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- Poster Presentations: A Presenting Opportunity in Conferences for Medical Students.

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- Attitude towards New Packaging to Reduce Condom-carrying Embarrassment among Thai Youth, A Crosssectional Study.
- Sub-tenon Anaesthesia versus Intracameral Anaesthesia in Patients Undergoing Cataract Extraction: A Comparative Study of the Level of Pain, Visual Perception and Anxiety.

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## INTERNATIONAL JOURNAL *of* MEDICAL STUDENTS

### *International Journal of Medical Students*

The *International Journal of Medical Students* (IJMS) is a peer-reviewed open-access journal, created to share the scientific production and experiences of medical students worldwide.



### *Schisto SXiez*

Sand Art. Scene from "Neglected: A Story of Schistosomiasis Infection in Ghana"

By Shelly Xie (with authorization).

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# Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) in the International Journal of Medical Students

Aisha Gharaibeh,<sup>1</sup> Sahil Koppikar,<sup>2</sup> Francisco J. Bonilla-Escobar.<sup>3</sup>

Observational studies are the foundation of all biomedical and clinical research.<sup>1</sup> While clinical trials and meta-analyses offer the highest levels of evidence and are therefore considered the gold standards of human research, experimental studies would be hardly possible without any evidence from the hypothesis-generating observational studies. It is by the help of well-conducted epidemiological studies that scientists can inform public health decisions and clinical practice guidelines.

Nevertheless, observational epidemiological studies are not always conducted by expert epidemiologists. In such cases, fundamental deficiencies in reporting have been identified.<sup>2</sup> Conflicting results from epidemiological studies on the risks of common daily products, such as the use of coffee, hair dyes, or hormones, are frequently and eagerly reported in the popular press, providing a constant source of anxiety and confusion to the public. This raises the need for guidelines on reporting such studies as medical journal editors might face problems upon reviewing these papers.

In the last few years, the STROBE checklist has been used frequently to analyze the reporting quality of published studies.<sup>3</sup> This ensured that each section of the paper included the relevant items that would allow other researchers to reproduce, compare and analyze the information presented, such as the background and objectives in the Introduction section; study and sampling design, setting, participants, variables, data sources, bias, study size, quantitative variables and statistical analysis in the Methods section; participants and descriptive information, outcome data, main results and additional analysis in the Results section; and, finally, key results, limitations and generalizability in the Discussion section.<sup>1</sup>

In September 2004, a meeting was held in the United Kingdom to identify and create common guidelines that could be used internationally for publication of observational studies. Experts in various fields attended this meeting, including epidemiologists, methodologists, statisticians, and editorial staff from the *Annals of Internal Medicine*, *British Medical Journal* (BMJ), *Bulletin of the World Health Organization*, *International Journal of Epidemiology* and the *Journal of the American Medical Association* (JAMA). They identified the most important items to be included in a checklist for each type of study and the strategy for disseminating this information, referred to as the STROBE (Strengthening the Reporting of OBservational studies in Epi-

miology) Statement. In October 2007, the STROBE statement, a 22-item checklist, was published in a number of journals. These items should be addressed in all articles that are reporting cross-sectional, case-control or cohort studies. The aim of the statement is to provide guidance on reporting observational studies in a consistent and thorough manner that can be easily reproduced.<sup>1</sup>

While clarity of reporting is a prerequisite to evaluation, the checklist should not be regarded as an instrument to evaluate the quality of observational research. Good reporting does not necessarily translate into quality research. The importance of good reporting is that others—readers, fellow scientists, reviewers and editors—can form an informed opinion on whether the research was appropriate and what aspects might need more scrutiny.

Since its inception, additional efforts have been taken by the STROBE Group to promote the STROBE guidelines by creating a number of extensions or additional statements similar to the first set of guidelines, such as:

- Strengthening the Reporting of Molecular Epidemiology for Infectious Diseases (STROME-ID).<sup>4</sup>
- REporting of studies Conducted using Observational Routinely collected Data (RECORD).<sup>5</sup>
- STrengthening the Reporting of OBservational studies in Epidemiology: Molecular Epidemiology (STROBE-ME). It used 9 existing items of the STROBE Statement and provides 17 additional items related to molecular epidemiology.<sup>6</sup>
- Draft STROBE checklist for abstracts published on Sep 20th 2011. It has been tested at the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). The *International Journal of Medical Students* (IJMS) in the second Editorial of this issue is promoting its use.<sup>7</sup>
- Strengthening the reporting of genetic risk prediction studies: the GRIPS Statement. It was developed on the basis of other guidelines, such as STREGA, REMARK and STARD. The GRIPS statement consists of a checklist of 25 items to improve quality and transparency of the reporting of genetic risk prediction studies.<sup>8</sup>

The STROBE statement is referred to in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of Medical Journal Editors (ICMJE) (Available from: <http://www.icmje.org/icmje-recommendations>).

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[pdf](#), updated 2013 Dec; cited 2014 Jun 22). We, in the IJMS, refer to the STROBE Statement in the Authors Guidelines (Available from: <http://www.ijms.info/ojs/index.php/IJMS/about/submissions#authorGuidelines>, updated 2014 Jan 4; cited 2014 Jun 22). The IJMS Editorial Team is aware of this statement and the authors are requested to always follow the guidelines to improve the way that observational studies are reported. Furthermore, this helps achieve one of the main objectives of the IJMS, that is, to teach young scientists how to conduct transparent studies and to promote ethical and professional research among young professionals for scientific advancement.

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# Poster Presentations: A Presenting Opportunity in Conferences for Medical Students

Hulegar A. Abhishekh,<sup>1</sup> Neeraj Tandon,<sup>2</sup> Sunil Rangarajan,<sup>3</sup> Aisha Gharaibeh,<sup>4</sup> Francisco J. Bonilla-Escobar.<sup>5</sup>

Presenting research findings in conferences develops scientific abilities in early career scientists, facilitates early dissemination of information and provides opportunities for learning different research approaches.<sup>1</sup> A participant can learn about unpublished research which stimulates ideas much before the article goes through lengthy process of publication. Critical feedback and comments from peers might help in the process of improving a developing manuscript. Conferences provide a platform to build one's network and meet global leaders and new collaborators in one's field. For early career residents and fellows, this can improve the chance of getting long term mentorship that results in overall betterment of career development by various means like getting good opportunities to get into fellowship or early faculty jobs.

Unfortunately, medical students and specialists lack the training related with the process of writing an abstract, organizing a poster or preparing for a scientific conference, in general.<sup>2,3</sup> The International Journal of Medical Students (IJMS) as it aims to enhance the role of medical students in research publication, also believes in improving the chances of medical students and early physicians to participate in conferences by sharing the tips and information mentioned below.<sup>4</sup>

Conferences vary from small conferences such as symposia, those which discuss specific topics, have narrow research focuses, or are open for advanced research, to large conferences such as society meetings, those which have broad coverage of a field, are open for beginner researchers or interdisciplinary research. Choosing the right conference to participate in is the first step towards a fruitful conference experience.

The next step for the participant is to prepare the abstract. Recently, the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) initiative published a checklist for conference abstracts which includes a list of items and recommendations for abstracts to gain better positions in research conferences (Available from: <http://www.strobe-statement.org/index.php?id=available-checklists>. Cited 2014 Jun 22).

Generally, all conferences provide an opportunity to present as either a poster or oral presentation. Both kinds of presentations have distinct advantages. Poster presentations have the potential to attract larger audiences compared to oral presentations. Additionally, they provide opportunity for longer dis-

cussion compared to an oral presentation where time frame is limited to 10-15 minutes.

Another important difference between the two types of presentation is the way in which the presenter engages their audience. Poster presentations receive a diverse set of visitors who may be interested in particular parts of the poster relevant to their field of study or expertise. Since it is more interactive, it becomes challenging to the presenter to quickly gauge the interest and attention span of the audience and modify his presentation of the data. This makes it all the more important for the presenter to understand every bit of data that is presented along with the accurate in-depth methodology. Although oral presentations allow for more diagrammatic representation of results with the inclusion of supplementary data, which usually gets eliminated in poster presentations due to space constraints, there will be very few slots for oral presentations compared to poster presentations and many are given to faculty members. We recommend poster presentation for early career professionals. Details about oral presentation can be found elsewhere.<sup>5</sup>

Presenting poster provides several opportunities. Authors can find the opportunity to develop a national or international reputation, associate their name with a topic, generate network, find a job or a promotion, obtain funding and find help with manuscript preparation.<sup>6</sup>

It is advisable to design posters on a few key points. Some of the key issues in poster presentations include a comprehensive summary of the poster, better quality of diagrammatic data representation.<sup>7</sup> Recent study has shown that visually appealing representation of data is more likely to attract an audience than a poster filled with text.<sup>8</sup> The poster should be balanced in content such as text, data, diagrammatic representation, and adequate empty space to make sure it is not overcrowded. A very important aspect that needs to be noted is the font size that is used. Audiences usually like posters that can be read from at least 3-6 feet.

Basic sciences researchers are generally cautious while presenting their findings. Experiments involving cell culture and animal work take longer time when compared to clinical data. Many authors are cautious in the work they present in view of competition, more so if the data is novel and is in the preli-

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minary stages.

Whatever the type of presentation is, these are some important points to include: brief introduction, general methodology, results and brief discussion. Points such as Abstract, detailed methods or many references are unnecessary. The Title should attract reader's/listener's interest, summarize key findings and include less than 20 words. Avoid using questions, abbreviations or "new" or "novel" in the title. Readers can refer Wood and Morrison (2011) article for the example poster format.<sup>6</sup> Presenters are advised to prepare few handouts although it is not absolutely required.

A few studies were conducted to assess the discrepancy in the results presented in conference and subsequently published full length articles. Results showed significant disparity, suggesting the need for precaution while concluding/ making clinical decisions based on findings presented in poster form at a conference.<sup>9</sup> It cannot be assumed that conference attendees will always understand that the data presented in a poster or oral talk are many times preliminary and incomplete, and do not represent the entire picture. Authors should be aware of this issue and be sure to clarify when findings are due for further testing and validation.

Researchers in developing countries may encounter the additional challenge of getting funding for the travel. It should be noted that most of the international conferences have funding opportunities for minorities and scientists from developing countries. A few of the international organizations, for example International Brain Research Organization, have opportunities to fund the researchers (Available from: <http://ibro.info/professional-development/funding-programmes/travel-grants/>. Cited 2014 Jun 23).

In conclusion, poster presentations are very important learning opportunities in the career of a budding scientist. Beyond helping in the early dissemination of study data, the presentation of posters offers a chance to make excellent contacts among conference attendees, and greatly improves the curriculum vitae.

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# Correlation of Fine Needle Aspiration Cytology and Histopathology Diagnosis in the Evaluation of Breast Lumps

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## Abstract

**Background:** A large number of patients have been suffer from breast cancer worldwide and this trend is increasing. It is difficult to determine whether a lump is benign or malignant from clinical assessment; thus, the need for micropic and tissue analysis arises. **Methods:** This comparative retrospective cross sectional study was conducted in the Department of Pathology, Rehman Medical Institute, Peshawar, Pakistan from January 2006 to March 2013, to determine the value of fine needle aspiration cytology (FNAC) in the diagnosis of breast lump and to compare the result of FNAC with histological diagnosis to assess its accuracy. **Results:** Seventy-four cases with breast lumps were presented for FNAC. Of these, 32.4% were reported as a C2 lesion, 4.1% were reported as benign with atypical cells (C3), 8.1% cases were suspicious for malignancy (C4), and 55.4% were positive for malignancy (C5). On histopathology examination, out of 24 cases which were reported as C2 lesions, 95.8% were benign and 4.1% turned out to be invasive ductal carcinoma. Of the cases that presented as C3 lesions, one was diagnosed as benign duct ectasia, one with ductal carcinoma in situ, and one with invasive ductal carcinoma on histopathological examination. The cases that were diagnosed as C4 lesions all turned out to be carcinoma on histopathology. In this study, FNAC and histopathology diagnoses were strongly correlated [ $r = 0.92$ ,  $p < 0.001$ ]. **Conclusion:** Diagnosis of breast lump based on FNAC should be practiced as there is high correlation with histopathological finding. FNAC should be used as a routine diagnostic procedure due to its cost effectiveness, thus maximizing the availability of effective health care to patients with breast lesions.

**Keywords:** Breast Neoplasms, biopsy, Cytological Techniques, Fine-Needle Biopsy (Source: MeSH-NLM).

## Introduction

Breast cancer is the most common cancer in women both in the developed and developing world. In 2012 it were diagnosed 1.7 millions of cases worldwide and it is well-known that a half of cases and deaths occur in developing countries (International Agency for Research on Cancer, IARC. Available from: [http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223\\_E.pdf](http://www.iarc.fr/en/media-centre/pr/2013/pdfs/pr223_E.pdf), cited 2014 Jun 20).<sup>1</sup>

Breast lumps are one of the most prevalent presenting complaints in an outpatient department (OPD) in Pakistan.<sup>2</sup> About 90% are benign and of no grave consequences, but malignant lumps contribute to a consequential percentage of all breast lumps.<sup>3</sup> With growing vigilance in the general population, especially about breast pathologies, and the associated solicitude and stress that this condition may lead to, the knowledge that breast cancer can have grim consequences compels patients to seek medical advice.<sup>3,4</sup> It is difficult to determine whether a lump is benign or malignant from clinical assessment.<sup>5</sup> A confident diagnosis can be established in more than 95% of cases utilizing triple assessment (examination, imaging and histological studies).<sup>6</sup>

Fine needle aspiration cytology (FNAC) is a relatively simple, reliable, atraumatic, economical and complication-free technique for the evaluation of mass lesions. It can be facily reite-

rated if an adequate aspirate is not obtained.<sup>4</sup> FNAC is now a well-established technique for the investigation of women with suspected breast carcinoma.<sup>7</sup>

Fine-needle aspiration (FNA) has become one of the most important diagnostic tools for palpable breast masses and false-negative results have become a major concern. However, cytopathologists agree in certain parameters to the adequacy of an FNA specimen.<sup>8</sup>

It has been shown that FNAC has reduced the number of open biopsies because of its high diagnostic sensitivity and specificity. However, open biopsy is still preferred in some centers due to lack of expert cytologists.<sup>9</sup> The biopsy of the palpable breast lesion predicated on the histological study of the tissue specimens can provide all the reliable information to the surgeon and oncologist for modern therapeutic strategies as part of the decision-making regarding the patient's treatment. This technique permits the eventual use of neo-adjuvant therapy.<sup>10</sup> Different studies have determined that FNAC has a sensitivity ranging from 80% to 98% and a specificity of 99% to 100%.<sup>11</sup>

The purpose of the present study is to determine the value of fine needle aspiration cytology in the diagnosis of breast lumps and to compare the result of FNAC with histological diagnosis to assess its accuracy.

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## Methods

This was a comparative cross-sectional study conducted at Histopathology Department Rehman Medical Institute, Peshawar, Pakistan, from January 2006 to March 2013. Non-probability convenient sampling was used. The Ethical Review Board of Rehman Medical College, Peshawar, Pakistan approved the study. Attendants were informed of their right to refuse participation and of the respect of the confidentiality of their answers.

The guidelines of the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist for cross-sectional studies was followed in writing the present article.<sup>12</sup>

All female patients with unknown primary diagnosis of breast lump undergoing FNAC followed by excision biopsy, were included. Patients with recurrent malignancy, patients who underwent FNAC but did not undergo subsequent histopathological diagnosis, and patients under chemotherapeutic treatment were excluded from the study. The study included 74 cases.

FNA was performed utilizing a 5-millimeter (mL) or 10 mL disposable syringe for each sample and for each patient. No local anesthetic was utilized. The needle was inserted into the palpable lesions, either once or twice depending upon the size of the nodule. Cellular material was aspirated into a syringe and expelled onto slides. Three to four slides were prepared for each patient. A small or medium-sized drop of aspirate was put near the frosted edge of a slide that was placed on a table. A second slide was acclimated to spread the aspirated material in the same manner used to prepare a peripheral blood smear and one of the smears was wet fine-tuned in 95% methanol and stained with Hematoxylin and Eosin (H&E). The air dried smears were stained with Giemsa stain. The procedure was done within one hour, and the reports were signed-out within 2 to 3 days.

The biopsy specimens were fine-tuned in 10% formalin for 24 hours. Then gross examination was done in the Department of Pathology by consultant histopathologists. The gross and cut section findings were noted. Several bits were taken from opportune sites for processing and paraffin embedding. From each block, sections were cut at 4-5 microns thickness and stained with H&E.

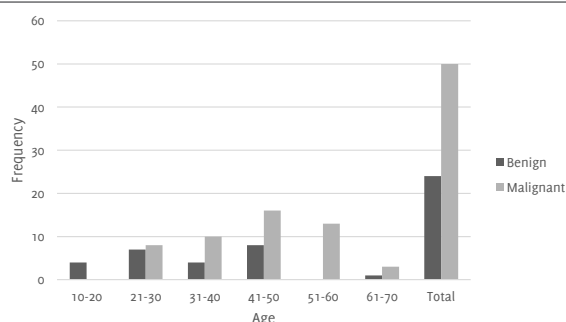
Statistical analysis was performed using the Statistical Package for Social Science (SPSS®) version 20.<sup>13</sup> Continuous data was displayed as the mean  $\pm$  standard deviation (SD), while the categorical and nominal data was presented as frequencies and percentages. Pearson's correlation was applied and a p-value of  $<0.05$  was taken as statistically significant with a confidence level of 95%.

## Results

The age range of the 74 patients included in this study was 15-70 years with mean age of  $41.43 \pm 13.421$ . The most effected age group was 41-50 years. Out of these 25 cases were benign and 49 were diagnosed as malignant. Highest frequencies of benign lesions were in the age group of 20-45 and the highest frequency of malignancy was in 30-55 year old women. The sensitivity of the test was 95.83% and specificity was 100%. Statistical

analysis by Chi-square test revealed a significant Chi-square value of 66.58 ( $P < 0.001$ ) (Figure 1).

**Figure 1.** Age Distribution of Patients with Benign and Malignant Breast Lump.



On cytology 24 patients (32.4%) had (C2) benign breast lesions. Out of these 24 cases, nine were reported as fibro-adenoma, five as fibrocystic disease, four as duct ectasia, three as proliferative breast lesion, two as lactating adenoma and one as pyogenic abscess. Out of 74 patients, three cases (4.1%) were benign with atypical cells (C3), six cases (8.1%) were suspicious for malignancy (C4), and 41 (55.4%) were positive for malignancy (C5) (Table 1).

Out of a total of 74 cases that underwent a surgical procedure, 24 were reported as benign lesions. Among these 24 cases, eight were reported as fibro adenoma, three were diagnosed as a phyllodes tumor, five as fibrocystic disease, six as duct ectasia and one had sub-acute mastitis along with duct ectasia. Among 24 cases one was reactive hyperplasia.

The remaining 50 cases were diagnosed as carcinoma of breast on histopathology. Among these, 39 were invasive ductal carcinoma, three with invasive lobar carcinoma, and two were diagnosed as infiltrating ductal carcinoma.

One case was of mixed invasive and mucinous carcinoma, one medullary carcinoma, one with ductal carcinoma with medullary feature, one with malignant adnexal tumor, and one with border line stromal sarcoma. One was a case of in-situ ductal carcinoma. Out of these 39 cases with invasive ductal carcinoma, 21 of them were grade III, 17 grade II and only one was grade I. One case was reported as a C2 lesion (proliferative breast lesion) on biopsy and it was proved to be invasive ductal carcinoma.

**Table 1.** Cytology Finding of Breast Lump on Fine Needle Aspiration (FNA)

Stage [n=74]	Freq. (%)
C2- Benign	24 (32.4)
Fibro adenoma	9 (12.2)
Fibrocystic	5 (6.8)
Duct ectasia	4 (5.4)
Proliferative breast lesion	3 (4.1)
Lactating adenoma	2 (2.7)
Pyogenic abscess	1 (1.4)
C3- benign with atypical cells	3 (4.1)
C4-suspecious for malignancy	6 (8.1)
C5-malignant	41 (55.4)

Of the cases that were diagnosed as C3 lesions (benign with atypical cells), one was diagnosed as benign duct ectasia, one with ductal carcinoma *in situ* and one with invasive ductal carcinoma. All six cases diagnosed as C4 lesions (suspicious for malignancy) turned out to be malignant on histopathology. Out of these, five were invasive ductal carcinoma and one was borderline stromal sarcoma. The correlation between FNAC and histopathology is shown in **table 2**.

## Discussion

Breast cancer is one of the most frequently occurring clinical conditions worldwide.<sup>14</sup> Although there has been little success in controlling the disease, it is of general accord that a confident preoperative diagnosis should be made before surgery, thus making FNAC a reliable diagnostic tool. It is a cheap and complication-free technique. The cost is economical, equipment is low-priced and the technique is relatively easy.<sup>15</sup> The procedure can also be performed anywhere. Furthermore, FNAC has a high accuracy, making it a reliable procedure.<sup>14</sup> The results can be obtained quickly and it is less invasive compared to tissue biopsy.

FNAC is an easily diagnostic method for determining the causes of a breast lesion. Its success is due to its accuracy and cost effectiveness for a breast lump. Therefore, it has many advantages for patients and physicians.<sup>16</sup>

In this study the sensitivity of the test was 95.83% and specificity was 100%. Statistical analysis by Chi-square test revealed Chi-square value 66.58 ( $P < 0.001$ ), which is statistically significant. In a similar study performed at Khyber Teaching Hospital, Peshawar, Pakistan, from August 2002 to May 2003 the sensitivity and specificity of FNAC was 91.66% and 96.96%, respectively.<sup>3</sup> The results of this study were similar to a study performed at the University Medical and Dental College, Faisalabad, Pakistan, from 2008 to 2011 which showed a sensitivity of 96.42%.<sup>1</sup> Similarly, a study performed by Waqar describes the sensitivity of FNAC as almost 92.6%.<sup>17</sup> In the literature, sensitivity ranges from 94-99% and specificity reaches up to 100%.<sup>11,19</sup>

Keeping in mind the aim and objectives of the present study, 71 of the 74 cases were diagnosed on FNAC as malignant and were correlated with their histological diagnosis. All the cytologically-diagnosed malignant lesions were proven to be malignant on histology. On FNAC, 24 were benign with one of the cases of benign breast lump turning out to be malignant on histological diagnosis. Fibro adenoma is a common benign breast lump in the majority of the young females.<sup>19</sup> Three cases out of 74 on FNAC were C3 lesions (benign with atypical cells) on histological finding, with one turning out to be benign and

two being malignant. Six cases were diagnosed as C4 lesions (suspicious for malignancy) on FNAC with all of them being malignant on histological examination. FNAC of the breast can reduce the number of open breast biopsies.<sup>8</sup> The procedure has some challenges due false positives or uncertain test results in the diagnosis of fibrocystic disease, adenosis, epithelial hyperplasia with or without atypia, apocrine metaplasia, radial scar, and papilloma.<sup>20</sup>

The current study showed that FNAC is a reliable method. It helps in diagnosing breast lumps without surgical intervention and it also helps in pre-operative decision-making. From this study we can presume that FNAC has an association with histopathological findings and ought to be performed on standard premises. FNAC is also a good tool for follow up if there is recurrence of breast lesions. In the presence of budget constraints and personnel shortage, hospitals are required to demonstrate even great cost effectiveness in the diagnosis of breast lesions. Confident preoperative diagnosis is becoming increasingly important. FNAC should be practiced on routine basis as it is cost effective and reliable and thus maximizes the availability of health care for patients with breast-related pathologies.

There are some difficulties and limitations that need to be mentioned about FNAC, first at all, both false-negative and false-positive results can occur.<sup>21</sup> The most significant difficulty in making a diagnosis is the overlapping features of different lesions.<sup>22</sup> Other limitations to this procedure include, for example, that the lack of cellular pleomorphism can often give a false negative diagnosis. Our study was of a retrospective design where patients not undergoing an operation were not included. This suggests the possibility that false-negative cases may have been missed.

FNAC has certain limitations on accounts of inadequate sample and suspicious diagnoses. The overlapping of cytological features can cause cytodiagnostic errors and wrong diagnoses when the histological architecture from Inflammatory lesions mimics Malignancy.<sup>23</sup>

The normal surgical protocol in Pakistan is in which the biopsy is not preceded by FNA; the FNA has not been given its due importance in Pakistan. The protocol of doing a FNA before a biopsy has been established in a few pathology labs and hospitals. This study shows how much of a useful procedure FNA can be, perhaps reinforcing the paradigm shift in modern medicine where minimal invasive or non-invasive procedures are beginning to replace invasive procedures.

**Table 2.** Comparison of Fine Needle Aspiration Cytology (FNAC) and Histopathology Findings.

Cases (%)	FNAC	Histopathology Finding	
		Benign (n=24)	Malignant(n=50)
0 (0)	C1-unsatisfactory	0	0
24 (32.4)	C2-Benign	23	1
3 (4.1)	C3-Benign with atypical cells	1	2
6 (8.1)	C4-Suspicious for malignancy	0	6
41 (55.4)	C5-malignant	0	41

Note: Fine needle aspiration cytology and histopathology diagnosis were strongly correlated,  $r(72) = 0.71$ ,  $p < 0.001$ .

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## Author Contributions

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# Attitude towards New Packaging to Reduce Condom-carrying Embarrassment among Thai Youth, A Cross-sectional Study

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## Abstract

**Background:** Human Immunodeficiency Virus (HIV) incidence has been increasing in Thai youth, mostly from unsafe sex. Embarrassment with carrying condom was one of the main reasons. This study aims to evaluate attitude towards condom use, sexual behavior and the new condom packaging that merges with daily life products in Thai youth. **Methods:** A cross-sectional study was conducted among volunteers aged 15-24. New packaging were demonstrated and the volunteers were provided with questionnaires to complete in privacy booth and submit anonymously. **Results:** Of 680 participants with mean age of 19.7±2.7 years and 59.9% females, half of them thought condom should be carried and used. However, the same group did not actually do. Two-thirds of participants were interested and would use the packaging, citing these reasons charming, convenience, and disguise of condom. Females preferred the packaging significantly more than males. **Conclusion:** Disguising condom packaging, as phone charm and key ring, might be another safe and practical way to encourage youth to carry condoms around.

**Keywords:** Condoms, Product Packaging, Adolescent, HIV, Sexual Behavior (Source: MeSH-NLM).

## Introduction

Human Immunodeficiency Virus (HIV) is a retroviruses founded in 1980s.<sup>1</sup> This virus infects and depletes CD4+ T cell, which is a lymphocyte serving in immunological response. After getting infected, the person is known as HIV-positive. When the CD4+ T cell count is less than 200/μL, the current Centers for Disease Control and Prevention (CDC) classification system defines this person to have Acquired Immunodeficiency Syndrome (AIDS), which might further develop opportunistic infection such as *Pneumocystis jiroveci*, atypical mycobacteria, and *Cytomegalovirus*.<sup>1</sup>

In 2007, it was estimated that there were 546,578 people living with Human Immunodeficiency Virus (HIV) in Thailand.<sup>2</sup> The significant modes of transmission include spouse transmission, male sex with male (MSM), injecting drug user (IDU), sex worker, and casual sex.<sup>3</sup> Most of them get infected from unsafe sex.<sup>3</sup> Somehow, these population tend to have more risky behaviors.<sup>4</sup>

Because most Thai people have better HIV education, they accept living with AIDS victims more than the past.<sup>2,5</sup> However, the infected people feel that the stigma is still strong and they are discriminated from the society.<sup>2</sup> This stigma was reported to cause depression, social isolation and shame.<sup>6,7</sup>

Despite a huge collaboration, the HIV incidence has not declined but increased in youth and adolescents, which could be illustrated by an increase in HIV prevalence of military recruits (18-24 years old), blood donors (21-30 years old), and sexually transmitted infection (STI) clinics (15-24 years old).<sup>8-11</sup> Despite good HIV knowledge and negative attitude towards risky behavior, a large number of youth have unsafe sex; almost 50% had sex without condoms and several of them have multiple partners.<sup>12,13</sup> This trend could lead to an even higher HIV prevalence among young people.

Male condom is a barrier tool used during sexual intercourse for contraception and prevention of sexual transmitted disease.<sup>14,15</sup> It prevents male ejaculated semen from entering partner's body and also block secretion from partner to enter his own body. It was reported that the pregnancy rate was 2% per year and the rate of sexual transmitted disease was significantly decreased if condom was used properly.<sup>16,17</sup>

There are many HIV preventive programs which promote the use of condom including campaigns such as "100% Condom Program".<sup>10,13-15</sup> One of the main reasons why youth do not use condom is the embarrassment of carrying condom.<sup>18-20</sup> The reasons against carrying condom were reported that males are

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afraid of being publicly exposed and humiliated while females are afraid of parent disapproval, gossiping, or being considered as anticipating having sex and being promiscuous.<sup>21,22</sup> To solve the problem, new male condom packaging merged with daily life products, such as phone charm and key ring, was developed to promote carrying condom. This study aims to assess Thai youth's attitude towards condom use and sexual behavior, evaluate the new condom packaging in encouraging youth to carry condom, find the key factors in good condom packaging, and find the association between the findings.

## Methods

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement is followed in writing this article.<sup>23</sup> This was a cross sectional study using self-administered questionnaire which took place in Siam Square, which was the most famous and crowded youth center in Bangkok, the capital city of Thailand, August 2009.

Participants were chosen by purposive sampling. Inclusion criteria was youth, which is defined as aged 15-24 years old by the United Nations.<sup>24</sup> They also had to be Thai and hang out in Siam Square. The study was announced in the national and local television channels, radios, and newspapers a week earlier to invite Thai youth to participate in the study. Participating in this study, the participants were emphasized that their participation was voluntary. They did not have to answer questions they did not want to and their information would be confidential. The study objectives were explained to the participants and the new condom packaging demonstrated. Later, they were asked to completed questionnaire in privacy booths and submitted anonymously.

New condom packaging was designed to merge with daily life products, such as mobile charm, earrings, and bag accessory because they were things youth love to use in their daily life and condom could be in disguise, or designed beautifully despite seeing condom in these products. The packaging was made by students at the Faculty of Medicine, Chulalongkorn University, Thailand. This packaging was piloted in 111 1st – 3rd year volunteer medical students because their age fell in the range of the study participants (*Figure 1*). The packaging was demonstrated by five volunteers. After seeing the demonstration of carrying condom, the subjects were asked for their opinions about the condom products. Their responses were grouped and used to develop the questionnaire.

The questionnaire development was based on previous literatures and the mentioned student responses. The questionnaire was piloted in 20 volunteer medical students. It consisted of four parts: general information, attitude towards condom use,

sexual behavior, and attitude towards AIDS and new condom packaging, respectively.

With 95% confidence interval, the estimated proportion derived from pilot study which students liked the new packaging 71.2%. The desired precision was 0.07. The sample size required was 161.

Data analysis was conducted by using SPSS© software (version 16.0 for Windows, copyright 2007, SPSS Inc.). Percentage was used for descriptive data. Because the participants could choose not to answer any questions that they felt uncomfortable with, missing values were omitted and the percentage calculation was based on the total amount of answers, which was not similar to the total number of participants. Open question answers were grouped into categories and reported as frequency. Cross tabulation and Chi-squared test were used to find the association between categorical variables. Fisher exact test was used in the paired categorical variable with expected value less than 5. A p value less than 0.05 was considered statistically significant.

**Table 1.** Socio-demographic characteristics of participants.

Characteristic	Freq. (%)
Gender	
Female	406 (59.9)
Male	272 (40.1)
Sexual preference	
Heterosexual	497 (75)
Homosexual	70 (10.5)
Bisexual	96 (14.5)
Current Education Study level	
Undergraduate	438 (64.9)
High school	220 (32.6)
Postgraduate	17 (2.5)
Occupation	
Student	549 (81.5)
Employee	84 (12.5)
Business people	28 (4.2)
Merchants	7 (1)
Government officer	6 (0.9)
Other history	
Drinking alcohol	380 (56.4)
Smoking	294 (18.6)
Drug user	39 (5.8)

**Figure 1.** Condoms Packaging Designs.



## Results

### *Socio-demographic Characteristics of Participants*

There were 1,104 participants in this study; 324 were excluded because they were out of age range (15-24 years). Six hundred eighty participants were included in the analysis. Their mean age was  $19.7 \pm 2.7$  years. Their socio-demographic characteristics were described in *Table 1*.

### *Attitude Towards Condom Use*

Most of participants (72.1%) thought it was necessary to always use condom no matter whom they had sex with while 3.4% said they would not use condom in any circumstances. When the participants were asked about their attitude towards carrying condom, 10.8% thought the condom should not be carried. Three major reasons were given including; they could go and buy (44.8%); carrying condoms made them look bad (26.0%) and they did not intend to have sex before marriage (19.8%), respectively. However, embarrassment about buying condoms was reported to be the main reason why the participants did not use condoms (49.0%).

### *Sexual Behavior*

It was found that 30.4% of participants had already had sex. Among the participants that had already had sex, majority of them (44.7%) had sex less than once a week and 33.5% used condom every time. About 13% had multiple partners; over a third of them thought there were differences between having sex with their partners and casual partners. An open question was used to assess the differences. They reported that the differences were difference in sexual emotion between loved and unloved partners (77.5%) and difference in physical appearance (12.5%). Only 6.7% reported safety issues to be the reason for the difference. On the other hand, 88.2% said that there was an increased risk in getting infected from casual partners, while the other 11.8% said there was no increased risk.

The age of first sex experience ranged from 9-23 years with a mean of  $17.9 \pm 2.5$  years. About 40% did not use condom during their first sex. Only 8.9% of the participants actually carried condoms, while most of them (91.1%) did not.

### *Attitude Towards AIDS and the New Packaging*

Most participants thought that AIDS was a very important public health problem and sexual transmission was the major way to get infected.

A lot of participants (85.1%) found that the new condom packaging was interesting. Among the interested respondents, the first three products they liked most were mobile charm, key ring, and accessory that attached to belt, neck tie, shoes or hat. The first three reasons were the product's charming design, the disguise of condom, and the convenience of carrying, respectively.

The products that the participants did not like were earrings, and other accessory such as bracelet and necklet. The reasons were the obviousness of the condom and the bad design.

Most respondents (66.4%) said that they would be confident in using the products and 33.6% said they would not. The reasons why they were confident were similar to the reasons why they

**Table 2.** Summary of results.

Topics	Freq. (%)
Condom attitude (What participants thought)	
Using condom	
Always use before marriage	486 (72.1)
Only with casual partners	42 (6.2)
Would try to use	77 (11.4)
Would not try to use	46 (6.8)
Not use at all	23 (3.4)
Why not use condom?	
Embarrassment by buying	308 (49)
Laziness to buy	110 (17.5)
Embarrassment by carrying	79 (12.6)
Decrease in pleasure	72 (11.5)
Unnecessary to use	59 (9.4)
Carrying condom	
Should carry	602 (89.2)
Should not carry	73 (10.8)
Sexual behavior (What participants really did)	
Frequency of sexual intercourse per week	
<1	88 (44.7)
~1	47 (23.9)
2-3	36 (18.3)
>3	26 (13.2)
Condom use	
Every time	65 (33.5)
>50%	50 (25.8)
<50%	62 (32)
Never	17 (8.8)
Condom use with casual partners	
Always	81 (75)
Occasionally	20 (18.5)
Never	7 (6.5)
If there was no condom at the time they were going to have sex	
Stop having sex	28 (26.2)
Go to buy condoms	51 (47.7)
Continue having sex	28 (26.2)
Condom use in first sex	
Yes	122 (60.4)
No	80 (39.6)
Carrying condom	
Yes	18 (8.9)
No	185 (91.1)
Attitudes toward AIDS	
AIDS problem	
Very important	583 (86.8)
Important	79 (11.8)
Not much important	9 (1.3)
Not important at all	1 (0.1)

**Table 2 (continue).** Summary of results.

Topics	Freq. (%)
Major mode of transmission	
Sexual transmission	639 (96.5)
Intravenous drug use	16 (2.4)
Vertical transmission	7 (1.1)
Attitudes towards the new packaging	
Most interesting packaging	
Mobile charm	283 (45.2)
Key ring	153 (24.5)
Accessory	110 (17.6)
Least interesting packaging	
Earrings	318 (50.8)
Other accessory	204 (32.6)

liked the products. If this new packaging were launched, 72.9% said it would not affect their daily lives. Moreover, 78.3% of the participants said that the government should promote the idea of new packaging, and 66.5% said they would buy if the products were on sale.

#### Attitude and Behavior in Condom Carrying

There were two significant associations between attitude and behavior. Concerning carrying a condom, only 10.1% of the participants, who thought they should carry condom, actually carried condoms and 89.9% of them did not carry condom; however, all of the participants, who thought they should not carry condom, did not carry condom ( $p < 0.001$ ). Concerning using condom, only 54.5% of participants, who suggested using condom every time, actually used condom every time, while 6.0% of participants, who suggested not to use condom every time, really used condom every time ( $p < 0.001$ ).

Females were significantly more interested in the products than males. Females were interested in the products 86.0%, while males were interested 80.7% ( $p = 0.025$ ). However, there were no associations between gender and the intention to use the product ( $p = 0.204$ ), gender and the intention to buy the products ( $p = 0.053$ ), and gender and the effect of condom products to daily lives ( $p = 0.292$ ). Summary of results is described in **Table 2**.

## Discussion

Most participants thought that condom should be carried and used. However, they did not actually carry and use. The new packaging was also interesting and attractive to use, especially for female.

In this study, there is discordance between attitude and behavior. This might be resulted from social stigma. Sarkar, revealed that the main factors contributing to the failure in promoting condom use in Thailand were social and cultural factors, especially the life style, prostitutes and brothel system and the stigma to HIV/AIDS.<sup>25</sup> This study also showed that the embarrassment with buying or carrying condom is the main factor why Thai people did not carry condoms. Carrying condoms makes young women look like desiring sexual intercourse.<sup>26,27</sup> To sum up, social stigma might cause the discordance between

attitude and behavior, resulting in embarrassment with buying or carrying condom; thus, decreasing this stigma was the key to success for all the HIV campaigns in Thailand. This is also in concordance to previous studies.<sup>28,29</sup>

Although almost all respondents knew that the major mode of HIV transmission was sexual intercourse, only part of them had safe sex or use condom every time. This result is similar to other study findings.<sup>30,31</sup> One study showed that although Thai people knew about HIV and its burden, only about a quarter of the adult and 20% of youth realized that they were at risk of the infection, resulting in the high rate of unsafe sex (United Nations Development Programme, UNDP, Opinion poll on HIV/AIDS Thailand. 2004. Available from: [http://www.undp.org/content/thailand/en/home/library/hiv\\_aids/AIDSOpPoll/](http://www.undp.org/content/thailand/en/home/library/hiv_aids/AIDSOpPoll/), updated 2004 May 1; cited 2014 Mar 30). Similarly, UNGASS Country Progress Report Thailand indicated that despite high awareness of safe sex and the condom effectiveness in preventing HIV and STI, there is still lack of concern and skill in condom use; therefore, only 20-40% of students reported using condom every time they had sex (United Nations Programme on HIV/AIDS, UNAIDS, United Nations General Assembly Special Session, UNGASS, country progress report Thailand. 2010. Available from: [http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2010countries/thailand\\_2010\\_country\\_progress\\_report\\_en.pdf](http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2010countries/thailand_2010_country_progress_report_en.pdf), updated 2010; cited 2014 Mar 30). Moreover, this study showed that even though the participants knew that they should carry and use condom, they did not actually do it. This showed that, apart from social stigma, there was also a lack of personal concern, which might cause many campaigns to fail.

Most participants appreciated the new condom packaging. The beautiful design is the main reason why they like the packaging. Clement explained that packaging design had an influence on purchasing the products.<sup>32</sup> The more attractive they are, the more likely the consumers would buy the products. Since female participants were interested in the products more significantly than the males, further studies were highly recommended to find the reason why males were less interested in the product than females and how to encourage them to carry condom more.

Limitation of this study includes the fact that it was conducted at Siam Square which was a youth center of Bangkok, the participants had their uniqueness. They were well educated, medium to high socioeconomic group of the population. Moreover, there were differences between Thais and other country citizens as such this study result might not be generalized.

There are discordances between attitude and behavior in using and carrying condom. A new condom packaging could reduce embarrassment of carrying condom. In dealing with youth, charming and disguising condoms are important. Disguising condom packaging as phone charm and key ring, might be another safe and practical way to encourage youth to carry it.

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## Author Contributions

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# Sub-tenon Anaesthesia versus Intracameral Anaesthesia in Patients Undergoing Cataract Extraction: A Comparative Study of the Level of Pain, Visual Perception and Anxiety

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## Abstract

**Background:** Phacoemulsification is a modern method of cataract extraction. Sub-tenon anaesthesia used to be the preferred anaesthetic technique for this procedure before intracameral anaesthesia gained its popularity in recent years. Nevertheless, many surgeons still believe that sub-tenon anaesthesia is better than topical anaesthesia. This study aimed to evaluate and compare the experiences of patients who were treated for cataract by phacoemulsification surgery using either sub-tenon or intracameral anaesthesia. **Methods:** Cross-sectional study conducted at Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia. Participants were asked to complete a questionnaire within 1-2 hours following surgery. The questionnaires were designed to gather information on the patient's level of anxiety, visual perception and amount of pain experienced during cataract surgery. **Results:** A total of 62 patients were included in the study. Thirty-one patients received anaesthesia by sub-tenon injection, whereas another 31 patients received anaesthesia by intracameral injection. There were no significant differences in the level of pain experienced by the two groups of patients during instillation of anaesthesia and during surgery ( $p=0.205$  and  $p=0.592$ , respectively). There were also no significant differences in terms of visual perception and anxiety levels during surgery between the two groups ( $p=0.178$  and  $p=0.731$ , respectively). **Conclusion:** Intracameral anaesthesia obviates the need for an injection during cataract surgery and is as comfortable for patients as sub-tenon anaesthesia in terms of visual perception, level of pain, and anxiety.

**Keywords:** Phacoemulsification, Cataract Extraction, Anesthesia Local, Anxiety (Source: MeSH-NLM).

## Introduction

Phacoemulsification is a modern and popular method of cataract extraction. Sub-tenon anaesthesia, also known as parabolbar anaesthesia, pinpoint block, or episcleral block, is a popular alternative to peribulbar or retrobulbar anaesthesia.<sup>1,2</sup> Sub-tenon space is a potential space between the capsule and the outermost layer of the eyeball, namely, the sclera. Local anaesthetics instilled into this space produces immediate analgesia and akinesia of the eyeball by diffusing posteriorly into the retro-orbital space to block the traversing sensory and motor nerves.

Intracameral anaesthesia is another method used in cataract surgery. It involves the injection of anaesthetics directly into the anterior chamber of the eye at the beginning of the surgery. It has gained popularity recently, with lidocaine being the commonest drug used for this purpose.<sup>3</sup> The advantages of intracameral anaesthesia include the ease of application via a preexisting corneal wound. Many studies have been conducted to compare the level of pain during phacoemulsification with various techniques of local anaesthesia.<sup>2,4,7</sup> Although intracameral anaesthesia is known to provide pain-free surgery, many surgeons still believe that regional anaesthesia via the sub-tenon route is better than topical anaesthesia.<sup>2,5</sup>

The aim of this study was to compare the level of pain experienced during phacoemulsification in patients receiving either intracameral or sub-tenon anaesthesia. Other variables, including the level of anxiety and visual perception, were also examined. Comparison between sub-tenon and intracameral anaesthesia in terms of anxiety and visual perception has not been reported in previous studies.

## Methods

A cross-sectional study was conducted at the Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Malaysia, from March to June 2010, and the protocol was approved by the ethics committee of UKMMC. Written informed consent was obtained from every patient participating in this study. The study subjects were men and women aged between 45-80 years old who were undergoing phacoemulsification surgery for cataracts. Patients included in the study were those willing to undergo routine cataract surgery performed by a trained ophthalmologist using either sub-tenon or intracameral anaesthesia. Exclusion criteria were as follows: subject age < 18 years; known diagnosis of anxiety or psychiatric disorders; patients requesting or requiring sedation; and complicated or prolonged (>1 hour) cataract surgery.

*About the Author: This study was conducted by a group of medical students with a supervisor. Majority of the authors were graduated in 2012 and they are currently doing their internship in various field.*

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Patients were selected using universal sampling. All patients received standard preoperative medications, which included a combination of guttae tropicamide 0.8% (Alcon laboratories, USA) and guttae phenylephrine 5% (Alcon laboratories, USA) for pupil dilatation. Topical bupivacaine was instilled preoperatively to reduce the stinging sensation during cleaning with 5% povidone iodine. None of the patients received any preoperative or intraoperative sedation. Three experienced surgeons who routinely operated with sub-tenon anaesthesia and three other surgeons who routinely operated with intracameral anaesthesia performed the surgery for this study. The anaesthetic agents used were intravenous 2% lidocaine hydrochloride (lignocaine injection 2%, Pfizer Ophthalmics, New York, USA) for the intracameral group and a combination of lidocaine and bupivacaine for the sub-tenon group. Phacoemulsification surgery was performed after routine preparation and draping and using routine methods. Complicated surgeries were excluded from the study.

**Table 1.** Comparison of Pain Level during Instillation of Anaesthesia and during Surgery.

Pain Level	During instillation of anaesthesia		During surgery	
	Intracameral n (%)	Sub-tenon n (%)	Intracameral n (%)	Sub-tenon n (%)
Grade 0	9 (28.1)	18 (56.3)	16 (50.0)	18 (56.3)
Grade 1	20 (62.5)	8 (25.0)	14 (45.16)	10 (31.3)
Grade 2	2 (9.4)	2 (7.5)	1 (3.1)	2 (6.25)
Grade 3	Nil	2 (7.5)	Nil	1 (3.23)
Grade 4	Nil	1 (3.7)	Nil	Nil

Note: Mann-Whitney U test: During instillation of anaesthesia  $p=0.205$ , During surgery  $p=0.592$ .

All patients were requested to complete a questionnaire within 1-2 hours following their surgery. The questions mainly concerned the levels of pain, visual perception and anxiety levels experienced during instillation of anaesthesia and during surgery. In cases where the patient was illiterate or had difficulty in reading, the scales used in the questionnaire were explained and a verbal response was obtained.

Patients were asked to grade the levels of pain experienced during delivery of anaesthesia and during surgery on a visual analogue pain scale (VAS). Patients were asked to grade the pain they felt on a linear scale of 0 to 4 (grade 0 = no pain, grade 1 = mild pain, grade 2 = moderate pain, grade 3 = severe pain, grade 4 = maximum imaginable pain). Patients were also asked about their visual perceptions during surgery.

Anxiety level was assessed using the State-Trait Anxiety Inventory (STAI). Calculations were conducted online. For the purpose of analysis, the scores were grouped into four categories: grade 1 (mild anxiety), grade 2 (moderate anxiety), grade 3 (severe anxiety) and grade 4 (very severe anxiety).

Statistical analysis was performed using SPSS 13.0 for Windows (SPSS Inc). Analyses of categorical data were performed using the Chi-square test. Comparison of the mean age between the two groups was conducted using the independent samples t-test, while comparisons for ordinal and other numerical variables were mainly conducted using the non-parametric Wilcoxon Mann-Whitney test.  $p$ -values of less than 0.05 were considered statistically significant.

## Results

A total of 62 patients were included in the study. Thirty-one patients (mean age  $68.6 \pm 6.7$  years) received intracameral local anaesthesia and 31 patients (mean age  $67.3 \pm 7.2$  years) were given sub-tenon anaesthesia. Age difference was not statistically significant between the two groups ( $P=0.497$ ).

Most patients in this study reported no pain (Grade 0) or mild pain (Grade 1) during instillation of both types of anaesthesia ( $P=0.205$ ). Similarly, majority of the patients in both groups reported pain scores of grade 1 or 0 during surgery, and no significant difference was observed ( $P=0.592$ ) (Table 1).

Patients in both groups reported seeing various types of images during the procedure, ranging from hand motions, lights, and various colours or combination of images. Six patients reported seeing no images at all. For the purpose of analysis, these various images were grouped based on the number of

images reported (Table 2, 3). Most patients in the sub-tenon group saw one to two images during surgery, with 28.12% of them seeing two images. For the intracameral group, majority of the patients (40.62%) saw two images, and 34.38% saw only one image. There were no significant differences between the two types of anaesthesia in the number of images reported ( $P=0.178$ ). Anxiety levels in the two groups were approximately equal, with more than 50% of patients in both groups reporting only mild (Grade 1) anxiety during surgery with no significant difference between the groups ( $P=0.178$ ) (Table 4).

**Table 2.** Qualitative Description of Visual Sensation during Surgery for Both Groups.

Visual sensation	Sub-tenon [n (%)]	Intracameral [n (%)]
Nothing	4 (13%)	2 (6%)
Light	9 (29%)	6 (19%)
Movement	4 (13%)	3 (11%)
Colours	Nil	1 (3%)
Light and movement	14 (45%)	19 (61%)

**Table 3.** Number of Visual Sensation Reported by Patients.

Number of images	Sub-tenon [n (%)]	Intracameral [n (%)]
Nothing	4 (12.5)	2 (6.3)
1 image	14 (43.8)	11 (34.4)
2 images	9 (28.1)	13 (40.6)
3 images	5 (15.6)	1 (3.1)
4 images	Nil	5 (15.6)

Note: Mann-Whitney U test  $p=0.178$ .

**Table 4.** Comparison of Anxiety Level between the Sub-tenon and the Intracameral Group.

Anxiety level	Sub-tenon [n (%)]	Intracameral [n (%)]
Grade 1	23 (72)	22 (69)
Grade 2	7 (22)	7 (24.3)
Grade 3	1 (3.1)	2 (6.2)
Grade 4	1 (3.1)	Nil

Note: Mann-Whitney U test p=0.178.

## Discussion

Numerous studies have reported various complications of regional anaesthesia in comparison with topical or intracameral anaesthesia during cataract surgery.<sup>4,8</sup> Until recently, peribulbar anaesthesia was deemed to be the superior technique for cataract surgery as it allows for a less painful and less difficult surgery.<sup>9</sup> However, papers published more recently suggest that regional anaesthesia is unnecessary for routine phacoemulsification.<sup>10,11</sup> Pain is not the only significant factor when describing patient's experience during phacoemulsification. Visual analogue pain scale (VAS), which was used in this study, is known to provide reproducible results.<sup>12</sup> In our study, patients receiving intracameral anaesthesia reported levels of pain similar to those reported by patients who received sub-tenon injection. The combination of preoperative topical bupivacaine administration and intracameral injection of lidocaine was found to be more superior than using topical anaesthesia alone.<sup>13</sup> Iris manipulation and stretching of the uveal tissue can irritate patients under topical anaesthesia, and additional anaesthesia is required in such circumstances.<sup>13</sup>

Intracameral anaesthesia utilises short acting lidocaine 2%, whereas the combined regime of lidocaine and bupivacaine used for sub-tenon injection may have an anaesthetic effect that lasts for up to an hour. For this reason, difficult cataract cases for which duration of extraction surgery could potentially be longer may not be suitable candidates for intracameral anaesthesia. Nevertheless, experienced surgeons may still opt for intracameral injection to avoid the unnecessary complications of regional anaesthesia and in view of the ease of instillation and cost-effectiveness.

STAI is a set of questionnaires used to assess the anxiety level in adults. The simplicity of the STAI instrument makes it ideal for this purpose, even for evaluating individuals with lower educational backgrounds.<sup>14,15</sup> Adapted in more than forty languages, the STAI is the leading measure of personal anxiety worldwide. STAI contains 40 questions, each with four possible responses: not at all, somewhat, moderately so and very much so. Au Eong *et al.*, reported that up to 15.4% of patients admit suffering from fright during surgery with topical anaesthesia.<sup>16</sup> In the present study, both groups of patients reported similar levels of anxiety, and most of them were having only mild anxiety throughout the procedure. Anxiety during surgery may arise from pain experienced during the procedure, but the surrounding environment and the visual perception during surgery may play an important role as well. Reaffirmation from the surgeon, friendly personnel, as well as relaxing environment may help to put patient at ease and keep them calm throughout the surgery. The possible role of environmental factors was not examined in this study; similar ambient was created

for both groups of patients by using the same medical staff for all cases.

Subjective visual sensations during cataract surgery were previously described as seeing light, various colours, movements or even instruments.<sup>16</sup> Previous studies reported that almost 80-87% of patients with sub-tenon block perceived light during surgery, compared to 94%-100% of patients with topical anaesthesia.<sup>16-19</sup> In this study, patients reported similar visual sensations, which were described as seeing different colours, movements and even instruments during the procedure. Interestingly, the visual experience was not significantly reduced by the use of sub-tenon anaesthesia. Theoretically, intracameral lidocaine injection has no effect on the optic nerve, and it is thus expected that more patients in the intracameral group would experience more visual sensations compared to the regional block group.<sup>19</sup> Chung CF *et al.*, suggested that bright light from the microscope might induce bleaching of photoreceptors, which could, in turn, affect the vision even under intracameral anaesthesia and hence reduce the visual sensation during surgery.<sup>20</sup>

Limitations of this study include the lack of a control group, non-random sampling design, and the use of self reporting and subjective description by the patients. Although the bias of variability had been partially eliminated by the use of standard questionnaires, pain and anxiety levels were still subjected to patient's perception, which may vary individually.

Choice of anaesthesia should always be made based on several considerations. Status of the patient and the surgeon's experience must be considered to ensure that the best choices are made. Surgeon's experience is an especially important consideration in choosing the best anaesthesia for patients undergoing complicated cataract surgery.

In conclusion, this study further supports the effectiveness of intracameral anaesthesia, as compared to sub-tenon regional anaesthesia, in maintaining patient's comfort and alleviating anxiety and pain during routine cataract surgery. Apart from akinesia, sub-tenon administration does not provide additional benefits for routine cataract surgery. Therefore, we believe that surgeons can safely select intracameral anaesthesia for patients undergoing uncomplicated cataract surgery.

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# Awareness and Practices of Non-Pharmacological Approaches for Management of Hypertension in a Geriatric Population

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## Abstract

**Background:** There is an increase in the prevalence of hypertension all over the world, including India. Hypertension can be initially managed with non-pharmacological measures. This study aims to assess the knowledge of non-pharmacological measures to control hypertension and its application in a geriatric hypertensive population. **Methods:** The study was conducted at the Department of Physiology, SVU, Vadodara, India. A total 110 hypertensive patients were included in the study and a non-validated survey was conducted to examine knowledge of non-pharmacological measures to control hypertension in this group of patients. Frequencies, percentages, means and standard deviations were calculated and reported. **Results:** Only 10% of the respondents knew the normal values for blood pressure. Approximately 38% of the subjects did not measure their blood pressure regularly. A total of 24% subjects knew that body weight has a correlation with hypertension. About 27% said that there was no correlation between salt intake and hypertension, and 88% of the study population did not carry out any form of physical activity. **Conclusion:** Hypertension can be controlled by life style modifications such as exercise, weight management and a healthy diet. Public health and education measures targeting hypertensive population need to be taken to decrease the risk factors for cardiovascular diseases and, therefore, improve people's health and quality of life.

**Keywords:** Hypertension; Health Knowledge, Attitudes, Practice; Exercise; Geriatric Assessment (Source: MeSH-NLM).

## Introduction

Hypertension (HTN) is a chronic disease which is independently associated with cardiovascular diseases in the elderly. It constitutes one of the most frequent risk factors for cerebrovascular diseases.<sup>1-3</sup> Hypertension is a major public health problem in many parts of the world.<sup>4,5</sup> Known as “the silent killer,” it may exist for prolonged periods without symptoms and may manifest only after causing serious complications. It has been identified as the most common, most potent and most universal contributor to cardiovascular mortality, which accounts for 20-50% of all deaths.<sup>6</sup>

Assessment of knowledge, attitudes and practices is a critical aspect of hypertension control. Limited information is available from developing countries regarding this aspect of hypertension control, despite the fact that hypertension has been implicated as a major health problem in these countries.<sup>7</sup>

Blood pressure can be controlled not only with medications but also with non-pharmacological management strategies such as exercise, weight reduction, salt restriction, and fruit and vegetable consumption. These non-pharmacological measures play an important role in the management of hypertension. The present study was conducted to assess the knowledge of

non-pharmacological measures to control hypertension and its application in a geriatric hypertensive population.

## Methods

This is a cross-sectional questionnaire based study. It was carried out from October to December 2013 at the Department of Physiology, S.B.K.S Medical Institute and Research Centre, Vadodara, India.

A non-validated self-administered questionnaire was prepared consisting of 10 questions in the local language (Gujarati) to assess knowledge, attitude and practice among the subjects about non-pharmacological measures to control hypertension.<sup>8</sup> These were closed questions with a YES/NO response.

Subjects more than 50 years of age of either gender with a history of hypertension who were willing to participate and give consent were included. The exclusion criterion was refusal by the subject to sign the informed consent form.

The protocol was explained to the subject and written informed consent was obtained. A detailed clinical history was collected through face-to-face interviews, while blood pressure readings were obtained using a sphygmomanometer.

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Data analyses were performed with Microsoft Office Excel®. Frequencies and percentages were reported for categorical variables, while means and standard deviations (SD) were presented for quantitative variables.

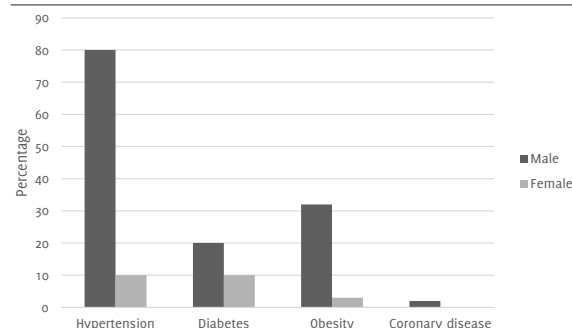
The study protocol was approved by the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC) and the Committee for the Purpose of Human Research Review Panel (HRRP) of the Sumandeep Vidyapeeth University (ethical approval code: SVIEC/ON/medi/BNPG-12/D13376). The reporting of this study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies.<sup>9</sup>

## Results

A total of 120 questionnaires were distributed to hypertensive individuals who fulfilled the inclusion criteria. Of these, 110 completed questionnaires were submitted, corresponding to a response rate of 92%. The mean age of the subjects was  $56.7 \pm 1.2$  (SD) years. The study respondents consisted of 91 males and 19 females.

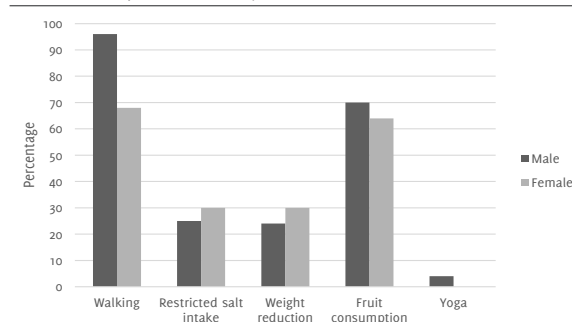
Out of the 110 respondents interviewed, 84% were suffering from hypertension, 32% were suffering from diabetes mellitus along with hypertension, 33% were suffering from obesity along with hypertension and diabetes mellitus and 2% were suffering from coronary heart disease with hypertension (Figure 1).

**Figure 1.** Percentage of Male and Female Subjects Suffering from Different Diseases.



About 94% male and 68% female subjects controlled blood pressure by walking. About 26% male and 31% female hypertensive subjects said that they had reduced salt intake to control hypertension. About 22% male and 31% female subjects tried weight reduction, and 69% male and 63% female hypertensive subjects took fruits in appropriate amount to control hypertension. Finally, 3% male subjects controlled hypertension by practicing yoga regularly (Figure 2).

**Figure 2.** Percentage of Practice for Control of Hypertension in Both Male and Female Subjects of the Study.



Only 10% of the respondents knew the normal range of blood pressure. About 62% of hypertensive subjects reported measuring their blood pressure regularly. Approximately 85% of the subjects used anti-hypertensive medications. Only 27% of the respondents were aware of the correlation between salt intake and hypertension. Approximately 24% of the subjects agreed that body weight is correlated with hypertension and weight reduction could, therefore, help with hypertension control. About 68% subjects took fruits in appropriate amount to control hypertension. History of smoking was positive in 74% of the male subjects. While history of tobacco consumption was positive in 53% of the male subjects none of the female subjects reported a history of tobacco consumption. Up to 90% subjects doing walking regularly. Only 12% patients practiced yoga and/or meditation regularly (Table 1).

**Table 1.** Knowledge and Practice of Non-Pharmacological Approaches to Hypertension Management among Subjects.

Type [n=110]	Follower [%]
Knowledge of normal values of blood pressure	10
Regular check-up of blood pressure	61.8
Taking anti hypertensive drug	85.5
Restricted salt intake	27.2
Weight reduction	23.6
Fruit consumption	68.1
Smoking	74.5
Tobacco consumption	52.7
Walking	90
Yoga, meditation	11.9

## Discussion

There is an increase in the prevalence of hypertension in the past few years. Hypertension can be controlled with drugs along with some non-pharmacological measures. The present study assessed knowledge of non-pharmacological measures to control hypertension in adult hypertensive patients. Findings from previous studies showed that half of the population was aware of the correlation between salt intake and blood pressure.<sup>8-11</sup> The majority of population did not know about the correlation between blood pressure and body weight.<sup>12,13</sup> The most important non-pharmacological therapy consists of a hygienic behavioral program aimed at changing the patient's lifestyle.<sup>14</sup> The nutritional and behavioral measures recommended in the management of high blood pressure improved the patients' general health status, as they also have a beneficial effect on other cardiac risk factors frequently associated with hypertension.<sup>15</sup> Impaired baro reflex sensitivity has been increasingly postulated to be one of the major causative factors of essential hypertension. A short period (3 months) of regular yogic practice for 1 hour/day is effective in controlling blood pressure in such individuals.<sup>16</sup>

Knowledge and practice of non-pharmacological strategies to manage hypertension were less than optimal in our study population. Hypertensive patients should be advised to stop smoking and tobacco consumption, reduce salt intake, and consume a diet rich in fruits and vegetables, such as banana, unsalted sunflower seeds, spinach, beans, baked white potato,

and soybean. Eating about 30 calories a day of dark chocolate could also reduce blood pressure without any adverse effect, although this option is not preferable for overweight people due to the high caloric content of chocolate.<sup>17</sup> Physical activities like yoga and daily walking could help in the reduction of both blood pressure and body weight.

The present study has a few limitations. Only patients with a systolic blood pressure higher than 160 mmHg and aged 50 years or older were included in this study; therefore, our findings may not be generalizable to other patient populations.

Knowledge and practice regarding body weight, smoking tobacco, salt intake, fruit and vegetable intake, yoga and physical exercise, and their roles in the management of hypertension were satisfactory in this study population. Further large scale studies need to be undertaken to obtain a clearer picture of the level of hypertension in the geriatric population. Training programs should be recommended to develop the necessary skills needed for optimal non-pharmacological management of hypertension.

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# Alzheimer's Disease: Current and Future Treatments. A Review

Evelyn Chou<sup>1</sup>

## Abstract

Alzheimer's disease (AD) is a currently incurable neurodegenerative disorder whose treatment poses a big challenge. Proposed causes of AD include the cholinergic, amyloid and tau hypotheses. Current therapeutic treatments have been aimed at dealing with the neurotransmitter imbalance. These include cholinesterase inhibitors and N-Methyl-D-aspartate (NMDA) antagonists. However, current therapeutics have been unable to halt AD progression. Much research has gone into the development of disease-modifying drugs to interfere with the course of the disease. Approaches include secretase inhibition and immunotherapy aimed at reducing plaque deposition. However, these have not been successful in curing AD as yet. It is believed that the main reason why therapeutics have failed to work is that treatment begins too late in the course of the disease. The future of AD treatment thus appears to lie with prevention rather than cure. In this article, current therapeutics and, from there, the future of AD treatment are discussed.

**Keywords:** Alzheimer's disease, disease-modifying drugs, beta-secretase inhibitors, gamma-secretase inhibitors, cholinergic, amyloid, tau (Source: MeSH, NLM)

## Introduction

The most common form of dementia is Alzheimer's disease (AD). It is a degenerative and currently incurable terminal disease, affecting about 75% of the 35 million people worldwide suffering from dementia. It is predicted that the prevalence of AD will double every 20 years, meaning an estimated 115 million individuals may be suffering from AD by 2050.<sup>1</sup> AD is thus becoming increasingly recognized as a major cause of medical and social burdens in the elderly population worldwide.<sup>2</sup> In its preclinical stages, AD cannot be diagnosed, while its clinical stages are characterized by impairment of cognitive functions (i.e. recent memory, language difficulties, spatial disorientation and visual agnosia), with behavioural disturbances significant enough to compromise activities of daily living (ADLs). Life expectancy is reduced, with patients generally living up to 5-8 years following diagnosis.<sup>3</sup>

Currently, no drugs are available to halt the progression of neurodegeneration in AD; the nature of AD treatment is symptomatic.<sup>2</sup> For instance, cholinesterase inhibitors (CIs) that promote cholinergic neurotransmission are used in mild to moderate cases of AD. Memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist, is used in moderate to severe cases to prevent excitotoxicity,<sup>4</sup> and antipsychotics and antidepressants are used in the treatment of neuropsychiatric symptoms.<sup>5</sup>

The future of treatment of AD lies in the targeting of neuritic plaques (NPs) and neurofibrillary tangles (NFTs), which has the potential to delay neurodegeneration.<sup>6</sup>

The daunting statistics and the impacts that AD has on suffer-

ers, caregivers and the society make it exceptionally vital that we review how AD is currently being treated and how this is likely to change in the near future with the possible development of disease modifying treatments.

## Search Strategy and Selection Criteria

The papers for this review article were identified by computerized advanced searches in Pubmed database and Google Scholar using the keywords 'Alzheimer's', 'beta-secretase' and 'gamma-secretase'. These papers included meta-analyses, original research articles, review articles and clinical trials. Information was also obtained from textbooks and Alzheimer's disease forums. This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.<sup>7</sup>

## Clinical Features

The progression of AD can be divided into a series of stages: pre-dementia, mild, moderate and severe.

The pre-dementia stage is often unreliably distinguished from normal aging or stress-related issues.<sup>3,8</sup> One of the first signs is the deterioration of episodic memory. No decline in sensory or motor performance occurs at this stage, and other aspects such as executive, verbal and visuospatial functions are slightly impaired at most. An individual remains independent and is not diagnosed as suffering from AD.<sup>8</sup>

During mild stages of AD, increased memory loss affects recent declarative memory more profoundly than other capacities, such as short-term, declarative and implicit memories.<sup>3</sup>

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Motor function remains normal, and sensory performance is not impaired extensively. However, some visual, auditory and olfactory functions may be affected.<sup>8</sup> Communication begins to decline as patients find themselves unable to recall certain words. The individual may be able to remain independent, but not without some assistance.<sup>3,9</sup>

Recent memory continues to deteriorate in the moderate stage. Due to an inability to create new memories, AD patients seem to live in the past.<sup>9</sup> Patients are still able to manage basic ADLs, but help is required in certain areas such as grooming and dressing.<sup>3,9</sup> Insight into their disease is commonly lost by this stage, with patients becoming delusional. A longitudinal study conducted in 1993 showed that it is at this stage that cognitive decline, aggression, depression and incontinence in patients become predictive factors for placement in nursing homes.<sup>10</sup>

In the severe stage, even early memories can be lost. Basic ADLs are now affected, declining gradually. Communication deteriorates further to single words or phrases, and language is thus significantly impaired.<sup>3,9</sup> Behavioural disturbances occur, causing disruptions to caregivers.<sup>3,11</sup> The most common cause of death in AD patients is pneumonia,<sup>12</sup> followed by myocardial infarction (MI) and septicæmia.<sup>3</sup>

## Risk Factors

Inheritance of certain genes is a risk factor for AD, with both familial and sporadic cases occurring. In sporadic AD, which is the more common form, there is a link with the apolipoprotein  $\epsilon 4$  (APOE4) allele, with the risk being greater in homozygotic situations.<sup>1,13</sup> It has been shown that transgenic mice expressing either mouse or human apoE develop neuritic plaques (NPs) associated with neuritic degeneration due to fibrillar amyloid- $\beta$  deposits. In contrast, in apoE negative mice, no neuritic degeneration was observed despite the presence of non-fibrillary amyloid- $\beta$  deposits. ApoE thus appears to play a critical role in the progression of NPs and degeneration.<sup>14</sup>

Environmental factors also contribute to the development of sporadic AD.<sup>15</sup> Familial AD, on the other hand, has been associated with mutations in presenilin 1 (PSEN1) and presenilin 2 (PSEN2), as well as the amyloid precursor protein (APP) gene, which is located on chromosome 21.<sup>1,13</sup> Many other candidate polymorphic genes have been associated with increased AD risks, including secretase, peptidase, microtubule, cytoskeletal, anti-apoptotic and protease genes.<sup>1</sup>

Vascular factors seem to affect the risks of developing AD. Metabolic syndrome,<sup>1</sup> comprising hypertension, dyslipidaemia, obesity and diabetes mellitus, has been associated with increased risk.<sup>16</sup> Hypertension contributes to the formation of neuritic plaques (NPs), neurofibrillary tangles (NFTs), and characteristic lesions seen in AD.<sup>17</sup> Dyslipidaemia and diabetes mellitus are not only implicated in the generation of NPs, but also cause cerebrovascular dysfunction.<sup>18</sup> In addition, obesity has been linked to cognitive decline and resistance to insulin the latter of which leads to hypertension, diabetes and cerebrovascular dysfunction.<sup>19</sup>

Psychosocial factors are also implicated in AD. With greater social, physical and mental stimulation, individuals are less likely

to develop AD later in life. The risk of cognitive decline is higher in those with lower physical activity. Additionally, the protective effect of physical activity is more prominent in apoE4 allele carriers. These three lifestyle factors appear to act together in a common pathway in their protection against dementia.<sup>1,20</sup>

## Causes

### Cholinergic Hypothesis

The cholinergic hypothesis of AD came about due to the combined observations of deficits in choline acetyltransferase and acetylcholine (ACh) and the fact that ACh is important in memory and learning. It was thought that reduction in cholinergic neurons as well as cholinergic neurotransmission led to the decline in cognitive and noncognitive functions. Cholinergic function loss correlated to cognitive decline, but no causal relationship was established.<sup>2,21</sup> Moreover, the use of cholinesterase inhibitors (CIs) does not have a significant effect in more than half of AD patients receiving treatment, indicating the presence of other important processes in the progression of the disease.<sup>21</sup>

### Amyloid Hypothesis

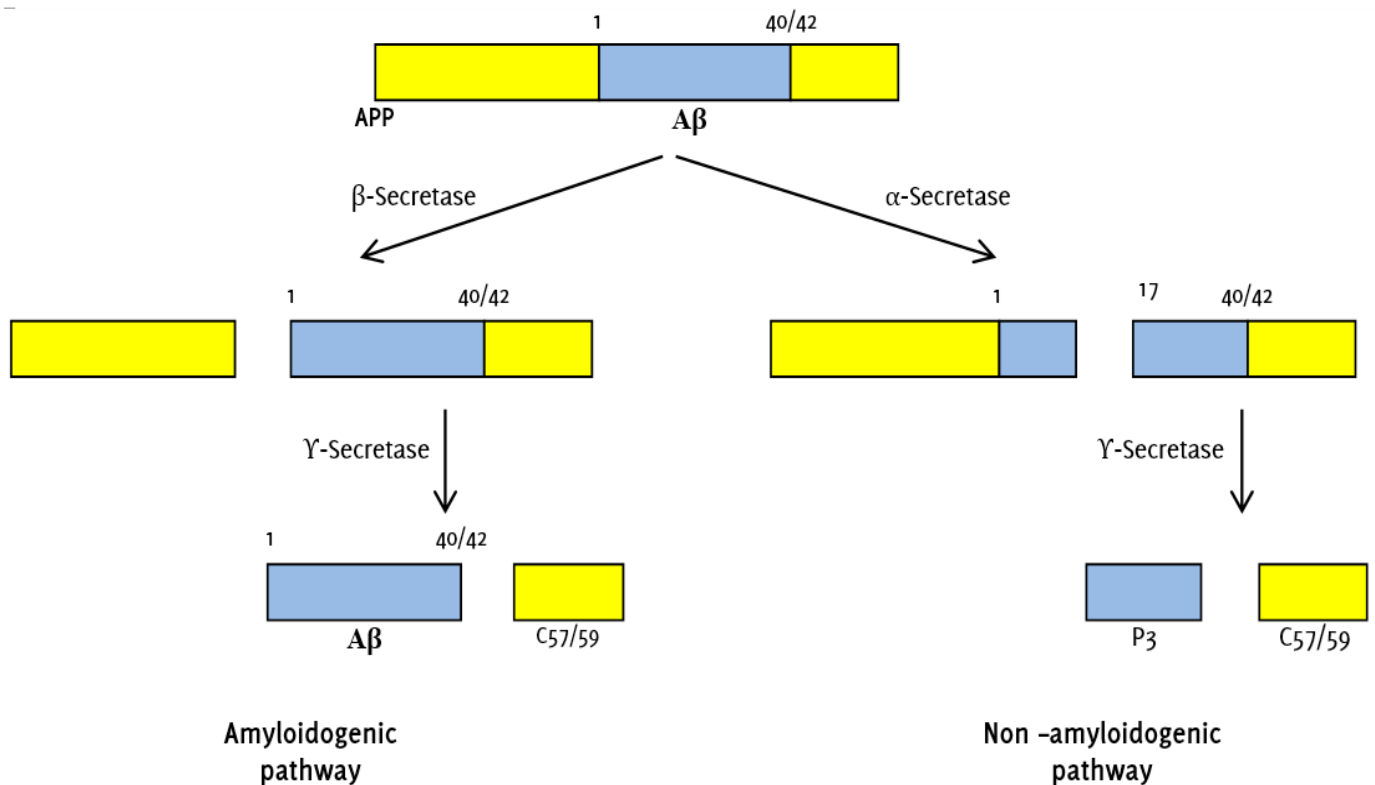
Amyloidosis is the abnormal deposition of amyloid proteins in tissues, with the altered amyloid proteins forming an insoluble  $\beta$ -pleated sheet. Reduced tissue and cellular clearance is observed in amyloid protein deposits. The membrane protein amyloid- $\beta$  precursor protein (APP) is proteolysed to form A $\beta$ , and it is the amyloid form of A $\beta$  that makes up the amyloid plaques (neuritic plaques) found in the brains of AD sufferers.<sup>6</sup>

According to the amyloid hypothesis, the basis of AD is the presence of A $\beta$  production in the brain.<sup>2</sup> Evidence for the amyloid hypothesis was compelling, as gene mutations encoding the amyloid- $\beta$  precursor protein (APP) was found to cause familial AD, with sites of major mutations found in  $\gamma$  secretase and APP.<sup>6</sup> A $\beta$  is derived from APP by proteolysis in the amyloidogenic pathway, mediated by  $\beta$  secretase (BACE1) and  $\gamma$  secretase, in the extracellular and transmembrane region, respectively. Cleavage by  $\beta$ -secretase produces APPs $\beta$  and C99. C99 is further cleaved by  $\gamma$  secretase to form either A $\beta$ 1-40 or the more hydrophobic, aggregation-prone A $\beta$ 1-42.<sup>22</sup>

A $\beta$ 40 is more predominant in cerebral vasculature.<sup>2</sup> APP can also be cleaved by  $\alpha$  secretase in the non-amyloidogenic pathway, producing APPs $\alpha$  and C83. Further evidence came from an experiment in the 1990s whereby transgenic mice expressing three different isoforms of mutant APP were found to have characteristic AD neuropathologies.<sup>23</sup>

Despite widespread support of A $\beta$  fibrils being the main cause of pathology seen in AD, it was suggested that oligomerization of A $\beta$ 1-42 plays a more important role. Oligomerization of A $\beta$ 1-42 produces soluble A $\beta$  oligomers which are known as A $\beta$ -derived diffusible ligands (ADDLs). Experiments showed that these ADDLs are potentially more toxic than A $\beta$  fibrils as they target synaptic spines and disrupt synaptic plasticity, thus affecting cognitive function. Their toxicity lies in toxin receptors on cell surfaces and in Fyn, a tyrosine kinase receptor overexpressed in AD (*Figure 1*).<sup>24,25</sup>

Figure 1. The Amyloid Hypothesis: Amyloidogenic and Non-amyloidogenic Pathways.



#### Tau Hypothesis

The Tau hypothesis revolves around the presence of neurofibrillary tangles (NFTs) in AD. As a result of increased phosphorylation of Tau (originally bound to microtubules), there is an increase in free tau accompanied by loss of functioning microtubules.<sup>26</sup> Phosphorylated Tau are subunits of paired helical filaments (PHFs), which form NFTs. The impaired microtubules affect axonal transport of proteins and eventually cause neuronal death.<sup>27</sup>

#### Neuropathology

The degeneration of neurons and synapses, declining cholinergic function, characteristic neuropathologic lesions of neuritic plaques (NPs) and neurofibrillary tangles (NFTs) all contribute to cognitive decline.<sup>28</sup> The neocortex and hippocampus, which are the regions of higher function, are most affected by these lesions.<sup>21</sup> NPs consist of aggregations of amyloid-β peptide, while NFTs are located within neurons and their projections and are composed of filamentous hyperphosphorylated tau. The distinction between NPs and NFTs being causative or mere markers of AD and the chronological order in which the pathologies appear are important to the understanding of AD pathology.<sup>6</sup> A study carried out to determine the role of NPs and NFTs in AD established that NP deposition occurs in early stages of the disease, but does not correlate with progression of illness once clinical stages have been established, whereas NFTs seem to correlate to decline in cognitive function in later stages.<sup>28</sup>

#### Current Symptomatic Treatments

It is through the understanding of the disease processes that underlie AD that targets can be ascertained and treatments developed.

#### Cholinesterase Inhibitors

Cholinesterase inhibitors (CI) aim to increase acetylcholine availability in synaptic neurotransmission in order to treat memory disturbances. Currently, three CIs are being used as the first-line treatment in mild to moderate AD: donepezil, rivastigmine and galantamine.<sup>2</sup> While donepezil and rivastigmine are both selective inhibitors, galantamine inhibits both ACh and butyrylcholinesterase. A meta-analysis collaborating 13 randomized, double-blind trials that were designed to evaluate the effectiveness and safety of CIs showed no improvement in ADL and behaviour. In addition, donepezil and rivastigmine showed no significant difference in their impact on cognitive functions, ADLs and behaviour. Overall, similar benefits were observed across all three drugs.<sup>29</sup> It is known that CIs are unable to halt disease progression, but they have been found to have effects for a substantial period of time. As seen in a randomized double-blind trial, patients undergoing long-term treatment with donepezil showed no beneficial loss for up to two years.<sup>30</sup>

In addition, there may be some added benefits to increased doses of CIs given. In a randomized, double-blind, parallel-group, 48-week study conducted to determine the efficacy and safety of a rivastigmine patch of a higher dose, deterioration of ADLs was significantly reduced and Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) was improved in patients treated with higher doses.<sup>31</sup> Side effects as a result of CIs are minimal and are usually limited to gastrointestinal symptoms such as diarrhea, nausea and vomiting.<sup>13</sup>

#### NMDA Receptor Antagonists

Memantine is a non-competitive NMDA receptor antagonist effective in the treatment of moderate-to-severe AD. The modu-



lation of NMDA receptors results in reduced glutamate-induced excitotoxicity. Its benefits were proven in a 28-week, double blind, parallel-group study which showed that treatment significantly reduced deterioration in patients. Most adverse reactions to the drug were not severe and were considered to be unrelated to the drug. The positive effect on cognitive function translates to behavioural improvements: patients were less agitated and required less assistance from caregivers.<sup>32</sup> Improvement of the behavioural and psychological symptoms related to dementia (BPSD) was also highlighted by a meta-analysis of 6 studies involving memantine treatment.<sup>33</sup>

#### Antidepressants and Antipsychotics

BPSD is a common occurrence in AD and a major source of burden on caregivers. CIs and memantine help to control these symptoms to a certain extent, but as patients continue to deteriorate, control by these drugs becomes insufficient.<sup>2</sup>

Depression is very common, especially in the early and late courses of the disease. Antidepressants such as: selective serotonin reuptake inhibitors (SSRI: citalopram, fluoxetine, paroxetine, sertraline, trazodone), tricyclic agents and combined serotonergic and noradrenergic inhibitors may be used to counter this.<sup>2,34</sup> Discontinuation of antidepressants in demented patients in a double blinded, randomized, parallel-group placebo controlled trial showed significant increases in depression when compared to those who continued treatment. These results are indicative of the beneficial effects of antidepressants.<sup>34</sup>

Atypical antipsychotics used in AD include olanzapine, quetiapine and risperidone, which are used to treat psychosis and

agitation. However, the use of such drugs appears to be controversial, with patients showing significant declines in cognitive function with antipsychotic drugs administration when compared to patients receiving the placebo.<sup>35</sup>

#### Disease-Modifying Treatments

While symptomatic treatments have proven helpful, it is the finding of a cure that is most vital. Since the amyloid hypothesis indicates that A $\beta$  generation and deposition from overexpressed APP cleavage make up the fundamental basis of AD, interest centers on anti-amyloid therapies. These therapies result in decreased production of A $\beta$ , increased clearance of A $\beta$  and the prevention of A $\beta$  aggregation into amyloid plaques.<sup>6,36</sup> Immunotherapy has also been an area of interest as it targets the clearing of A $\beta$  peptides, which can either directly or indirectly impact cognitive decline.<sup>37</sup>

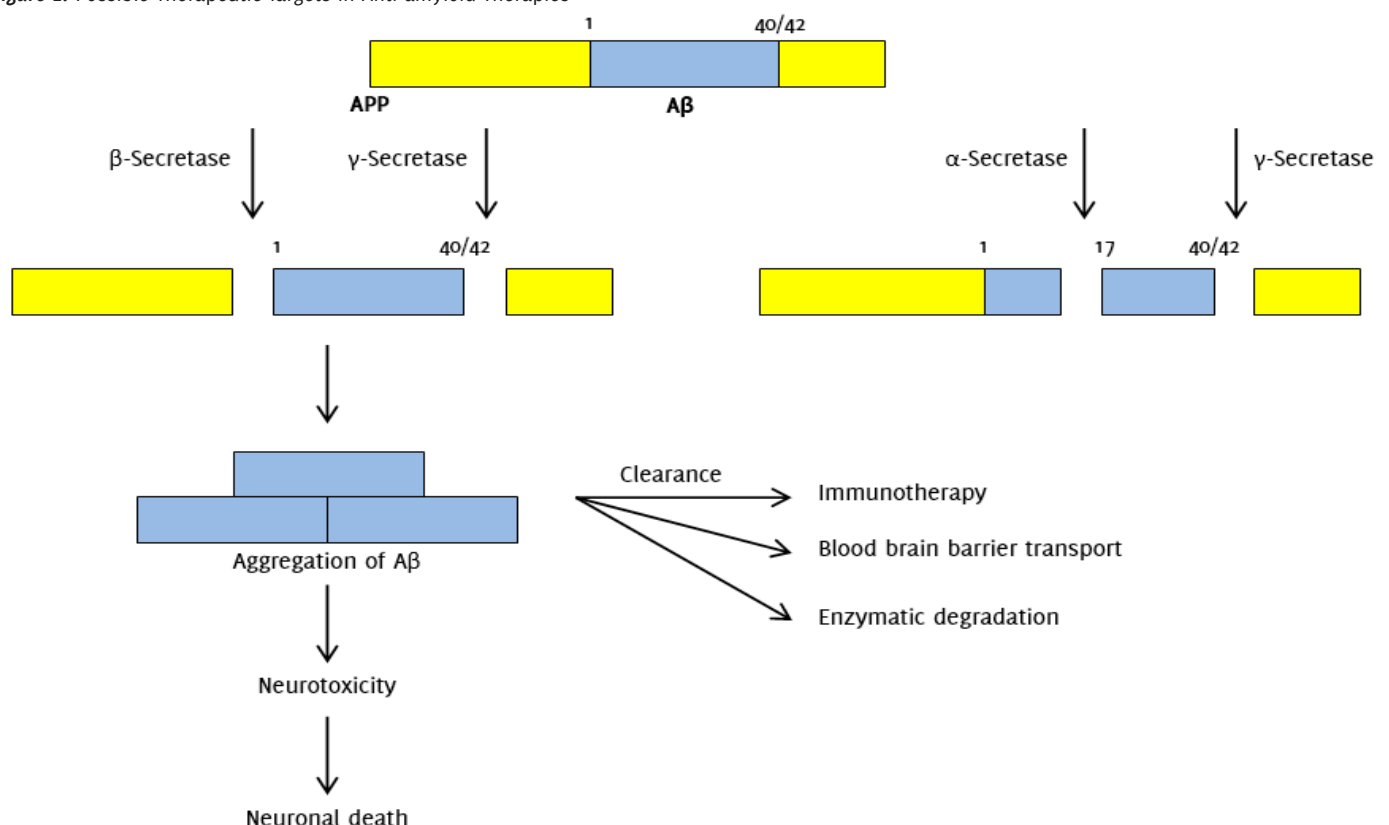
Focusing on decreasing A $\beta$  generation, several methods can be employed to achieve this, mainly by targeting the amyloidogenic and nonamyloidogenic pathways.  $\beta$  and  $\alpha$  secretases both compete for APP, with  $\beta$ - and  $\gamma$ -secretase processing ultimately resulting in amyloid deposition and  $\alpha$ -secretase generating soluble APPs $\alpha$ .<sup>2</sup> Inhibiting  $\beta$ - and  $\gamma$ -secretases while simultaneously potentiating  $\alpha$ -secretase action would thus reduce A $\beta$  generation and deposition overall.

#### Decreasing A $\beta$ Generation

##### $\beta$ -Secretase Inhibitors

The cloning of  $\beta$ -secretase has allowed for the investigation of its structural and catalytic properties.<sup>38</sup> Development of clinically effective inhibitors depends greatly on this detailed knowle-

**Figure 2.** Possible Therapeutic Targets in Anti-amyloid Therapies



dge of its structure.  $\beta$ -secretase is a rate-limiting transmembrane aspartyl protease beta-site APP-cleaving enzyme (BACE1) involved in the first proteolytic step of the amyloidogenic pathway of A $\beta$  generation. BACE1-deficient mice were used to determine the role of  $\beta$ -secretase. In mice with BACE1 $^{-/-}$  neurons, generation of A $\beta$ <sub>40</sub> and 42 was eradicated, thus confirming the role of BACE1 in the amyloidogenic pathway.<sup>39</sup> From this, it can be inferred that inhibition of BACE1 activity would be able to reduce A $\beta$  levels and ultimately reduce neuritic plaques. Thus, it has become a primary therapeutic target.

The close resemblance of  $\beta$ -secretase's catalytic apparatus to other aspartyl protease targets such as HIV protease has contributed to the development of its inhibitors.<sup>39</sup> However, the secretase's hydrophilic, long and shallow active site presents some problems to the development of its inhibitors. An effective inhibitor would need to be able to penetrate the blood-brain barrier (BBB) and the cell membrane of neurons. This has made the discovery of small yet potent inhibitors more difficult.<sup>36</sup> Another challenge is that  $\beta$ -secretase inhibitors act as substrates for P-glycoprotein that transports them out of the brain. Efforts have been made to overcome this through the design of inhibitors with higher selectivity for BACE1 over megalin 1 (BACE2) and cathepsin D (cathepsin D).<sup>2,39</sup> The low number of drugs reaching clinical trials reflects the difficulty of these challenges faced (Figure 2).

The earliest BACE1 inhibitors were peptidic, large, polar and clinically ineffective. These have been progressively improved and they have been made less peptidic. The first orally bioavailable drug-like non-peptidic BACE1-inhibitor LY2811376 was found to significantly lower A $\beta$  protein in animal models. Healthy volunteers later treated with the compound also demonstrated this decrease in A $\beta$  levels. Its safety, tolerability and efficacy were determined in a double blind, placebo controlled study in which subjects were assigned either the active drug or a placebo and participated in CSF and plasma sampling. The drug was discontinued due to its pathological effect on accumulations of autofluorescent material within the retinal epithelium, causing them to be enlarged. Although the drug did not go on to enter the later clinical trial stages, data recorded nevertheless provides support for BACE1 as a target for BACE1 inhibitors.<sup>40</sup>

Despite support for BACE1 inhibitors, certain concerns were yet to be dealt with. In particular, it was not known whether BACE1 played other important physiological roles apart from being involved in the amyloidogenic pathway.<sup>40</sup> In a 2006 study, it was discovered that BACE1 is involved in the myelination process of peripheral and central nerves. In BACE1-null mice, hypomyelination occurred. This hypomyelination was thought to be due to the role of BACE1 in the cleavage of neuregulin-1 type III, a myelination initiator. At this point, it was still unclear whether neuroglinin-1 cleavage is required for myelin sheath maturation, which would make BACE1 inhibitors potentially dangerous.<sup>41</sup> However, it was later found that neuroglinin1 signalling is in part independent of BACE1 function. Even though BACE1's processing of the gene does produce a myelin-inducing signal, this signal is not essential for myelination stimulation.<sup>42</sup>

The first  $\beta$ -secretase inhibitor to enter Phase I clinical trials was

announced in 2008.<sup>2</sup> This compound, CTS-21166, developed by CoMentis, was able to significantly lower A $\beta$  levels. It was not only potent (1.2-3.6 nM), but also selective. In cellular assays performed, CTS-21166 did not bind to 60 other enzymes.<sup>38,40</sup> This was an achievement, as non-specific binding was one of the major issues in developing a clinically effective  $\beta$ -secretase inhibitor. It also displayed desirable brain penetration, another problem associated with the development of other inhibitors (Strobel G. Keystone Drug News: CoMentis BACE inhibitor debut. <http://www.alzforum.org/new/detail.asp?id=1790>. Cited 2013 Sep 30). The injection of CTS-21166 into transgenic mice resulted in reduction of A $\beta$  40 and 42 by an average of 36.5% as well as reduction in amyloid plaques in hippocampal and cortical areas by about 40%. Using this knowledge, the compound was then tested on healthy male volunteers for its tolerability and safety in 6 volunteers, with a range of doses (7.5-225 mg) given intravenously. Results were positive, showing good tolerability over the range of doses administered and slow drug clearance (Strobel G. Keystone Drug News: CoMentis BACE inhibitor debut). Significant plasma A $\beta$  inhibition continued for up to 72 hours, with recovery to normal levels by 144 hours after the inhibitor was administered.<sup>39</sup> Later phase clinical trials have yet to be published.

## $\gamma$ -Secretase Inhibition

$\gamma$ -secretase inhibition is perhaps the most widely and frequently studied mechanism to reduce A $\beta$ . It is involved in the second step of the amyloidogenic pathway and is thus crucial in A $\beta$  generation. Another product derived from  $\gamma$ -secretase cleavage is the amyloid intracellular domain (AICD), which may have a role in gene expression downstream.<sup>6</sup>  $\gamma$ -secretase is an intra-membrane cleaving protease, consisting of 4 components: presenilin (PS), nicastrin (NCT), presenilin enhancer (Pen2) and anterior pharynx defective (Aph1). These 4 components were thought to be essential for the activity of  $\gamma$ -secretase, and the loss of any of the proteins appeared to abolish the activity of  $\gamma$ -secretase. However, in NCT knock-out mice, it was observed that a complex of PS1, Pen2 and Aph1a was able to function as a  $\gamma$ -secretase inhibitor, which indicated that NCT is not required for substrate recognition in  $\gamma$ -secretase. Instead, it is thought to have a role in the stabilization of the enzyme. This makes it much more complex than  $\beta$ -secretases.<sup>6,43</sup> Even though NCT may not be the most important component,  $\gamma$ -secretase activity is PS dependent. It was the combined knowledge of mutations in PS1 and PS2 resulting in early-onset of AD and PS mutations also causing increased levels of A $\beta$  that led to the belief that PS has a direct impact in  $\gamma$ -secretase mediated cleavage of APP.<sup>44</sup> In an investigation of PS-1 deficient mouse embryos, the cleavage of APP by  $\gamma$ -secretase was prevented, causing A $\beta$  levels to be significantly reduced, whereas cleavage by  $\beta$ - and  $\alpha$ -secretase was unaffected.<sup>45</sup> This thus confirmed the function of presenilin in  $\gamma$ -secretase.

Despite  $\gamma$ -secretases' complexity, the development of  $\gamma$ -secretase inhibitors has been easier than the development of  $\beta$ -secretase inhibitors. This is due to the hydrophobicity of its active site. Inhibitors developed were hydrophobic, which aided its permeability, and penetrating the BBB and neuronal membranes was less of a problem.<sup>6</sup> However, its development was not without challenges. The most serious concern faced was that  $\gamma$ -secretase had other physiological roles in development

via Notch signalling regulation. Normally, Notch is cleaved in the Golgi apparatus to produce mature Notch1 protein. Notch-1 undergoes further cleavage to release the Notch intracellular domain (NICD). NICD in turn modifies the transcription of target genes within the nucleus. In PS1 knock-out cells, it was observed that PS1 is vital in the cleavage of APP and Notch.<sup>46</sup> Hence, the use of  $\gamma$ -secretases in the treatment of AD can be expected to cause gastrointestinal toxicity, immunosuppression and anaemia due to the role of Notch-1 in haematopoiesis. PS is also involved in several other processes, such as the cellular trafficking of proteins. The knock out of PS would lead to the accumulation of protein fragments within the cell due to interrupted transport between subcellular compartments. It has also been suggested that PS plays a role in homeostasis of  $\text{Ca}^{2+}$ .<sup>47</sup> Efforts to overcome these challenges come from the development of selective  $\gamma$ -secretase inhibitors that target cleavage of APP only.

Notch-sparing  $\gamma$ -secretase inhibitors have also been developed, and these are able to reduce APP proteolysis in the amyloidogenic pathway, thus decreasing A $\beta$ , while preventing the cleavage of Notch.<sup>47</sup> One of the first compounds with this property was STI571 (Gleevec), an abl kinase inhibitor. STI571 was found to be able to reduce A $\beta$  production, albeit weakly, while at the same time did so without causing cleavage of Notch. These agents formed the basis of development of a number of more potent selective inhibitors, and several of such inhibitors have been reported to enter clinical trials.<sup>47,48</sup>

LY-450139 (Semagacestat), a selective  $\gamma$ -secretase inhibitor that is able to reduce A $\beta$  production, has been the most widely studied. LY-450139 resulted in dose-dependent decrease in A $\beta$  concentrations over a period of 6 hours post-administration, with maximum reduction of 40% relative to the baseline concentration.<sup>49</sup> This correlated with the fact that semagacestat is absorbed rapidly from the gut, reaching its peak 1.5 hours after administration and the fact that it is mainly excreted renally. In its phase I clinical trial, manageable adverse events were reported. In the Phase II 14-week study performed in 51 mild-to-moderate cases of AD, semagacestat was shown to be safe and tolerable.<sup>50,51</sup> However, during its Phase III trial in 2010, the drug was discontinued due to its detrimental effects on cognitive function of patients receiving it compared to those receiving the placebo. Semagacestat also appeared to be associated with increased risks of skin cancer. Such harmful effects were thought to be due to the involvement of the inhibitor with Notch cleavage and CTF $\beta$ , a neurotoxic precursor of A $\beta$  (AlzForum. Drugs in clinical trials. <http://www.alzforum.org/drg/drc/detail.asp?id=108>. Accessed: 2 Apr 2013).<sup>2</sup> Setbacks have also been faced in other trials, as seen in Phase III clinical trials of tarenflubril. These trials aimed to determine the efficacy, safety, and tolerability of the drug in the treatment of mild-to-moderate AD patients. However, results failed to show any benefit from tarenflubril in the cognitive function of patients. Possible reasons for this lack of success include insufficient doses and its low penetration across BBB.<sup>52</sup>

BMS-708163 (Avagacestat) is another example of a  $\gamma$ -secretase inhibitor. Its phase I clinical trial assessed its tolerability, safety and pharmacokinetic properties in young, healthy male volunteers. It reached its peak concentrations rapidly, in about 1.5

hours, with a plasma half-life of about 33 to 34 hours. There was a dose proportional increase in plasma concentration within the range of 0.3-800 mg of the drug. Avagacestat was able to reduce A $\beta$  by up to 88% 1 hour post-administration. Some minor side effects included nausea, dizziness and headaches, with no serious side effects or deaths reported. This phase I clinical trial thus demonstrated Avagacestat's tolerability for up to 800 mg dosage, and its suitability for progression into larger clinical studies.<sup>53</sup> In a phase II clinical trial, 209 patients with mild-to-moderate AD were randomized to receive either the active compound or a placebo. The phase II clinical trial established that daily doses of 25 and 50 mg were indeed well-tolerated, whereas 100 and 125 mg doses were not as well tolerated and had a tendency to cause worsening of cognitive function and GI disturbances related to Notch involvement.<sup>54</sup> These clinical trials have so far established an acceptable dose range for future studies of Avagacestat.

## Conclusion

Taking into account the amount of research that has gone into developing secretase inhibitors, the outcome has not been desirable. The trials so far have come up empty handed, showing no therapeutic improvements in AD patients. As a result, there has been reasonable concern that anti-amyloid therapies may have no therapeutic effect in patients, which would mean decades of wasted research and possibly the targeting of the wrong compounds. Hope that anti-amyloid therapies would have a significant positive impact on AD patients is slowly dissipating. This doubt is further enhanced by the immunization of patients with full length A $\beta$ -peptides in an attempt to clear the NPs from the brain. Previously, it was unknown whether active immunization of A $\beta$  was able to benefit patients. Thus, a trial was carried out to determine its beneficial effects. In this Phase I, randomized, placebo-controlled follow up on the long term effects of A $\beta$  immunization (AN1792), data obtained indicated that immunization was indeed able to significantly reduce A $\beta$  deposition in the AD brain, in comparison to patients receiving the placebo. Disappointingly, despite the pathological improvements observed, the drug failed to produce results of cognitive improvement in these patients. On top of this, some patients even progressed to clinically severe dementia.<sup>55</sup> What these results imply is that the removal of NPs alone may be insufficient in the disease-modifying treatment of AD. Perhaps challenges against the amyloid hypothesis are reasonable, and other factors such as tau hyperphosphorylation's contribution to AD should be re-examined in greater detail.

However, despite the disappointing lack of improvement in patients with A $\beta$  generation and deposition, there still is the possibility that these anti-amyloid strategies hold the potential to cure AD. Concluding that anti-amyloid strategies are futile at this point in time would be rash.

First of all, anti-amyloid therapies were indeed successful, as they were able to reduce NPs. Secondly, A $\beta$  deposition forming NPs was shown to be one of the earliest signs of AD, whereas cognitive decline correlated with NFT deposits.<sup>28</sup> NPs were thought to be the earliest signs of AD, as individuals with trisomy 21 on which the gene for APP is located developed AD much earlier.<sup>56</sup> Such observations were also made in individuals with familial AD. The initial A $\beta$  deposition is thought to set off

a series of secondary downstream events, such as the accumulation of tau and inflammatory processes that cause neuronal destruction.<sup>57</sup> Targeting NPs after a certain point would no longer be beneficial, as other processes become the main propagating factors of the disease. This indicates that perhaps the targeting of NPs much earlier on and in larger doses may be key to anti-amyloid therapies. As such, the way forward in the treatment of AD seems to be the switch from trying to cure AD to instead attempting to prevent it.

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# Social Media Etiquette for the Modern Medical Student: A Narrative Review

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## Abstract

Most medical students worldwide are using some form of social media platform to supplement their learning via file sharing and to stay up-to-date on medical events. Often, social media may blur the line between socialization and educational use, so it is important to be aware of how one is utilizing social media and how to remain professional. Research has yielded some troublesome themes of misconduct: drunken behaviour, violations of confidentiality and defamation of institutions. Because there is no universal policy to monitor online professionalism, there exists the potential for indiscretions to occur. It has been reported that misdemeanours can affect future residency placements and employment for medical students. Accordingly, studies suggest that educators need to recognize this new era of professionalism and adapt policies and reprimands to meet modern outlets where professionalism may be violated.

**Keywords:** Social media, Medical Students, Internship and Residency, Medical Education, Continuing Medical Education (Source: MeSH, NLM).

## Introduction

It has been observed that the majority of North American and European medical students use various social media platforms (Facebook®, Twitter®, YouTube®) for file sharing, circulation of educational resources and staying connected with peers.<sup>1-3</sup> Defining online professionalism is difficult, and there are a number of cases where lapses occur in the medical student population. Almost all medical schools in North America and Europe have an online presence, yet rarely are there guidelines or rules that punish unprofessional behaviour. Research shows that there is a potentially dangerous dichotomy between the online social lives of modern medical students and professionalism requirements of medical career for which they are training.<sup>4-6</sup> Though this is a problem in professional medical practice as well, this narrative review will focus on examining social media use by medical students, with a concentration on online professionalism and how education on the topic is, or should be, integrated into the world-wide medical school curricula. Twenty first century medical students ought to take care in using social media in the most effective way possible.

## Search Strategy and Selection Criteria

A literature search was conducted using Google Scholar, PubMed (Medline), and SCOPUS. Key word combinations included “medical student professionalism and social media”, “medical education and social networking”, and “undergraduate + medical school education + social media”. The 283 results acquired were then limited by year of publication; only articles published after 2007 were included in order to stay as current as possible. Twenty-two articles were chosen for analysis. The inclusion criteria incorporated articles on medical student-spe-

cific social media use. Articles pertaining to practicing physicians were excluded from the review. Emerging themes were assembled into this narrative review. This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.<sup>7</sup>

## Major Trends

The use of social media is common and growing in the medical profession, as more individuals obtain the technology and know-how to use these new platforms.<sup>2-3</sup> In a survey of 132 U.S. medical schools, 95% had Facebook® presence, and 25% had school-specific pages, while 10% had Twitter® accounts.<sup>2</sup> These numbers are comparable with those in Canadian and European literature; thus, most medical students in North America and Europe have some online presence.<sup>1</sup> Professionalism is a longstanding foundation of the medical profession, and as online presence becomes more common, perceptions of professional behaviour must evolve.

Social media has become an advantageous platform for a number of reasons. Students use social media to gain and share information, to communicate and discuss within study groups, and to motivate each other to generate discussion and share thoughts.<sup>8</sup> In addition, interaction with tutors can be easily facilitated via online platforms.<sup>8-10</sup> Facebook® and Twitter® may provide an opportunity for creativity, engaging students in educational settings beyond the scope of traditional medical education.<sup>8</sup> Also, Twitter® allows for quick contact with noteworthy physicians and scientists who would otherwise be difficult to reach.

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In addition to the increase in overall social media usage in the medical student population, it has been found that there are trends of usage across the span of the medical undergraduate program. Social media usage declines as medical students reach the end of their medical degree.<sup>12</sup> Thus, approaches to “technology-enhanced education” might need to be tailored differently for clinical versus pre-clinical students; pre-clinical students used more social forums, while clinical students used social media for obtaining information.<sup>13</sup> The above paragraphs note broad themes of social media usage in the medical student population.

## Atmosphere of Misuse

Medical professionals are increasingly participating in online social media, and evidence is emerging from studies, legal cases and media reports that its use can pose a risk in the medical community.<sup>14</sup> Information stored online is easily accessible and often permanent, so students ought to consider the virtual reach of their posts and comments.<sup>3</sup> Because of its multiple uses, social media may blur the line between socializing and studying/work.<sup>5</sup> Current medical students have grown up in a world where information is shared liberally, and social media is a part of everyday life. Many do not see social media as part of their professional identity, and it is difficult to differentiate between public and private content. It is for this reason that lapses in professionalism occur.<sup>5,10</sup>

Defining e-professionalism is difficult, but the most accepted definition is this: “the attitudes and behaviours reflecting traditional professionalism paradigms but manifested through digital media”.<sup>5</sup> In a 2009 study published in *Journal of the American Medical Association*, 47/78 (60%) of medical schools had had at least one case of unprofessional posting by one or more of their medical students.<sup>15</sup> At one U.K. medical school, 54% of students have seen unprofessional behaviour by their colleagues, most of which involve discussion of clinical encounters. Although there is no governing policy blanketing these issues, unprofessionalism can result in punishments as severe as expulsion from school.<sup>2</sup>

## Types of Inappropriate Behaviour

With every post on any social media site, the user creates a permanent and far-reaching digital footprint.<sup>15</sup> Across the literature, there are five common categories of inappropriate posting by medical students:

- Drunken behaviour;<sup>2,5</sup>
- Overt sexually related content;<sup>2,5</sup>
- Foul language/derogatory humour;<sup>2,5,12</sup>
- Breaches in patient confidentiality;<sup>2,3,5,15</sup>
- Defamation: activities that damage the reputation of an organization or individual.<sup>3</sup>

One study evaluated the Twitter® and Facebook® profiles of 501 medical students. It was found that some Facebook® groups that these students joined were vulgar in nature, and it was noted that 70% of these students’ profiles displayed drunkenness and foul language.<sup>12</sup> Some students seem to think social media is for venting, whereas older generations believe that this type of posting is inappropriate.

Of particular interest are the patient confidentiality concerns

that come up in the literature. According to Belean et. al., 30% of professional violations were linked to patient confidentiality.<sup>11</sup> One issue is the ubiquity of photographic devices, which pose a significant risk to clinical patients as well as standardized patients used in training. The absence of strong online professionalism tenets manifests itself, in one case, in the form of unauthorized recordings during demonstrations of pelvic exams.<sup>15</sup> The Australian Medical Association warns that the “anonymity potentially afforded online is no excuse for unprofessional behaviour”.<sup>14</sup>

## Professionalism Online

Almost all medical schools have a social media presence, but most have no method of addressing unprofessional behaviour,<sup>2,17</sup> nor do they have a set of solid rules pertaining to unprofessional postings.<sup>16,17</sup> With new technologies being integrated into the lives of medical students, there should be instruction on online professional behaviour to give students recommendations on how they ought to conduct themselves. In this area, there is significant room for improvement.<sup>2,7,19,20</sup>

Professionalism is a core pillar of most medical school curricula across the world; however, it is often unclear how e-professionalism is integrated into the teachings on this topic.<sup>17</sup> In a study of 130 U.S. medical schools, only 38% had policies on online student postings, but they were vaguely written and only 10% had policies explicitly mentioning social media or online social networking.<sup>2</sup> The challenges are the lack of systems for identifying, tracking and remediating professionalism lapses and the difficulty of anticipating new technological advances.<sup>19</sup>

In 2013, the Canadian Federation of Medical Students (CFMS) published guidelines on social media professionalism. Their goal was to have medical students, as proto-professionals, act in a way that they would feel comfortable observing their own physicians acting away from clinical duties.<sup>20</sup> The publication is divided into four sections:

1. Clear guidelines regarding professional boundaries online.
2. Suggestions for how medical students can present themselves in the best possible light.
3. Case samples with explanation and critique.
4. A survey of the literature on the topic of social media professionalism.

This set of guidelines will be updated as social media progresses and new platforms are created.<sup>20</sup> Documents such as this one are important for medical schools to add to their professionalism teaching, as social media is now a major aspect of the public presence of medical professionals.

## Consequences on Future Career

Owing to the permanence and worldwide reach of online posting, there are risks inherent in placing any content online. One of the more detrimental issues is that social media misconduct may affect placements in residency programs. Medical students may not associate their lack of professionalism with their current clinical or future career placements, for they may not understand how their opinions could be misinterpreted.<sup>12</sup> However, studies have exhibited that online indiscretions can

affect one's own future employment, that such indiscretions can compromise the public's perception of the medical field,<sup>10,15</sup> and indeed that online misconduct can translate into shaming the entire profession.<sup>15,16,21</sup> The trend is that employers are increasingly screening potential employees online; between one-fifth and two-thirds of employers conduct internet searches, including social networking sites.<sup>14</sup> The public now has online access to information about their physicians. Information on the Internet is permanent and can stay with a student until he or she is a qualified physician; for this reason, medical students should be prudent now about their posts.<sup>11</sup>

### How to Educate

It is clear that there are too few medical school policies on social media conduct. Most agree that instruction in professionalism needs to be addressed for the 21st-century medical student and this should begin at medical school matriculation.<sup>5,16,22</sup>

A few institutions have given advice on how best to address this shortfall. Not only will policies deter students from unprofessional behaviour,<sup>15,23</sup> but it has been suggested that it is the responsibility of medical educators to recognize the online environment that students are in and to tailor their professionalism courses to include this setting.<sup>17,23</sup> In addition, it has been recommended that engaging various users is the best way to create guidelines.<sup>16,17</sup> In addition, e-learning and social media sessions,<sup>9</sup> as well as facilitated group discussion followed by individual reflection,<sup>11,22</sup> should be incorporated into medical learning. Finally, because residents are generally closer in age to medical students, studies suggest they would be the best people to mentor students on the implications of online unprofessionalism.<sup>17,24</sup> Taken together, these measures may help students understand that they ought to be cautious about what they post online. The CFMS' new guidelines are attempting to control online professionalism issues in Canadian medical institutions; a number of medical schools around the world are joining in and integrating these teachings into their curricula.

### Conclusion

Social media and social networking platforms are becoming a ubiquitous source of information sharing in the realm of medicine. Medical students from Canada, and around the world, are engaged in this technology. Because of the permanence and reach of the Internet, it is important that caution is taken to ensure that lapses in professionalism do not occur, since these can affect residency and employment. In addition to the issue of future employment, students should, of course, avoid misconduct because it can shame both the profession for which they are training and the institution that they are attending. A number of suggestions have been made for integrating e-professionalism into medical education. Policy and research into the creation of guidelines will help to ensure that the integrity of the medical profession is not compromised.

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# Management of Vaccination Failure in a Case of HIV - HBV Co-infection: A Case Report

Andre Small,<sup>1</sup> Hilary Schroeder,<sup>2</sup> Raghu Maramraj,<sup>3</sup> Marianinha Joanes.<sup>4</sup>

## Abstract

**Background:** A 60-year-old African American female patient, with chronic HIV infection since 1999, presented with markers of acute hepatitis B virus (HBV) infection for the past 15 months. The patient was previously vaccinated for HBV. Immunoglobulin dysfunction was hypothesized, but electrophoresis yielded no conclusive result. **Results:** Investigation suggests that the patient is a non-responder: someone who fails to sero-convert to standard vaccinations. This condition can be linked to B-cell dysfunction due to chronic HIV infection. **Conclusion:** It is suggested that non-responders may require a 6-dose regimen to achieve sero-conversion for vaccination. Prevention of co-infection should be the mainstay of treatment, which is achieved by vaccination. However, immune system dysfunction can lead to complications.

**Keywords:** HIV Seropositivity, Vaccination, Antigens, Hepatitis B (Source: MeSH, NLM).

## Introduction

Human Immunodeficiency Virus (HIV) compromises the immune response by destroying cells paramount to the immune system, CD4 T-cells, eventually leading to morbidity and mortality from super-imposed infections, which commonly include *Pneumocystis jiroveci*, *Cytomegalovirus* and *Toxoplasmosis*. This makes prevention through vaccination and prophylaxis the cornerstone of HIV management. One such prophylaxis option is against the Hepatitis B virus (HBV). HIV-HBV co-infection is associated with dangerous consequences and as a result, prevention and/or management is extremely important. Despite antiretroviral therapy, around 10% of HIV patients who develop a super-imposed HBV co-infection develop liver disease.<sup>1</sup> Patients with this type of co-infection are at increased risk of developing cirrhosis and fibrotic liver changes.<sup>2</sup>

HBV co-infection is common in many HIV infected patients at time of diagnosis, mainly due to the fact that both conditions are sexually and parentally transmitted viruses prevalent in people who engage in IV drug abuse and unsafe sexual practices.<sup>3</sup> The use of highly active antiretroviral therapy (HAART) has led to increased survival, and subsequently increased prevalence of chronic viral hepatitis among people living with HIV.<sup>4</sup> It is estimated that the prevalence of chronic co-infection is 8-11% in HIV patients.<sup>5-8</sup> As a result, it is routine to vaccinate all HIV patients for HBV. The Center for Disease Control (CDC) recommends that all high-risk patients receiving adult vaccinations, be given a 3-dose vaccine series at 0, 1, and 6 months intramuscularly.<sup>9</sup> However, many co-infected patients fail to seroconvert with standard vaccine administration they are deemed non-responders. Since co-infection has been attributed to

### Key Points:

- HIV and HBV co-infection is a common occurrence amongst HIV patients. This co-infection increases morbidity and mortality, and calls for particular treatment solutions.
- HIV patients can present with unique immune problems, such as B-cell dysfunction.
- Viral infections and B-cell dysfunction can decrease the effectiveness of standard vaccinations, therefore making patients non-responsive to standard vaccinations.
- This article discusses a case study of an HIV-HBV co-infected patient who presents as a possible non-responder to standard HBV vaccination.
- We have suggested methods to deal with patients who present as non-responders to standard HBV vaccinations.

a 19-fold increase in mortality,<sup>10</sup> it is important to establish a care plan for non-responders. This article discusses the clinical presentation of a non-responder and discusses the methods of management for such a patient.

## The Case

A 60-year-old African American woman with chronic HIV infection presented to the clinic for a routine follow-up. She contracted HIV in 1999, and started treatment 4 months after the diagnosis. On her previous visit in January 2012, she showed serological evidence of an acute HBV infection, but with no clinical signs or symptoms. On that visit she was given treatment for HBV with raltegravir and HBV vaccine (**Table 1**). In April of 2013 the patient's blood tested positive for only HBc IgM antibody which was shown to be persistent for 15 months. Her CD4 count at this time was 947. She still denied any symptoms such as weakness, fever, or right upper quadrant pain.

Her past medical history included a diagnosis of HIV in 1999, hypertension in 1994, depression in 2000, hyperlipidemia, la-

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tent TB, HIV-related lipodystrophy syndrome, past history of gonorrhea, and an acute HBV infection. Her social history is significant for previous intravenous drug use she has been off drugs since the diagnosis of HIV. Her current anti-retroviral medications are atazanavir (Reyataz), ritonavir (Norvir) and raltegravir (Isentress). Medications to help control her hypertension are hydrochlorothiazide (HCTZ) and valsartan (Diovan). Finally, pravastatin (Pravachol) is used to control the hyperlipidemia. She has drug allergies to erythromycin and codeine.

On physical exam, the patient's vital signs were found to be within normal limits – meaning her temperature was 98.00 F, pulse was 78, respirations were 16 and her blood pressure was 110/70. She was found to be moderately obese with a BMI of 32.3 Kg/m<sup>2</sup> given her height of 65 inches and weight of 194 pounds. She did not seem to be in any obvious distress and showed signs of being normotensive and non-cachectic. Her head was normocephalic, pupils were equal and reactive, tympanic membranes were clear, mucosal surfaces were pink, and her throat was non-erythematous and free of exudates. Upon auscultation, her lungs were clear bilaterally, heart sounds were regular and there were not any murmurs or gallops and normal bowel sounds were heard in all four abdominal quadrants. Her abdomen was also soft, non-tender and there were not any signs of hepatosplenomegaly.

When the patient first presented in May 2012, her IgG and IgA were normal, and it was only her IgM that was subpar (1372, 246 and 31, respectively). A complete blood count (CBC) was drawn 4 months later (September 2012) and revealed a WBC of 5.5, hemoglobin (Hgb) 12.9, hematocrit (Hct) 38 and platelets were 192,000. During the same visit, a lipid panel was ordered and the results showed a total cholesterol of 254, low-density lipoprotein (LDL) of 17, triglycerides (TG) of 159 and high-density lipoproteins (HDL) of 52. Given her total cholesterol levels, the need to prescribe pravastatin was clear.

## Discussion

This patient has a chronic HIV infection and presents with signs atypical of an acute HBV infection. Although numerous past attempts had been made to vaccinate this patient, she later

presented with HBV after originally testing was negative. This patient classifies as a non-responder, due to failure to seroconvert, and produce IgG HBV surface antibodies. She has elevated levels of IgM core antibody, which typically presents during an acute infection. Furthermore, she has failed to produce IgG core antibodies or surface antibodies after 15 months of infection (**Table 1**). Thirty percent of viral hepatitis patients with associated drug use may present with isolated anti-HBc. These individuals tend to have a varied response to vaccination.<sup>11</sup> It has been suggested that such patients may present with an occult liver disease.<sup>11</sup> It was originally hypothesized that this particular patient may have had an IgG immunoglobulin deficiency. However, electrophoresis revealed the patient has IgG immunoglobulin the laboratory reference range.

Regardless of a typical or atypical presentation of HBV-HIV co-infection, a management plan is necessary. A review of literature has allowed advisement on suggested protocols to monitor and treat such patients.

Typically CD4 counts and HIV viral loads are used to monitor the disease process; however, B-Cells can also be affected in HIV.<sup>6</sup> HIV can affect and cause abnormalities in any lymphocyte group. Specifically, HIV can affect the frequency and composition of B-Cell subsets, especially in patients with chronic infection.<sup>12</sup> The B-Cell dysfunction usually manifests as a decreased responsiveness to antigens, despite hypergammaglobulinemia and hyperactivity of the B-cells.<sup>13</sup>

In a 2012 study, vaccine responders and non-responders were followed after the diagnosis of HIV and subsequent vaccination. The goal of the study was to determine if non-responders were at an increased risk of mortality. It was concluded that hepatitis B surface antibodies could assist in the prediction of the progression to AIDS from HIV-infected patients.<sup>6</sup> It was discovered that non-responders were associated with a 2-fold increase in AIDS and/or death. It is hypothesized that HIV may play a role in the dysfunction of the interaction between the ligand of CD4 T-cells and B-Cells.<sup>6</sup>

HBV vaccination in HIV patients should be done while CD4 cell

**Table 1.** HIV Patient Labs Showing Resistance to Hepatitis B Vaccine Series.

Vaccine/Test	Results [Date]
Hepatitis Vaccine	[09/1999, 11/1999, 02/2000, 04/2012]
Pneumovax	[2009]
Fluvax	[10/2011]
RPR	Negative [6/2011]
Viral Load: HIV-1	< 75 undetectable [01/2012], [5/25/2012]
HCV sAb titer	Negative date: [4/24/2013]
Hepatitis screen	HBc IgM(+) Ab, HBsAg(-), HBsAb(-), HCV (-) [5/25/2012], [4/24/2013]
CD4 count	796 [01/2012], 880 [5/25/2012], 947 [4/24/2013]
CBC	WBC 5.5, HGB 12.9, HCT 38, platelets 192,000 [9/29/2012]
Lipids	Chol 254, LDL 17, TG 159, HDL 52 [9/29/2012]
Immunoglobulin G	1372 mg/dl (ref range 694 - 1618) [5/25/2012]
Immunoglobulin A	246 mg/dl (ref range 81 - 463) [5/25/2012]
Immunoglobulin M	31 mg/dl (ref range 48 - 271) [5/25/2012]

Labels: Pneumovax = pneumococcal vaccine, Fluvax = influenza vaccine, RPR = rapid plasma reagin for syphilis testing, HIV-1 = human immunodeficiency virus type 1, HCV sAb = hepatitis C vaccine serum antibody, HBc IgM Ab = hepatitis B core immunoglobulin M antibody, HBsAg = hepatitis B surface antigen, HBsAb = hepatitis B surface antibody, CD4 = cluster of differentiation 4, CBC = complete blood count, WBC = white blood cells, HGB = hemoglobin, HCT = hematocrit, Chol = cholesterol, LDL = low-density lipoprotein, TG = triglycerides, HDL = high-density lipoprotein.

count is above 200, to achieve a higher probability of successful vaccination. Alternatively, patients who have a CD4 count below 200, should receive HAART first and then vaccinate when CD4 count is above 200.<sup>7</sup> Our patient has failed to seroconvert while having a CD4 count in the optimal range (**Table 1**).

Increased standard doses of hepatitis B virus vaccine, may prove to increase the results of seroconversion of non-responders.<sup>3</sup> The current standard dose is three 20µM of vaccine given at 0, 1, and 6 months.<sup>9</sup> In a study of 20 patients, it was discovered that non-responders receiving 6 doses had a seroconversion rate of >90%. The doses were given at 0, 1, and 2 months, followed by 3 additional doses at 3, 4, and 5 months.<sup>3</sup>

Co-infection of HBV and HIV requires special treatment. Co-infection can be treated with tenofovir.<sup>4</sup> Lamivudine, has been used to treat these types of infections however, there are some infections that show resistance to lamivudine, thus allowing tenofovir to be used as an effective agent. The goal of therapy is to have a patient who is HIV-seronegative, with a manageable chronic hepatitis B state. Management should include monitoring liver histology, and prolongation of the time to development of end-stage liver disease.<sup>14</sup>

The most important management step of a HIV-HBV co-infection is prevention. Therefore, obtaining seroconversion should be the primary goal of medical treatment. Patients with a CD4 count below 200, should be treated with HAART in an effort to increase the CD4 count above 200 and increase the chances of seroconversion. In a patient with increased co-infection risk factors, such as continued intravenous drug use, utilization of a 6-doses vaccination method may be warranted. Alternatively, this method could also be used after failure of the standard vaccination regimen. The current literature emphasizes the importance of preventing co-infection. Furthermore, if a patient does develop co-infection, treatment with tenofovir should be administered as it has been shown to have a decreased rate of resistance.

Co-infection with HIV and HBV has an increased risk of morbidity and mortality. Prevention of co-infection should be the mainstay of treatment, which is achieved by vaccination. However, immune system dysfunction can lead to complications with vaccination, and result in vaccination non-responders. By knowing that B-cell dysfunction can lead to vaccine failure, a physician can better understand why alternative vaccine dosing regimens may be appropriate. In situations where co-infection is already present, treatment with an antiretroviral such as tenofovir should be used. The ultimate goal of management is to decrease viral serology, achieve a state where HIV viral load is undetectable, and delay the progression of end-stage liver disease.

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# Research as a Student: Is It Worth a Try? An Insightful Experience from a Middle Eastern Student

Muneer Al-Husseini.<sup>1</sup>

*About the Author: Muneer Al-Husseini is fourth year medical student in Ain Shams University and a Regional Ambassador of the IJMS.*

## The Experience

I was standing in a long queue at Cairo International Airport, waiting for my flight, with a box on my back containing a poster; only at that time I realized I was not dreaming anymore. It was real and, a few hours later, I would arrive in Porto City, Portugal to attend the 8th Young European Scientists (YES) meeting. In that meeting, I was going to present my first research experience; it would also be my first time representing the International Journal of Medical Students (IJMS), a partner of the meeting and for whom I work for as an Ambassador.

It all started when I was attending an ordinary anatomy lecture during my 2nd year. A professor at my class announced training positions for students who are interested in conducting research as undergraduates and who wanted to dive deep into this amazing world. I asked the professor for a position. He then asked me to make a team to start. I established a team consisting of students in my class. We were learning our first steps in conducting research.

At that time it was a little bit strange for undergraduates to be working in research and many other students and even professors were asking us why would we waste our time in research instead of studying. We kept working, however, and we spent more than six months with many hours each day learning and gaining new skills in the lab, animal house (where we performed experiments on animals), and with the technical issues regarding the preparation of biological samples. This latter technique was necessary for microscopic studies using an ordinary light microscope, scanning electron microscope, and the energy dispersive X-ray spectroscopy (EDS) which is used by geologists to analyze the elemental composition of stones as well as by biologists to analyze the chemical composition of biological samples.

## First Personal Independent Student Research Experiences

My research was about the corneal ulcer. It is a devastating complication and one of the common causes of blindness in Egypt. The major causes of corneal ulcers are trachoma and alkaline chemical burns. Trachoma, caused by the bacterium

*Chlamydia trachomatis*, is highly endemic in Egypt, especially in rural areas.<sup>1</sup> I started the research project with my team in spite of the limited resources. After six months of hard work in addition to studying for my 3rd year, my group came up with a manuscript.

The team decided to present the research in an international medical student conference so I browsed the internet looking for a conference and got a long list of conferences. We chose to submit the abstract in the 8th YES meeting as it was the most professional and suitable for our research. Later on, the abstract was accepted as a poster presentation.

As a medical student from the Middle East, I used to think that scientific meetings were just about presenting research. I was, however, quite wrong. The YES meeting was more like spending three full days of learning new knowledge, enjoying time in a new culture, and making like-minded friends from all over the world. The scientific program included the plenary, poster presentation, and oral presentations. There were workshops for different skills related to clinical, academic, and even human resources. I had two presentations: the first one was my poster presentation and the second one was about the IJMS. The program also included social activities in which I enjoyed seeing the most beautiful sights of Porto, a city full of historical and touristic attractions.

The part I liked the most was meeting with the scientists where we had the chance to chat with professors and experts from around the world. The professors were so friendly with students, supporting, advising, and willing to exchange scientific, personal, and career experiences. I made a lot of friends from different countries and cultures. There were students from Portugal, Russia, Turkey, Serbia, amongst others. What gathered us together was that we all shared the same interests in medical research.

## Why Research?

Evidence-based medicine (EBM) has become the most effective paradigm in making clinical decisions, according to the most updated guidelines. Teaching EBM in medical schools has

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increased dramatically worldwide.<sup>2,3</sup> However, most medical schools in developing countries have not included EBM training courses in the curriculum.<sup>4</sup> That is why I would like to emphasize the importance of learning the practice of EBM and building a strong research background to help implement these practices in one's future career.<sup>5</sup>

Even if a medical student does have a busy schedule, the research practice should continue along at the same pace as one's medical study; the earlier students start this process, the more benefits they will get. For example, early involvement in research allows for the better understanding of published work and it also allows one to discover a passion for a specific specialty in medicine - possibly influencing one's future career.<sup>6</sup> The idea may seem difficult and even impossible for many different reasons but as a personal experience, I really recommend taking the very beginning steps towards becoming involved in research. I also recommend traveling for learning; whether traveling for an exchange program, doing clinical electives, or attending conferences, it's worth investing some time and resources on one's education.<sup>7</sup>

In addition, conducting research in a place where it is not that empowered is not only beneficial on the scientific level but it is also beneficial as a journey of awareness for other students, supervisors and program directors, encouraging them to direct more effort towards research. This is especially important in developing countries who already face many obstacles

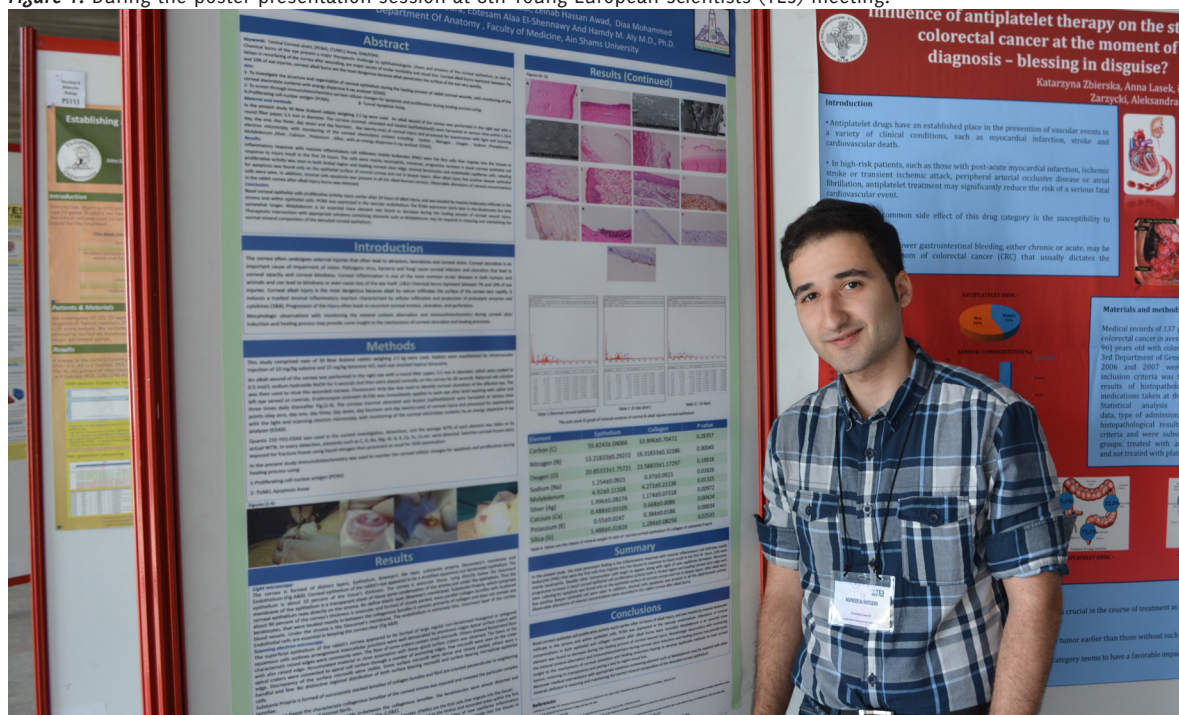
that include little funding, the lack of human resources, and ill-defined research goals. By considering research as one of the fundamental priorities, it will certainly lead these countries toward achieving innovative solutions to provide better health-care practices and productive research environments.<sup>8-11</sup>

Today's medical students are the future physicians. From here on comes the important role of students in understanding the concepts of research and its contribution to the progress of medicine and the service of humanity. That is one of the reasons why the IJMS has been created to promote the understanding of the concepts of research to medical students through several strategies. These include providing a feedback system on how to improve manuscripts to potentially achieve publication, gaining the exceptional experience to develop skills on the critical evaluation of manuscripts under the guidance of expert editors, and also introducing the internal functioning and workings of a peer-reviewed journal.<sup>12</sup>

### Final Words for the Curious Minds

So what are the final take-home messages? Be initiative and start your independent research journey early by forming a like-minded team under the supervision of an inspiring mentor. Be Patient, Persistent and Passionate (the magical 3 P's). Manage your time efficiently. Improve your English language skills. Work on your presentation skills. Love what you do, do what you love, and if you have a curious mind, seek Research!<sup>13-14</sup>

**Figure 1.** During the poster presentation session at 8th Young European Scientists (YES) meeting.





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# A Nobel Day in Lisbon, Portugal – A Unique Experience for Someone who Loves Science

Catarina Alves-Vale.<sup>1</sup>

**About the Author:** Catarina Alves-Vale is a third-year medical student (Faculdade de Medicina, Universidade de Lisboa, Portugal) of a six-year course. She is also doing research about regulation of gene expression at Instituto de Medicina Molecular (Lisboa). In 2013, Catarina won the prize for the Best Plenary Presentation at the Annual International Medical Students Meeting (AIMS Meeting).

## The Experience

June 25th 2013. I will never forget that sunny and busy day in Lisbon, Portugal. After exiting the subway and walking for a few minutes, a huge and magnificent building in the middle of the city appeared on my horizon. It was there, in Culturgest, where I had the opportunity to listen and learn from a group of eminent scientists and Nobel Laureates in physiology and medicine. "A Nobel Day in Lisbon" was an open event supported by Cunha Vaz Associates, a leading communication company, and hosted by Renata Gomes who is a reputed Portuguese scientist affiliated with the University of Oxford and the University College London, who is interested in nanotechnology for cardiovascular regeneration (Cunha Vaz Associates. A Nobel Day. Available from: <http://www.anobelday.com/>. Cited 2013 Sep 5).

The morning topics included discussion regarding the financial difficulties in science and the future of scientific research, which were explored through panel discussions addressed to the public. Basically, the scientists talked to the audience about their work and career, their feelings towards science and how they deal with roadblocks. In some cases, what they were talking about could be applied to areas outside of medicine, in everyday life. For example, many interventions focused on the importance of thinking outside the box when we are trying to plan the future, like a new research project. However, this also should happen when we need to find a key to solve problems, which are quite usual in science, but provide great opportunities to make changes in the way we work and think. Furthermore, it was highlighted, for several times, that being sufficiently persistent to pursue our goals, and specially our dreams, is a requirement to be successful. Another discussed topic was the responsibility of scientists to communicate with society the relevance of their work and discoveries because all the citizens are contributing to the public science funding.

During the afternoon, more specific scientific sessions took place. We had to choose between two "Professional Sessions", because they would be occurring at the same time in different places. I chose the "Vascular Science" session, in which Professor Paul Riley, director of the Oxbridge British Heart Foundation Centre of Regenerative Medicine and Chair of Development and

Reproduction at University of Oxford, told us about his research "en route to mend a broken heart" (University of Oxford. Paul Riley - Oxford Cardiovascular Science. Available from: <http://www.cardioscience.ox.ac.uk/bhf-centre-of-research-excellence/researcher-profiles/paul-riley>. Cited 2013 Sep 6). Specifically, Professor Riley explained how his team used stem cells to treat ischaemic cardiac disease, the leading cause of mortality worldwide (World Health Organization, WHO. The top 10 causes of death. 2013. Available from: <http://who.int/mediacentre/factsheets/fs310/en/>. Cited 2013 Sep 5).<sup>1</sup> The presentation that I enjoyed the most was integrated in this session "Where do Ideas Come From". It was given by Professor Oliver Smithies, Excellence Professor of Pathology and Laboratory Medicine at University of North Carolina and the Nobel Prize laureate in 2007 for introducing starch as a medium in gel electrophoresis (Smithies O. Turning Pages. In: Grandin K, editor. Les Prix Nobel. The Nobel Prizes 2007. Stockholm; 2008. Available from: [http://www.nobelprize.org/nobel\\_prizes/medicine/laureates/2007/smithies\\_lecture](http://www.nobelprize.org/nobel_prizes/medicine/laureates/2007/smithies_lecture). Cited 2013 Sep 5). Professor Smithies, a very kind and enthusiastic 88-year old scientist, also provided advice to the audience in the room; for instance the importance of keeping appropriate lab-book notes and choosing to work in a subject that you really enjoy. I found myself asking what keeps Professor Smithies going? According to his own testimony, it is simply curiosity.

As a second year medical student, and an aspiring scientist, having the possibility of learning with reputed scientists was an amazing opportunity. I was lucky because the Instituto de Medicina Molecular, Lisbon, advertised the event among collaborators, including undergraduate students conducting research. There is still a long way to go to successfully convey to society what scientists actually do. It is really important that scientists themselves strive to be active players in the communication of science to the general audience. This unique day was a very positive step, but more of these steps are needed, and I wish to be part of them.

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## A World Leader in Medicine

Omar Mousa.<sup>1</sup>

**About the Author:** Omar Mousa is a second year internal medicine resident at SUNY Upstate Medical University, Syracuse – New York – USA. The internal medicine program is of 3 years duration. He is a recipient of the Gold Foundation Humanism and Excellence in Teaching Award for the year 2013.

Professor Anna Suk-Fong Lok, MD is the Alice Lohrman Andrews Research Professor in Hepatology, Director of Clinical Hepatology, and the Associate Chair for Clinical Research in the Department of Internal Medicine at the University of Michigan Health System. Dr. Lok obtained her medical degree from the University of Hong Kong in 1977 and her hepatology training under the late Dame Sheila Sherlock at the Royal Free Hospital in London, UK in 1982-83. She rose through the ranks at the University of Hong Kong until she moved to the United States in 1992. More than 30 fellows and junior faculty from all over the world have been trained by Dr Lok. She has received many awards throughout her career, including the Distinguished Scientist Award from the Hepatitis B Foundation, the Distinguished Women Scientist Award from the American Gastroenterological Association and the Distinguished Service Award from the American Association for the Study of Liver Diseases. Dr. Lok is the true triple threat having received awards from the University of Michigan for research excellence in 2011, distinguished mentor in 2012, and clinical excellence in 2013 (Anna Suk-Fong Lok. 2013. Available from: <http://www.uofmhealth.org/profile/425/anna-suk-fong-lok-md>. Cited 2013 Dec 18; Councilor 2013-2015 - Anna Suk-Fong Lok. 2013. Available from: <https://www.aasld.org/aboutus/leadership/Pages/lok.aspx>. Cited 2013 Dec 18).

Dr. Lok's research focuses on the natural history of hepatitis B and C and their pathogenesis and treatment. She also focuses on the prevention of liver cancer. Her research receives funding from the National Institute of Health, as well as multiple pharmaceutical companies and federal and private foundations. She has more than 350 publications on viral hepatitis and liver diseases. She is also the coauthor of the American Association for the Study of Liver Diseases (AASLD) guidelines on Hepatitis B. Dr. Lok served as an Associate Editor of Hepatology, a Co-Editor of the Journal of Viral Hepatitis, and a Senior Associate Editor of Gastroenterology. Dr. Lok is currently a Councilor for the AASLD.

I asked Dr Anna Lok if she could tell the readers of the IJMS and myself about her journey in the field of medicine and scientific research. She was very happy to share her great experience with us. Here is our interview:

**Figure 1.** Anna Suk-Fong Lok, MD, FRCP.



1- Dr Anna Lok, can you please tell us about yourself and what made you choose to become a doctor?

I grew up in Hong Kong and back then – more than 30 years ago, there were only two universities and very limited choices in career paths for students interested in science. I was interested in becoming a doctor because I wanted to work with people. I grew up in a conservative Chinese family. When I told my father I was planning to apply for medical school, he thought medicine was a profession for men and suggested I apply to nursing school instead. However, he was extremely delighted when I was accepted into the only medical school in Hong Kong at that time.

2- What made you interested in Hepatology?

My first rotation as a medical resident was gastroenterology. We had a lot of liver patients on the service. My attending was

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a hepatologist and an inspiring teacher, and we happened to have a visiting professor who was the head of the Liver Unit at UCSF, and who rounded on the service with me for 2 weeks. After that, I knew I wanted to be a hepatologist.

3- During your career, you had important achievements and great successes. Can you describe your most successful accomplishment?

I have my share of successes and failures – this is life. It is important that young people realize that those of us who have made it had our struggles and our failures also. So do not feel discouraged when things are not going your way. It is important to remember that our journey in life and our career is a marathon and not a sprint; there will be ups and downs and those who persevere will reach their destination. I am most proud of the accomplishment of all the fellows and junior faculty I have trained and the outstanding Hepatology program I built at the University of Michigan. It is extremely gratifying to see that many of my mentees are now full Professors and heads of departments, to read their work in scientific journals, and to hear them lecture at scientific meetings.

4- What challenges did you have to overcome while pursuing your career including becoming a successful hepatologist, as well as coming to the United States?

I had very limited research experience when I arrived in London for my fellowship training. It took a long time and a lot of effort to convince others I was committed to research and I was trainable. I did not have any training in the US and I was not familiar with the health system so it took a while to learn how the health system works – I never had to bill my patients or had to understand health insurance before as Hong Kong has a socialized health care system at least back when I was working there. Despite having published more than 100 papers and having established myself as a promising young investigator, I had to prove myself all over again when I moved to the US and to show others that I could make it. I was very lucky in that many people extended a helping hand along the way.

5- What do you like the most about medicine?

We can help others and make a big impact on their health. Our work is never boring as each day brings different challenges and rewards. Although many complain that medicine is not a rewarding profession anymore, I disagree; we are well rewarded by that inner satisfaction that we improve the lives of others and most patients are appreciative.

6- In your opinion, what are the most important values the medical students and residents should learn for their future?

Recognize the impact of every little thing you do on your patients', and their family's, lives. Understand how privileged you are. While we cannot be perfect, we can and should always try our best. Also, remember that medicine is not just a science, it is also an art. Even when our hands are tied and modern medicine cannot save our patient's life, we can still make a difference by being compassionate and understanding.

7- Based on your research expertise, can you tell us why medical students should be encouraged to participate in medical research?

Without research, we would be practicing medicine like our great grandfathers did. Research stimulates us to ask questions and to find answers so we can provide better care to our patients. Even for those who do not plan to pursue an academic career, research trains us how to think, how to analyze problems, and how to interpret other people's work.

8- Finally, I would like to ask you for advice to help the new generation of trainees, including myself, to be great doctors and excellent practitioners?

Set your goals high but be focused, work hard, and never give up. Remember that medicine is not just a science but also an art. Learn how to communicate and how to listen, and always try to imagine if you or your loved one is on the other side of the consultation room.

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## Key aspects of an effective surgical curriculum for medical students

To the Editor,

Surgery is a competitive specialty that a proportion of medical students choose to pursue however, many individuals find enhancing their portfolio difficult at such an early stage. This letter aims to provide a structured way in which surgically minded medical students can take advantage of opportunities to start to build a strong portfolio. There are 5 key areas to address throughout medical school: anatomy, clinical skills, management, research and mentorship. The overriding theme is that we must not only show an enthusiasm for surgical education, we must also be provided with an innovative and inspirational training programme.

### Anatomy Teaching

Anatomy is traditionally taught by cadaveric dissection or prosection in medical schools. The use of cadaveric dissection and prosections must be preserved in medical schools, as this is the most realistic simulation of the internal workings of the human body that pre-clinical students achieve prior to entering the operating theatre. Integration of newer techniques like 3D computer simulations of the human body will allow students to explore interactive prosections to understand and learn anatomy. For example, Anatomy TV® is an internet based interactive learning tool derived from human dissection ([www.anatomy.tv](http://www.anatomy.tv)). Orientating anatomy teaching around these tools will provide an innovative curriculum for pre-clinical students to learn.

There are several approaches to anatomy teaching however, we believe a case-based approach can help to teach normal anatomy and facilitate understanding of what problems abnormal pathology can cause. For example, when exploring the anatomy of the lungs this should be in the context of a disease such as cystic fibrosis; after learning the pathophysiology of the disease students will better understand the normal anatomy of the lung and how disruptions, such as bronchiectasis cause airway collapse, impaired clearance of secretions and increased susceptibility to infection.<sup>1</sup> This approach can also help provide pre-clinical students with surgical treatments to these

cases. For example, in the above case, the definitive treatment is a lung transplant. A case-based approach can help stimulate enthusiasm to learn anatomy.

Furthermore, the dissection room is also an ideal place for students to be introduced to the importance of good clinical practices such as hand washing and handling sharps. These skills are of vital importance for both patient and staff safety and have particular importance in a sterile surgical environment.

### Clinical and Technical Skills

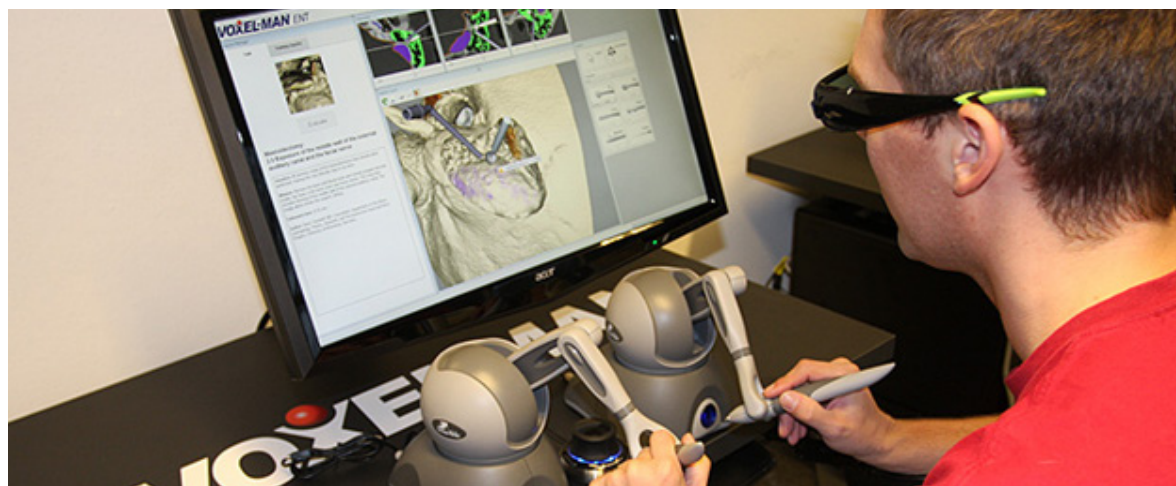
We must maximize all the learning opportunities available to us as medical students; this is especially important for those who train in the European Union because the European Working Time Directive restricts trainees to 48 hours of work per week, therefore surgeons of the future have less time to achieve the competencies held by surgeons of today.<sup>2</sup> To achieve this, medical students must attend all clinical opportunities available to them, reading before and after each clinical experience to reinforce their knowledge base.

Surgical simulation has been shown to enhance (rather than substitute for) time in the operating room and surgical trainees and medical students widely agree that it should be added to their curriculum.<sup>3,4</sup> Maximizing the use of surgical simulators available in some centres, will help budding surgeons build the necessary dexterity in order to succeed in surgical fields where procedures are progressively becoming minimally invasive.<sup>5,6</sup> These early exposures will help clinical students develop and aspire to become the surgeons of tomorrow (**Figure 1**).

### Management and Leadership

Surgery is more than a technical exercise; surgeons are team builders and leaders. Surgeons lead a multi-disciplinary team in the operating theatre and early experience of leadership can help develop communication and teamwork skills so that tomorrow's surgeons can become better leaders. Students should participate in and lead student bodies, such as the Student British Medical Association (BMA) and surgical societies in order to gain experience in management and healthcare politics. Meanwhile, universities should provide opportunities for students to gain formal training in leadership and management

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as successful surgeons of tomorrow must have these qualities in their armamentarium of skills.<sup>7</sup>

### Research

All medical professionals must innovate within their respective specialties and therefore as medical students we must involve ourselves in research, both opportunistically and through further degrees, to expand the evidence base from which we practice in the future. As students in active research centres, approaching senior practitioners to help with research projects and audits in a field of interest can be a great way of learning how boundaries can begin to be pushed and practice improved in surgery. The early development of analytical and critical thought to challenge and improve surgical care is important; the best surgeons need to move their specialty forward.

As future surgeons we have a unique chance to improve a specialty that is not traditionally academic there is a big push for clinical research with less than 1% of surgical patients currently involved in trials.<sup>8</sup> Currently, despite a call for multicenter and even multinational collaboration, there is a reluctance by clinicians to recruit for research and therefore by improving our understanding of research methodology as students we can significantly contribute to evaluation of surgical procedures in all fields.<sup>9,10</sup>

### Mentorship

Lastly, we believe excellent surgeons need enthusiastic and committed mentors. Mentorship has been shown to ultimately maintain and improve patient surgical care.<sup>11</sup> Mentors motivate, advise and may also be able to offer extra clinical or research exposure to enthusiastic students. Furthermore, it has even been shown that early preclinical mentorship positively influences student's decisions when embarking on a surgical career.<sup>12</sup>

Therefore, universities should give students access to mentors that can guide and advise students on the correct path towards a successful future in a surgical speciality. As medical students, we can attempt to seek out these mentors ourselves by asking for opportunities to shadow and become involved in projects with surgeons that we take a liking to, that operate in a potential field of interest, or seem enthusiastic to teach.

Finally, during medical school, some students decide to embark on a surgical career than others. Regardless of the stage at which this decision is made it is important to maximize opportunities to give the best chance of success in our chosen field. We strongly believe that not only is embracing anatomy and clinical skills is important but also actively seeking leadership opportunities, research projects and mentors will give medical students the best chance of a successful career in surgery.

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## Enhancing the Student Surgical Learning Experience

To the Editor,

In this issue, Okonkwo *et al.*, have discussed areas of improvement for the undergraduate medical curriculum that are needed to promote the next generation of surgeons.<sup>1</sup> With an ever-present trend of decreasing interest in surgery, this is now more important than ever.<sup>2</sup> However, Okonkwo *et al.* are short in their discussion in what medical students can do themselves to enhance their surgical training experience. The steps that medical students can undertake begin in the anatomy lab and progress into the clinical surgical rotation. In addition to these, joining student surgical societies and finding effective mentors will assist surgically-minded medical students on their surgical career path.

### Anatomy Teaching

Anatomy has forever been one of the corner stones of medical education, often marking the entry of students into the world of medicine. However, in the past decade anatomical teaching has seen a decline, with a reduction in both time and resources directed towards developing the anatomical curriculum.<sup>3</sup> While there is still much debate in how the future of anatomical teaching will look, it would indeed be difficult to argue against the importance of a solid foundation in the anatomical sciences.<sup>4</sup>

Regardless of whether a student will be using cadavers, specimens, or electronic images, preparation is key for a successful anatomy lab. Due to the limited amount of time available in the anatomy labs, students should begin with a preliminary understanding of the topics to be covered. Too frequently students arrive without sufficient background knowledge to efficiently use their time in the lab. In addition, surgically-minded students should always keep in mind the clinical relevance of their dissection experience.<sup>5</sup> For example while studying the anatomy of the knee, students should explore the different clinical presentations of ligament tears. This helps to promote learning through understanding, rather than superficial memorization. Studies have shown that in order to promote long-term anatomical learning, students should take multiple approaches in their learning of anatomy.<sup>6</sup> These steps should ensure a solid foundation of anatomical knowledge and will serve students well as they enter their surgical rotations.

### Surgical Rotations

As the surgically minded students advance from the preclinical stage into their clinical rotations, they will soon face their daunting first surgical rotation. Indeed, many students enter their surgical rotation with concerns of fatigue, mental abuse, and proficiency.<sup>7</sup> The surgical rotation has historically been described as having a unique learning environment with an emphasis on teamwork, but with less personal connections with staff members.<sup>8</sup> Students need to quickly adapt to make the most of their experience. Students may be initially disappointed with the passive nature of learning in the operating room (OR). However, those hours standing in the OR do not need to be wasted. To fully take advantage of their OR experience, students need to be familiar with clinical history and

presentations of the patients that they will be seeing. Meeting the patient pre-operatively also has the added advantage of increasing the likelihood of being permitted to attend and actively participate in the patient's operation. What students frequently forget is that clinical learning does not have a strict syllabus that is seen in the preclinical curriculum. This means that students are partially responsible for their learning. This means taking the responsibility to ask questions, demonstrate enthusiasm, ask for feedback, and discover their own learning opportunities. These are the traits that will help medical students succeed in a surgical rotation, and ultimately, secure a surgical training position.

### Finding the right mentor

Okonkwo *et al.*, have discussed the importance for medical schools to provide access to surgical mentors.<sup>1</sup> However, this service is not always provided by medical schools; indeed, the majority of medical students do not have effective surgical mentors.<sup>9</sup> Ultimately, it falls upon the student to find and create that personal connection. Students frequently misconceive that mentors must be consultant/attending-level surgeons. While senior mentors have the benefit of being well known among the academic community, provide convincing reference letters, and have a wealth of experience, the benefits of junior mentors are often overlooked. One study demonstrated that students who were exposed to surgical residents that enjoyed teaching and acted as role models, were more likely to pursue a career in surgery.<sup>10</sup> As a result, students should strive to have several mentors from varying stages of proficiency, benefiting from the time that junior doctors have to offer and the experience of senior experienced surgeons. Students should also strive to find a mentor with a similar learning style and outlook on medicine. A mismatched pair of mentor-mentee can be an ineffective tool and may potentially act as a deterrent to enter the field of surgery.

### Student surgical community

While surgical training is habitually based in the hospital, surgical training is not limited to the OR. In such a dynamic field, surgical excellence is reliant on continuous learning, which is made possible through strong and active surgical communities found both locally and globally. Medical students have founded surgical societies which create a platform for students to engage with members of their own surgical departments. These societies also highlight local windows of opportunity for students interested in further developing their surgical knowledge. In addition, membership in these societies demonstrates to training directors a trainee's commitment and interest.<sup>11</sup> National and regional surgical societies bring together members of the larger surgical community. Membership in such societies provides students with a wide array of exposure to this ever-changing field and is routine for students with a surgical interest.<sup>12</sup> These groups also frequently host extracurricular lectures, workshops, and conferences where pre-clinical and clinical medical students alike have the opportunity to engage with all facets of surgical training. Taking active steps to get involved with such groups is an invaluable way of ensuring a well-rounded and cutting-edge surgical education.

In conclusion, Okwonko *et al.*, have discussed how the undergraduate medical curriculum needs to help support medical

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students on a surgical training path;<sup>1</sup> however, it is important to note that there are several steps that medical students can take themselves to enhance their surgical training experience in the undergraduate setting. These steps take the form of self-directed learning in the anatomy lab, in the OR, finding motivational mentors, and collaborating with the activities of a student surgical society. Together, the curriculum improvements highlighted by Okwonko et al. and the student factors mentioned here will ensure the development of the next generation of surgical trainees.

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