal mucosa (BM)
d. floor of mouth (FOM)
e. gingiva

2.) Which of the following appearances of a white patch in the mouth is most concerning?

a. white friable slough
b. mixed red and white patch, indurated
c. corrugated, rough
d. faint white lines, fisherman's net appearance
e. multiple white/yellow 2-3mm spots

3.) You are working as a ward doctor in cardiology. A nurse asks you to review a 92 year-old gentleman that they notice has a large white patch in the left cheek. You notice that the white patch is in the cheek next to where the teeth bite, it is a diffuse white patch, striated and is not sore to palpation. The patient informs you that it was a little sore after drinking orange juice. What is the most likely diagnosis?

a. frictional keratosis
b. leukoplakia
c. lichen planus
d. linea alba
e. pseudomembranous candidiasis

4.) You are working as a ward doctor in haematology. A nurse asks you to review a 50 year-old female patient with acute myeloid leukaemia who has had a bone marrow transplant. They inform you that the patient is complaining of a growth on her tongue. On examination, there are a few smooth red areas on the front of the tongue surrounded by flat white ring-like patches. There is no growth, swelling or roughness and it is not particularly sore to touch. The patient reported that she only noticed it yesterday and that last week there was a similar lesion on the back of her tongue which has now disappeared. What is the most likely diagnosis?

a. oral hairy leukoplakia
b. squamous cell carcinoma (SCC)
c. related to graft-versus-host disease (GVHD)
d. geographic tongue
e. coated tongue

5.) Which intra-oral white patch is the most urgent to carry out an incisional biopsy on?

a. lichenoid reaction
b. pyostomatitis vegetans
c. frictional keratosis
d. leukoedema
e. chronic hyperplastic candidiasis (CHC)

MCQ answers

1.) The answer is *d. floor of mouth.* This area is often missed on examination under the tongue.

2.) The answer is *b. mixed red and white patch*, indurated, as these clinical signs make the lesion more likely to be dysplastic or an in-situ carcinoma. (a. is most likely to be frictional keratosis, c. leukoplakia, d. lichen planus and e. Fordyce spots).

3.) The answer is *c. lichen planus* – the key clues here were the striated appearance and soreness on drinking orange juice. Frictional keratosis usually presents as a lesion that is rough and sore to palpation. Pseudomembranous candidiasis would wipe off, sometimes leaving an area of redness.

4.) The answer is *d. geographic tongue*, given the classically described clinical appearance and the intermittent nature of the lesions. You would think about graft-versus-host disease given the patient's history, however its appearance is usually more severe than described and would not be intermittent.

5.) The answer is *e. chronic hyperplastic candidiasis (CHC)* as it has the highest risk of malignant transformation compared to the rest of the options. Leukoedema and pyostomatitis vegetans have no potential for malignant transformation.

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The British Student Doctor, 2021;5(3):74-75
doi: 10.18573/bsdj.218
Reflections

Remember to thank the patient

REFLECTIONS

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No conflicts of interest to declare

Accepted for publication: 02.04.21

Doctors, medical students and even books emphasise to say it. Whether it is an examination, administrating an injection or taking a history, it is not complete without saying a simple "Thank you" to the patient. Of course, with everyone else around uttering this phrase, you would look rude if you do not speak these words yourself. Does this mean we are just thanking patients for mere common courtesy?

What I thought was just another day on placement, happened to change my appreciation for patients for the rest of my career. After gulping down a can of expresso, I hurried to the ward only to be trailing behind a consultant and a couple of stressed junior doctors. I anticipated a doctor would at least glance at me and give an opportunity to introduce myself. Soon enough my hope faded as I realise this was going to be an hour of 'self-directed learning'. It was only when a junior doctor waited for me to enter prior to closing the curtain that I became aware that I did, sort of, exist. Having not seen the patient before, it was a matter of deciphering the diagnosis from the conversation between the consultant and the patient, as is often the case for medical students on ward rounds.

After an hour of scribbling down a list of misspelt drugs, I was back. Only this time, I was also holding a cannula and smiling at the patient to hide my fear. I was back as this opportunity was so rare. I was back to feel more involved. I was back to have a more productive day. I introduced myself to the patient, and my teaching had begun. Before I tore open the cannula pack, I took the time to ask the patient about the history of his condition and how his life had been affected. You can argue that you can learn more from a book about colon cancer than from patients. However, medicine is not just about how many drugs in the British National Formulary (BNF) you have memorised, how dextrous you are at venepuncture, or how you managed to diagnose Takayasu's arteritis. It is also about having conversations with patients who are going through shock, anxiety and grief. Medical schools train students for such scenarios with actors. But, when you know they are faking their

pain, are you not faking your emotions yourself? When a real patient who has gone through so much pain explains their condition, you learn and remember. You remember their words more strongly than any black and white page of a book!

A book may teach you how to express empathy but not how to feel it. During that conversation, not only did I learn what empathy feels like, but also how I naturally reacted to it without regurgitating patronising phrases from a page. Paul Kalanithi explains in his autobiography 'When Breath Becomes Air' the importance of seeing each patient as a person and not a problem. (1) When I first read this, I thought I understood this. However, it was not until I met this patient that I fully appreciated the genuine human to human connection in the care of patients. I was truly interested in his experience of cancer. In return, he was truly interested in my learning. He knew that he could have asked a well-experienced doctor, who would have been safer and more accurate, to cannulate him. Instead, he wanted me to cannulate him. After I had inserted the cannula, he smiled and was very grateful for it. It did not matter to him that I needed two attempts because he wanted me to become better at cannulation. He wanted to be a part of my training to be a competent doctor.

I thanked him not only for his selflessness in giving me an opportunity to be more competent, but also for his encouraging smile at the end that boosted my confidence. You need confidence to interact with patients and practice clinical skills. From my conversation with him, I learnt how his life was much more restricted in terms of socialising and exercising, such as swimming, due to lowered self-confidence from having a stoma bag. To make matters worse, he had recently lost his job and was struggling financially. By having a difficult conversation, I learned to connect with the patient at an emotional level and understand his story. Therefore, I was emotionally more prepared to actively listen to patients talk about their lives and suffering. Through expressing genuine interest in his story, I had learned to build the patient's trust in me to understand all aspects of his suffering and not just the superficial pain. I have been trusted to respect their vulnerability caused through sharing aspects of their life that they have not even revealed to their closest friends and family.

I was fortunate to have met such a gentleman. Not all patients will be as generous in nature. However, they are all still unique learning opportunities. There is no book or communication workshop that can fully prepare you to interact with patients that are emotional, depressed or partly conscious because you cannot predict your emotional reaction in a real situation. As medical students, we have the privilege of never being on our own when facing challenging patients as you can take another student or staff with you. Also, leaving the room is always an option, as there is no pressure to talk to patients. Therefore, it is less stressful to learn to deal with a patient that is aggressive and shouting at you now than when you are a junior doctor running late with a multidisciplinary team (MDT) meeting in five minutes. Of course, at this point, the thought of your consultant's passive aggressive stare for being late will make your hand tremble. Naturally, a doctor may have an emotional breakdown in such stressful situations.

Whilst the patient that is smiling away and having friendly chats with nurses may seem ideal, you will be limiting your experience by solely approaching friendly and talkative patients. By meeting patients varying in age, gender, ethnicity, socioeconomic status and mental health, you will gain a broader knowledge of hardships influenced by the patients' different backgrounds. However, in order to learn the most from patients, you will need to tailor your questions, tone and manner for each patient. Consequently, you can develop a stronger rapport with them so that they feel more comfortable with sharing their story. Initially, you may find these conversations awkward, but this is from inexperience in such situations. Therefore, the more often you are exposed to learning from patients, the more natural conversations will feel, the stronger the relationships will be, and the better your understanding of their holistic needs will become. By respecting the different aspects of their needs when making medical decisions and involving the patient more in medical discussions, you can provide a higher quality of care. Essentially, we need patient-centred learning as today's medical students, in order to deliver patient-centred care as tomorrow's doctors.

As medical students, creating positive experiences for our patients, not only develops us as clinicians, but also paves the way for future generations of medical students to learn from patients, through setting a positive example of patient care. Next time a clinic is cancelled, a lecture is postponed, or a consultant is too busy, walk straight to a ward where you can find a teacher on each bed.

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The British Student Doctor, 2021;5(3):76-78
doi: 10.18573/bsdj.134
Reflections

Anatomical renaissance: How important is the cadaver?

REFLECTIONS

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No conflicts of interest to declare.

Accepted for publication: 20.03.21

The Anatomy Lesson of Dr Nicolaes Tulp is one of Rembrandt van Rijn's early works (1632) and is displayed in Mauritshuis Museum, The Hague, Netherlands. It depicts the official city anatomist of the Amsterdam Guild of Surgeons, Dr Nicolaes Tulp (right), dissecting the forearm musculature of the cadaver of Aris Kindt, previously a petty criminal. (1)

Figure 1: *The Anatomy Lesson by Dr Nicolaes Tulp, oil on canvas by Rembrandt van Rijn. (2) Image courtesy of Mauritshuis, The Hague.*

Rembrandt was famous for using light and shadow to emphasise protagonists; (3) the centrally placed cadaver is clearly the most well-lit subject of the scene. This prompted me to question the importance of the cadaver and its dissection to the study of human anatomy. Additionally, the assembly of surgeons around the cadaver – each with differing levels of attention to the prosected forearm – made me think of my own experiences in the dissecting room. This led me to reflect on the extent to which human anatomy education, and perceptions of it, have changed since the 17th century and whether the changes are positive.

Throughout history, cadaveric dissection has been an indispensable part of studying of human anatomy (the word anatomy originates from the Greek anatomein: to cut open), and consequently has become a prominent feature of medical education. The first recorded public dissection occurred in early 14th century Bologna; however, it was not until a century later that dissections became more common. One reason for this was the difficulty of acquiring cadavers. From this time until the 19th century, it became typical for cadavers to come from executed criminals. (4) Andreas Vesalius (1514-64), widely considered to be the greatest of early anatomists and father of modern human anatomy, was a prolific dissector who realised that the human body was not always as previously described; dissection allowed him to see for himself and be the first to accurately describe several anatomical structures, including the uterus. His book De humani corporis fabrica (open in the painting) was the first to be primarily based on evidence from cadaveric dissections. The desire of Vesalius to see the evidence behind the anatomy and not blindly trust preceding literature had become widespread by the time of Rembrandt, (4) so dissection was essential to anatomical studies.

In recent years, there has been a shift in how anatomy is taught; less emphasis is placed on dissection and prosection – some medical schools have no dissecting rooms at all, relying instead on non-cadaveric models and computer software for anatomy teaching. (5) However, it must be acknowledged that the accuracy and efficacy of these new methods of teaching would not be possible without cadaveric dissection in the first instance.

As a lay member of the public, my reaction to Rembrandt's painting would have been repulsion. Dissection has been widely regarded as debasing and morally repugnant through the ages. This has been reflected in cadaveric dissection being illegal for large parts of history. Consequently, the public image of medicine was damaged by body-snatching and murder to provide a supply of cadavers for dissection. (4) The implication of these serious crimes would be that the benefits to anatomical knowledge outweighed the risks to the professionals at the time. The fact that Aris Kindt had been executed for his crimes before becoming a cadaver suggests that in 17th century Christian societies, becoming a cadaver was an undesirable fate. The church did not approve of dissection; however, it was more accepting if the cadavers came from criminals who were not involved with the church. (6) This view is still alive today in those who see their religious beliefs as incompatible with the practice of cadaveric dissection. (7) Furthermore, as medical students, we are taught of the four prima facie principles of medical ethics; one being non-maleficence or the duty of the doctor to 'do no harm' as stated by the Hippocratic oath. It is my opinion that this principle does apply after death, and therefore dissecting a cadaver could be considered contradictory to this. Despite its educational benefits, dissection could still be seen as mutilation, placing it in direct opposition with the public expectation of medical professionals (such as Dr Tulp) and the social contract between medicine and society. As such, the valid consent of the donor prior to their death is an absolute requirement. Unfortunately, regardless of his criminal status, Aris Kindt is unlikely to have been consented for dissection prior to his death.

Another reaction I would have had as a lay person is intrigue; the human body and study of its anatomy is deeply fascinating and relatable to everyone. This can be demonstrated as true both at the time of Rembrandt's painting and today. The Amsterdam Guild of Surgeons aimed its annual dissection or 'anatomy lessons' at trainee surgeons, with educational purposes in mind. However, these events became extremely popular in the Dutch Republic – prominent guests attended, and new theatres were built to accommodate large numbers of paying spectators. Additionally, artists such as Rembrandt were commissioned to paint these events. (6) In modern times, the anatomist Gunther von Hagens performed the first autopsy since the 19th century to 1.4 million people on live television in the UK. Whilst this kind of public dissection was illegal under the Anatomy Act 1984, it was performed in full without authoritative intervention. His travelling exhibition Body Worlds has received millions of visitors and recently became a permanent fixture in London. (8)

As a medical student, the painting also evoked positive emotions in me; it reminded me that anatomy is not merely theoretical, but a living and moving subject. In the painting, the wrist of Dr Tulp is flexed as he is demonstrating the action of the muscles in the dissected forearm. This led me to consider the relevance of cadaveric dissection in developing intricate knowledge of the human body for medical practice. Historically, anatomists have had backgrounds in surgery – examples include Fabricius ab Acquapendente as well as William Hunter and Henry Gray of St. George's Hospital, London. (4) It cannot be denied that accurate knowledge of anatomy is relevant when navigating structures during surgery in these disciplines. Furthermore, understanding structure is key in understanding function for physicians. But do we need cadavers to obtain this knowledge? In the painting, Rembrandt creates a vivid contrast between the pale grey skin of the cadaver and the healthy, flushed cheeks of the living. This highlights the fact that knowledge of in vivo anatomy necessary for practice is different from cadaveric anatomy. (5) However, I do not believe this should be an influential factor for medical schools to abolish cadaveric dissection altogether.

Sophisticated imaging techniques and hence minimally invasive procedures are increasingly becoming a larger part of medical practice. (1) Cadaveric dissection enables students to better understand three-dimensional anatomical structures and therefore develop the essential spatial reasoning skills needed to interpret the imaging data and target therapy to a specific site. (9) It therefore still holds importance in producing competent and up-to-date practitioners today.

Cadaveric dissection has been directly associated with anatomy learning for hundreds of years and remains so today. It has also been significant in directing public perceptions of the medical profession. (4) While the ethical implications of cadaveric dissection need to be considered, there is undeniable value in the use of education of medical professionals. Rembrandt's painting serves as a reminder of the historical significance of cadaveric dissection, allowing its viewers to reflect on its role in the modern day.

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The British Student Doctor, 2021;5(3):79-80
doi: 10.18573/bsdj.219
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The power of positive feedback

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No conflicts of interest to disclose

Accepted for publication: 25.06.21

Dear Editor,

As I reflect upon my clinical placements at medical school thus far, a common trend emerges. Rotations with regular feedback and encouragement positively impacted my opinion of that area of medicine, attracting me and increasing the likelihood that I will consider that field in the future. Although few, negative experiences of depreciation or public humiliation due to a lack of knowledge, completely turned me off a specialty and formed a negative lasting impression (regardless of my initial thoughts).

As a doctor and medical teacher, do you take the time to introduce students to the team or include them in discussion? Do you create a supportive and encouraging learning environment, a safe space where students are comfortable asking questions? You may not realise the impact that such simple gestures have on students' learning experiences (and cortisol levels). Being encouraged and included makes learners feel at ease and willing to engage in positive learning opportunities – providing you with plenty of chances to persuade them that your specialty is the best!

There is a lot to be said for the Irish proverb 'Mol an óige agus tiocfaidh sí – praise the youth and they will flourish', especially in terms of medical education. As human beings, our brains are wired to respond positively to encouragement, boosting our mood and self-esteem.(1) This plays a role in the evaluation we make of ourselves, making us feel competent and motivating us to reach our potential.(2) Medical students, both in my experience and in literature, commonly display perfectionistic personality traits, setting unrealistic standards and using negative reinforcement to aim for flawlessness.(3) I, too, am guilty of this nature. The overwhelming volume of medical information distracts us from the vitality of self-reflection – a time to consider what we already know and pinpoint the goals we wish to achieve.

Nonetheless, constructive criticism, in the form of feedback questionnaires or open discussion, cannot be undermined.(4)

Identifying strengths and personalising feedback educates scholars about their learning styles and how these can be manipulated to achieve their personal objectives. The Pendleton model, a learner-centred feedback strategy, uses open questions to highlight positive behaviours, initiate reflection and actively develop plans to address an area that requires improvement. This feedback style, which I encourage you to consider, has been particularly useful in the optimisation of my medical training. In fact, I plan to incorporate this approach in my future facilitation of feedback as it encompasses the essential elements of being a good teacher; motivating students to assess and refine their learning in a non-judgemental and unthreatening environment, while kickstarting reflective practice early in training.(4,5) After all, a good start is half the work.

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The British Student Doctor Journal

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