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The role of head CT prior to lumbar puncture in patients with suspected meningitis in a Johannesburg emergency department

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The role of head CT prior to lumbar puncture in patients with suspected meningitis in a Johannesburg Emergency Department

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A Research Report submitted to the Faculty of Health Sciences, University of Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Masters of Medicine in Emergency Medicine.

Johannesburg, February 2021

DECLARATION

I, Lana Cronje, hereby declare that this research report is my own work. It is being submitted for the degree of Masters of Medicine in Emergency Medicine to the University of the Witwatersrand, Johannesburg. It has not been previously submitted or presented for any degree or professional qualification at this or any other Institute.

Signature of Student: 

Date: 2021/02/11

Name of Supervisor 1: Prof F Motara

Signature of Supervisor 1: 

Date: 2021/02/11

Name of Supervisor 2: Dr M Moolla

Signature of Supervisor 2: 

Date: 2021/02/11

DEDICATION

To Jenna, Bryan and my mother, Lenie: without your support this project would not have been possible.

ACKNOWLEDGEMENTS

For their support with this project, I would like to thank my supervisors, Dr M Moolla and Prof F Motara. Their time, guidance, effort and patience are deeply appreciated.

SUBMISSION FORMAT OF THIS RESEARCH REPORT

As per University of the Witwatersrand Faculty of Health Sciences guidelines, this research report is being submitted in the following format: submission for publication ready format. The article is to be submitted to the SAMJ.

TABLE OF CONTENTS

DECLARATION i
DEDICATION ii
ACKNOWLEDGEMENTS ii
SUBMISSION FORMAT OF THIS RESEARCH REPORT iii
SAMJ AUTHOR GUIDELINES ..... - 1 -
MANUSCRIPT FOR SUBMISSION ..... - 6 -
SUBMISSION LETTER TO THE EDITOR ..... - 8 -
ARTICLE ..... - 9 -
Abstract ..... - 9 -
Background ..... - 10 -
Methods ..... - 10 -
Results ..... - 11 -
Discussion ..... - 15 -
Conclusion ..... - 17 -
References ..... - 18 -
RESEARCH PROTOCOL ..... - 20 -
APPENDIX 1: ETHICS CLEARANCE CERTIFICATE ..... - 35 -
APPENDIX 2: TURN-IT-IN REPORT ..... - 36 -
APPENDIX 3: CERTIFICATE OF FINAL SUBMISSION SIGNED BY STUDEN……..….- 37 -
APPENDIX 4: CERTIFICATE OF FINAL SUBMISSION SIGNED BY SUPERVISORS……...- 42 -
APPENDIX 5: LIST OF CORRECTIONS……-44-
APPENDIX 6: HOD APPROVAL LETTER…….-46-
APPENDIX 7: EDT PAYMENT RECEIPT……..-47-

SAMJ AUTHOR GUIDELINES

General article format/layout

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, which will delay publication.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and ºC), e.g. '40 kg' and '20 cm' but '50%' and '19ºC'.
- Please be sure to insert proper symbols e.g. µ not u for micro, a not a for alpha, b not B for beta, etc.
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- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published

previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text.

Structured abstract

- This should be 250-400 words, with the following recommended headings:
    - **Background:** why the study is being done and how it relates to other published work.
    - **Objectives:** what the study intends to find out
    - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
    - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
    - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.

- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF or jpeg form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Endnotes must* ***not*** *be used.*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.

- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
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    - Click Actions > Cite
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    - Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

MANUSCRIPT FOR SUBMISSION

TITLE PAGE

TYPE OF ARTICLE

Original research

TITLE OF MANUSCRIPT

The role of head CT prior to lumbar puncture in patients with suspected meningitis in a Johannesburg Emergency Department.

RUNNING TITLE

Scanning prior to lumbar puncture. How careful should we be?

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CONFLICTS OF INTEREST

The author hereby certifies that this submission is not under publication consideration elsewhere and is free from any conflict of interest.

AUTHOR CONTRIBUTIONS

Lana Cronje- Primary author, study design, data collection, data analysis, manuscript write up and approval of the final manuscript.

Feroza Motara- Assisted with study design, data analysis, interpretation of results, editing of manuscript and approval of the final manuscript.

Muhammed Moolla- Assisted with study design, data analysis, interpretation of results, preparation of manuscript and approval of the final manuscript.

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None

SUBMISSION LETTER TO THE EDITOR

Dear Editor: The South African Medical Journal:

Thank you for considering our article entitled: “Scanning prior to lumbar puncture. How careful should we be?”

It is common practice to perform a CTB prior to lumbar puncture in patients with suspected meningitis to exclude contra-indications to lumbar puncture. There are however several documented limitations to this practice. These include increased costs, prolonged ED length of stay and delays to antibiotic administration, contributing to morbidity and mortality.

South Africa is unique in that it has the largest number of people living with HIV who depend on public healthcare resources. Recommendations by FIDSSA guide which patients should receive CTB prior to lumbar puncture, but little is known about this practice in South African ED’s.

We believe that or findings will provide significant insight into this practice in public emergency departments. This article will appeal to the readership of the South African Medical Journal as it is applicable to multiple disciplines as well as hospital managers and carries a high citation potential.

ARTICLE

Scanning prior to lumbar puncture. How careful should we be?

Abstract

Background: Significant considerations exist when establishing which patients require a computed tomography scan of the brain (CTB) prior to lumbar puncture for suspected meningitis. Over-scanning patients have numerous implications including increasing healthcare costs and emergency department (ED) length of stay. Data on the imaging practices of doctors working in South African EDs is limited as well as whether they are considering the Federation of Infectious Diseases Society of Southern Africa (FIDSSA) guidelines around this practice. Hitherto there is no consensus regarding which patients require a CTB and which should proceed to a lumbar puncture without one.

Objectives: To describe current practices and the usefulness of the FIDSSA criteria relating to CTB prior to lumbar puncture and CTB results in patients with suspected meningitis in an academic, tertiary emergency department.

Methods: A retrospective, descriptive chart review was conducted of 284 adult patients presenting to Charlotte Maxeke Johannesburg Academic Hospital ED who had a CTB prior to lumbar puncture for suspected meningitis between 1 November 2016 and 31 October 2018. Data analysed included patient demographics, indications for CTB, presence of FIDSSA criteria, laboratory findings and CTB results.

Results: Two hundred and eighty-four patients with suspected meningitis who had a CTB scan prior to lumbar puncture were identified. Patients had a mean age of 39 years (range 18-81 years) and a male predominance (n= 157, 55%). HIV co-infection rates were 67%, the CD4 count was less than 200 in 47% of patients and cryptococcal meningitis was diagnosed on cerebrospinal fluid (CSF) analysis in 41% of subjects. Altered mental state (61%) was the most common indication for imaging, followed by headache (39%) and focal neurological deficit (31%). FIDSSA criteria for imaging were absent in 31% of patients. CTB scans revealed intracranial abnormalities in 121 patients (43%) and major findings which could preclude lumbar puncture in 32 (11%). Major abnormalities were found in 23 patients (16%) with FIDSSA criteria and 7 (8%) without. This association between the presence of FIDSSA criteria and major CTB scan abnormalities was not statistically significant (p=0.114).

Conclusion: There is poor guideline adherence regarding CTB prior to lumbar puncture with consequential delays in appropriate treatment, diagnosis and increasing healthcare costs. However, the FIDSSA guidelines require prospective validation for use in an ED setting as the absence thereof may not identify major abnormalities in several patients.

Background

Meningitis is a life-threatening disease frequently encountered in an ED. In Southern Africa, an inpatient mortality rate of more than 40% highlights the need for rapid diagnosis and swift treatment of this disease process (1,2). Diagnosis requires analysis of CSF obtained via lumbar puncture (3,4). Owing to the brain's remarkable, but limited potential for autoregulation of cerebral perfusion pressure, classic signs of raised intracranial pressure such as focal deficits or papilloedema maybe be absent (5). Cerebral herniation, a much feared catastrophic complication of performing a lumbar puncture in patients at risk of raised ICP, often necessitates a CTB prior to the LP (6,7).

The use of CTB prior to lumbar puncture is not without implications: high costs, limited availability, cancer risks and, very importantly, delays in antibiotic administration and patient disposition contribute to ED overcrowding and increased mortality (3,8-10). A conservative imaging strategy is therefore appealing in the South African context.

The presence of one or more criteria from the FIDSSA guidelines assists in determining which patients should receive a CTB prior to lumbar puncture. It includes a Glasgow Coma Scale (GCS) of less than 10, papilledema, a ventriculoperitoneal shunt, unexplained new focal neurological deficits excluding isolated cranial nerve palsies, and unexplained seizures. (4). Interestingly, a study done in the Western Cape found that although seizures in HIV positive patients are often a result of space occupying lesions and cerebral oedema, the vast majority of these are actually safe to LP (11).

This novel South African study, in an academic, tertiary ED describes the demographics, indications and characteristics of patients who received a CTB prior to lumbar puncture for suspected meningitis, as well as the use of the FIDSSA guidelines. It also describes the findings from laboratory investigations and CTB scans.

Methods

This retrospective, descriptive study was completed between 1 November 2016 and 31 October 2018 in the ED at Charlotte Maxeke Johannesburg Academic Hospital. It is a tertiary, academic facility in Gauteng affiliated to the University of the Witwatersrand. A chart review was performed of all adult patients presenting with suspected meningitis, who received CTB prior to performance of a lumbar puncture. Patients with known intracranial abnormalities prior to presentation, head trauma in the preceding month and those whose records were unavailable were excluded.

Data pertaining to CTB scan results was collected from the online picture archiving and communication system (PACS). This included patient demographics, indication for CTB and whether these included FIDSSA criteria, clinical characteristics (as written on CTB request form by clinician) and CTB scan results. These results were reported by the radiology registrar on duty and subsequently reviewed by a radiology consultant. They were classified as either normal or abnormal. Results were considered abnormal if there were any findings other than atrophy or uncomplicated sinusitis. Abnormal findings were further subdivided into minor or major abnormalities. Abnormalities were considered major if there were features suggestive of raised intracranial pressure (ICP) which would preclude a lumbar puncture. This included effacement of the basal cisterns, obliteration of the fourth ventricle, space-occupying

lesions with brain shift or obstructive hydrocephalus. Minor abnormalities included all other abnormal results.

Laboratory results were collected from the National Health Laboratory Service (NHLS) Track Care system and included CSF result, blood culture result, HIV infection status and CD4 count. CSF results were further categorized as suggestive of bacterial, viral, cryptococcal, tuberculous meningitis or other pathology. Once collected, data was transferred anonymously onto an Excel spreadsheet, version 2010 (Microsoft, USA).

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 25. The Pearson-chi square test was used to determine the relationship between quantitative variables and CTB scan findings. The Fischer exact test was used (assuming p-value <0.05) to test qualitative variables.

The study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences, University of the Witwatersrand (Ethics clearance certificate number M180123) and institutional permission was obtained. The study was conducted according to the internationally accepted ethical standards and guidelines of the Declaration of Helsinki, the South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

Results

Of the 781 patients with suspected meningitis who were identified, 284 patients were included in our study as depicted in figure 1. The mean age of patients was 39 years (range 18-81years), with a slight male predominance (55%, n=157). One hundred and ninety patients (67%) were HIV infected and 134 patients (47.1%) had a CD4 count of less than 200, accounting for 70.5% of the HIV infected patients. In 63 patients (22.2%) the HIV status was not known.

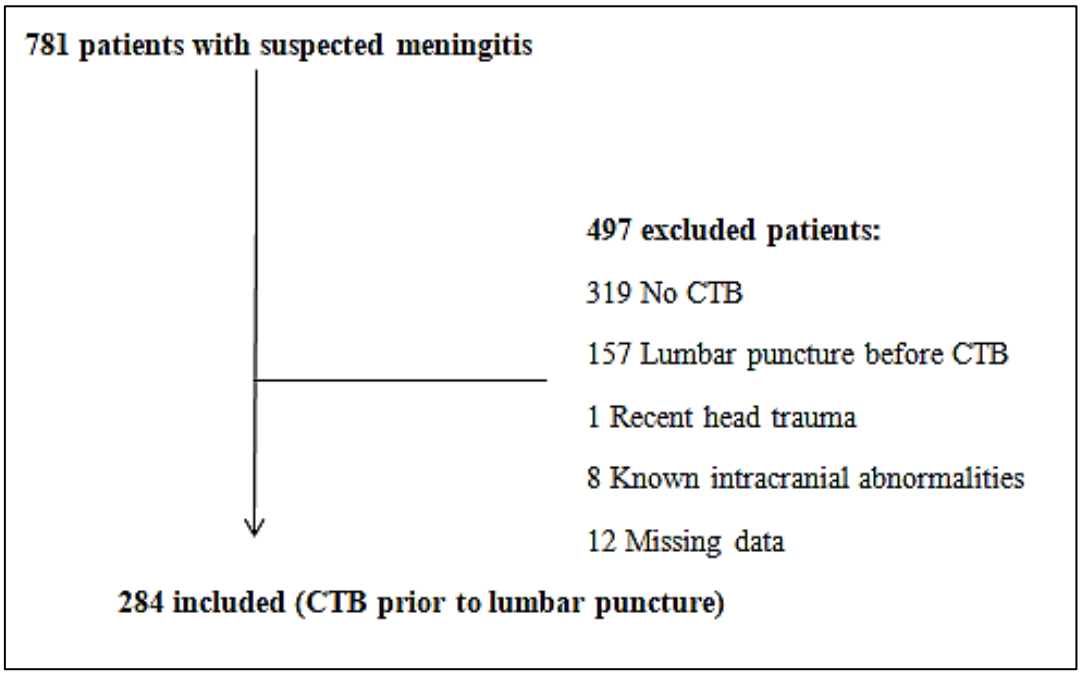


Figure 1: Breakdown of included patients

Clinical indications for requesting a CTB prior to decision regarding lumbar puncture were collected from CTB request forms. The most frequent clinical indications for CTB were altered mental state (61%), headache (39%), focal neurological deficit (31%), unexplained seizures (27%) and nausea or vomiting (22%). Indications are described further in Table 1.

Table 1: Clinical characteristics and indications as per CTB request forms

Indications & clinical characteristics of study population	**Total= n (%)**
Altered mental state (all)	173 (61%)
Altered mental state GCS <10	17 (6%)
Altered mental state GCS >/= 10	78 (27%)
Altered mental state GCS not specified	78 (27%)
Headache	111 (39%)
Focal neurological deficit (all)	87 (31%)
Focal neurological deficit- Isolated to cranial nerves	32 (11%)
Focal neurological deficit- not isolated to cranial nerves	55 (19%)
Unexplained seizures	77 (27%)
Nausea or vomiting	63 (22%)
Meningism	50 (18%)
Fever	38 (13%)
Visual symptoms	20 (7%)
Photophobia	13 (5%)
Elevated blood pressure	12 (4%)
Pupillary abnormalities (excluding papilledema)	12 (4%)

Known immunocompromise	11 (4%)
Papilledema	11 (4%)

Only 147 (51.8%) of the 284 included patients met FIDSSA criteria for a CTB prior to lumbar puncture, while 88 patients (31%) did not meet the criteria. The GCS score was not stated in 49 patients (17.3%) and therefore it could not be determined whether they had a recommended indication for CTB prior to lumbar puncture.

Blood cultures were obtained in 163 patients (57%). In 49 patients (30%) a microbiological organism was isolated. Lumbar puncture was performed for CSF analysis in 258 patients (91%) and 137 (53%) had abnormalities on analysis. Figure 2 depicts the distribution of the most likely cause of meningitis as per CSF analysis in these patients.

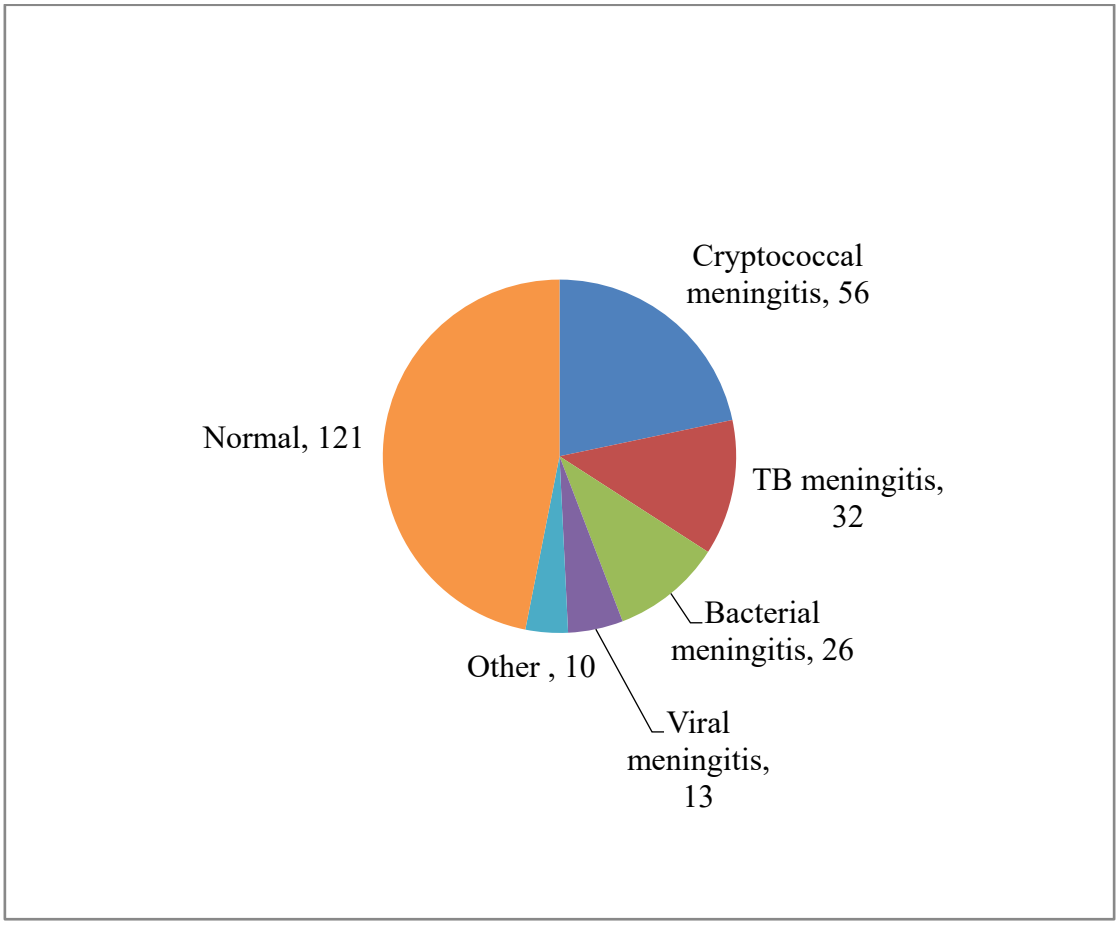


Figure 2: Distribution of most likely cause of meningitis as per CSF analysis in patients who underwent lumbar puncture in the study population (n=258)

Abnormalities on CTB scans were present in 121 patients (43%). Owing to the presence of more than one abnormality in a few of these scans, a total of 166 abnormal findings were present. These findings are described in Table 2. Major findings, which theoretically preclude the performance of a lumbar puncture, were present in 11% of the study population. This accounted for 21% of all abnormal findings.

Table 2 Breakdown of abnormal findings on CTB scans

Abnormal CTB Findings (N=166)		N (%)
Major	Space occupying lesion- with brain shift	15 (9)
	Features of raised intracranial pressure without the presence of a space occupying lesion	13 (8)
	Obstructive Hydrocephalus	7 (4)
Minor	Meningeal enhancement	48 (29)
	Communicating hydrocephalus	24 (15)
	Infarction	17 (10)
	Space occupying lesion- No brain shift	14 (8)
	Complicated sinus disease	6 (4)
	Venous Thrombosis	5 (3)
	Mastoiditis	5 (3)
	Inflammatory changes	4 (2)
	Oedema (without features of raised intracranial pressure)	3 (2)
	White matter hypodensities	3 (2)
	Metastases	1 (1)
	Involution/ Atrophy	1 (1)

A comparative analysis of the data was performed to find associations between different variables and the presence of abnormalities on CTB scan. The analysis revealed that females had a significant association with major abnormalities on imaging results (p= 0.021).

HIV infected patients and those meeting FIDSSA criteria for imaging prior to lumbar puncture were more likely to have major abnormalities on imaging. Major abnormalities were present in 7(8%) of patients who did not meet FIDSSA criteria for CTB prior to LP. These results are shown in Table 3.

Table 3: Comparison of abnormal CTB scan results according to the presence of FIDSSA criteria

FIDSSA criteria, N=284	**Total**	**Abnormal CTB** N (%)	***p*-value**	**Major abnormality on CTB** N (%)	***p*-value**
Present	147 (52)	65 (44)	0.684	23 (16)	0.114
Absent	88 (31)	36 (41)		7 (8)	
Unknown	49 (17)	20 (41)		2 (4)	

Discussion

This study was the first of its kind in South Africa, making comparisons only possible with international data. Seven hundred and eighty-one patients were identified with suspected meningitis over a two year period which was significantly more than numbers quoted for similar studies in more developed countries (12). The most reasonable explanation for this is the high rate of HIV infection in South Africa with an estimated prevalence of 19% in the young adult population (13).

At least 67% of the study population was HIV infected and 78% of these patients had a CD4 count below 200. This was in line with the co-infection rate quoted in Lesotho in 2014 (2) and indicates a concerning rise from the 37.3% present in an earlier SA study (1). That study furthermore predicted a predominance of cryptococcal and tuberculous meningitis as the HIV epidemic worsens, which was clearly visible in our study population as well as a study performed in Cape Town (14). Nuances in the clinical management of cryptococcal and tuberculous meningitis, makes it necessary for South African guidelines to deviate from international recommendations.

Most international guidelines include immunocompromise as a criterion for CTB prior to lumbar puncture, however their HIV coinfection rates of 10.4 -20.7% are much lower than the 67% seen in our study (12,15–17). This lower rate of HIV infection in these studies and resultant lower incidence of immunocompromise makes it feasible to image all of these patients prior to lumbar puncture. In our limited resource environment and HIV prevalent population, imaging all patients with HIV will increase the healthcare financial burden and lead to detrimental treatment delays.

Consistent with international guidelines, altered mental status was the most common indication for obtaining a CTB prior to lumbar puncture (17). Existing guidelines are, however, not in agreement over the GCS threshold for CTB (4,12,15,17–19). Some international studies suggest that for any alteration in mental status, a CTB should be obtained prior to lumbar puncture (12,15) whereas the FIDSSA guidelines suggest imaging for GCS less than 10 (4). Botswana guidelines, with a comparative patient population to ours, suggest that an emergency CTB should be done for all patients with suspected meningitis and a GCS<8 or posturing, unless presumed to be caused by cryptococcal meningitis (20). Their imaging strategy is thus more conservative than ours possibly as a result of an even more resource-strapped healthcare sector. Comparative data between CTB scan results and level of GCS would provide useful insight into resolving this uncertainty and pave the way for further research in this field.

Many ED practitioners are, unfortunately, not aware of the respective guideline recommendations. Poor adherence to the FIDSSA guidelines with regards to neurological indications for CTB prior to lumbar puncture was noted in the study. Only 51.8% of patients had contraindications to lumbar puncture without imaging documented on their CTB request form. Multiple international studies found poor adherence to national guidelines with over-investigation by means of CTB in all of these studies (17,21). We also observed deviation from FIDSSA guidelines regarding blood culture sampling on patients with suspected meningitis.

Blood cultures are critical in patients who will experience a delay to lumbar puncture due to imaging, as sterilization of blood cultures post antibiotic administration can occur rapidly (4). This is especially important in overcrowded South African EDs, where there are often significant delays to CTB being performed. The study found that only 57% of patients had a blood culture performed with an organism cultured in 30% of these patients. This can lead to significant diagnostic uncertainty and unnecessary prolonged antibiotic therapy.

Papilledema, a clinical sign of raised ICP and one of the FIDSSA imaging recommendations, was only documented to be present in 4% of patients whilst 11% of patients had features suggestive of raised ICP on CTB scan. This suggests that either papilledema was missed or it wasn't screened for in more than half of the patients in which it was likely present, reflecting another area of deviation from the guidelines. Traditionally, fundoscopy is used to detect this at the bedside, however, for myriad reasons, this skill is notoriously poorly performed by non-ophthalmologists in the ED (22). An emerging alternative to fundoscopy is the use of ocular ultrasound to detect widening of the optic sheath (23,24): a sign well recognized as a surrogate for papilledema and perhaps a skill more ED clinicians should be embracing as part of their armament.

The study was performed in an academic hospital where neuroimaging is readily available. It is thus likely that our rates of imaging far exceed those of most regional and rural centres in South Africa. Abnormalities on CTB scan were present in 43% of cases and 11% of all scans had major abnormalities. This rate is much higher than numbers found in the literature of 15-24% for abnormal findings and 2.7% for major findings (12,16,17). The presence of major abnormalities theoretically precludes the performance of a lumbar puncture. However, 20 out of the 32 patients with major abnormalities on CTB scan still had a lumbar puncture performed within their hospital stay. Normal CSF analysis was present in 6 (30%) of these potentially harmful lumbar punctures. This brings into question the utility of CTB prior to lumbar puncture if this practice is not going to lead to a change in management of these patients.

Of all the variables compared to CTB outcome, only female sex was found to be significantly associated with abnormal CTB scan results. Surprisingly, HIV infection and a CD4 count of less than 200 were not significantly associated with major abnormalities on CTB scans. This once again supports the FIDSSA guidelines in their exclusion of immunocompromise as an independent indicator for imaging prior to lumbar puncture. As one would expect, the presence of guideline criteria identified more patients with major abnormalities on CTB scans, There were however 7 (8%) patients with major CTB scan abnormalities who had no FIDSSA criteria documented on their CTB request forms, emphasizing the need for prospective validation of the use of these guidelines in our emergency departments.

Despite being a novel South African study that looked at critical facets of patient management, our study had several limitations. It was a single centre study in a tertiary hospital and results cannot be generalized to other, rural centres in South Africa. The study was retrospective and heavily reliant on adequate record-keeping, resulting in missing data.

Using CTB request forms for information regarding clinical characteristics and indications for CTB means there might have been significant findings present that were not documented. Furthermore, the majority of our study population was HIV infected and the results must be applied with caution in the population that is not HIV infected**.**

Conclusion

Our study highlights the high incidence of patients presenting to a South African ED with complicated meningitis and reflects a society in which HIV is still rampant. Our results highlight the lack of FIDSSA guideline adherence. Increased awareness amongst emergency medicine practitioners could prevent unnecessary imaging and the implications thereof. Importantly, the use of these guidelines in the emergency department setting lack prospective validation and the absence of FIDSSA criteria may not identify major abnormalities in several patients. Prospective studies are needed to validate the use of these guidelines in South African emergency departments.

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RESEARCH PROTOCOL

The Role of Head CT prior to lumbar puncture in patients with suspected meningitis in a Johannesburg Emergency Department

Dr Lana Cronje

Student Number: 1935836

Research protocol in partial fulfilment of the degree for Master in Medicine

(Emergency Medicine)

Supervisor: Prof Feroza Motara

Co- supervisor: Dr Muhammed Moolla

INTRODUCTION

Meningitis is an inflammatory condition of the meninges covering the brain and the spinal cord. This may be caused by infection with bacteria, viruses other microorganisms or in rare circumstances drugs or cancer. The mortality varies between different pathogens and populations with in-hospital mortality of more than 40% recorded in a South-African hospital (Bergemann and Karstaedt, 2013). This condition is regarded as a medical emergency because of this high rate of morbidity and mortality.

Meningitis is suspected in adult patients presenting with fever, neck stiffness and altered mental status. This classic triad of symptoms was found only to be present in 44% of adults, however, almost all patients presented with at least two of the four symptoms of fever, neck stiffness, headache or altered mental status (van de Beek *et al.*, 2004). Atypical symptoms are therefore common.

The presentation of meningitis can vary significantly in developing and developed countries. Several factors contribute to atypical clinical presentations of meningitis. There is often a delay in health seeking behaviour, difficulties with health access due to lack of available health facilities, long distances to travel for medical care, lack of transport or inability to pay for transport (van der Hoeven, Kruger and Greeff, 2012). This leads to more patients presenting with complications of the disease. The increased prevalence of immunocompromise in developing countries is another factor leading to atypical presentations in these regions.

Immunocompromised hosts lack the ability to respond normally to an infection. This is due to a weakened immune system. This can be caused by a number of conditions like diabetes, malnutrition, drugs and HIV. In 2016, the estimated number of HIV positive people in South Africa was 7.03 million (Statistics South Africa, 2016). Furthermore, 40% of patients do not know their HIV status (UNAIDS, 2016). This makes it a challenge for clinicians to identify patients in whom a higher index of suspicion for atypical meningitis symptoms is necessitated.

The diagnosis of meningitis is made on an analysis of the cerebrospinal fluid. This is obtained by a lumbar puncture. Lumbar puncture is an inherently invasive procedure and not without risks. Of particular concern is the risk of a rapid decrease in cerebrospinal fluid pressure leading to brainstem herniation and death (as cited by van Crevel, Hijdra and de Gans, 2002). Performing a lumbar puncture is thus contra indicated in patients with elevated intracranial pressure. A computed tomography (CT) scan of the head is often performed to evaluate for this.

Despite lacking validation, several decision rules exist to selectively perform head CT's in patients who are the most likely to have raised intracranial pressure or mass lesions (April, Long and Koyfman, 2017). Most of these are departmental guidelines and differ depending on

local practises. According to Dutch guidelines patients with a Glasgow coma scale less than 10, new paresis of an arm or leg, papilledema, immunocompromise or new onset seizures should receive neuro imaging before lumbar puncture (as cited by Costerus *et al.*, 2016). This is similar to South African recommendations. The Federation of Infectious Diseases Society of Southern Africa (FIDSSA) recommend CT prior to lumbar puncture in patients with a Glasgow Coma Scale of less than 10, papilledema, the presence of a ventriculoperitoneal shunt, unexplained seizures or unexplained new focal neurological deficit, excluding isolated cranial nerve palsies (Boyles *et al.*, 2013). From experience, current practise in most emergency departments are guided by clinician gestalt, it is thus difficult to determine whether these practices are appropriate.

Head CT is unfortunately not without limitations. It carries a high financial burden, especially in a resource limited country like South Africa and patient exposure to ionising radiation can lead to higher incidence of cancer, especially in younger patients (Gibson *et al.*, 2014). It also carries with it the potential for delay in antibiotic administration. Patients undergoing head CT prior to lumbar puncture have been shown to experience delays in antibiotic administration, despite existing guidelines and textbooks recommending empiric therapy prior to imaging (April, Long and Koyfman, 2017). Any delay in antibiotic administration greatly impacts patient outcomes, resulting in increased case fatality rates with higher time intervals to antibiotic administration (Proulx *et al.*, 2005). This can have dire consequences in a country like South Africa with a large population of immunocompromised patients. It is thus crucial to carefully select which patients require neuroimaging prior to lumbar puncture.

In 2009, a revision of Swedish guidelines removed impaired level of consciousness and new onset seizures as contra-indications to lumbar puncture. They found that these changes were associated with improved outcomes due to less treatment delays. Treatment was commenced 1.2 hours earlier on average and mortality decreased from 11.7% to 6.9% post guideline

implementation. They found that CT before lumbar puncture didn't add to the management of patients, unless focal neurology or signs of imminent herniation were present (Glimaker *et al.*, 2015). Even though this study population differs markedly from patients in developing countries with a high burden of immunocompromise, it does beg the question of whether our scanning practices are appropriate.

This novel South African study will for the first time interrogate the current South African guidelines by the FIDSSA as well as the usefulness of CT prior to lumbar puncture in emergency departments in South Africa. The findings of this study could influence patient selection for head CT prior to lumbar puncture in a developing country.

AIM

To evaluate the role of head CT before lumbar puncture in patients who received CT scan prior to lumbar puncture for suspected meningitis.

OBJECTIVES:

To describe the demographics of patients with suspected meningitis who received a head CT prior to lumbar puncture for suspected meningitis.

To describe the indications and clinical characteristics of patients with positive head CT's in patients who received CT scan prior to lumbar puncture for suspected meningitis.

To compare indications for head CT and laboratory findings in patients with positive and negative CT scans.

To describe the use of current FIDSSA guidelines to use CT scan prior to lumbar puncture.

METHODS

Design

The study will be retrospective, observational and transverse, with descriptive and comparative elements.

Study population and sample

The study will be conducted at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) with record review taking place in the adult medical Emergency Department, areas 165 and 167.

The study population will consist of the records of all adult patients who presented to the medical Emergency Department of CMJAH in the period from 1 November 2016 to 31 October 2018

This study will make use of a convenience sample of all adult patients (18 years and older) who presented to the Medical Emergency Department of CMJAH over a 2 year period with an admission diagnosis of suspected meningitis who had a CT scan performed prior to lumbar puncture.

The required sample size is 280 patients. This was calculated using Epi info 7.2 and data from previous research. The incidence of positive head CT's for meningitis in the literature is 24% (Hasbun *et* al., 2001) and a confidence level 95% was used. The study site performs on average 20 CT scans prior to lumbar puncture on patients in a month. The estimated time for study inclusion was hence determined as 2 years, retrospective to the date of study approval.

Inclusion criteria:

- All adult patients, 18 years and older, admitted to CMJAH from areas 165 and 167 with an admission diagnosis of suspected meningitis over a 2 year period, who had a CT scan performed to rule out contra indications to lumbar puncture.

Exclusion criteria:

- Patients with confirmed intracranial abnormalities preceding their admission for meningitis
- Head trauma in the last month
- Patients whose records are not available for review

Data collection

A retrospective review of the records of patients included in the study will be done. Patients will be identified on the basis of an admission diagnosis of suspected meningitis, as documented in the admission book. The file number of the patient will be used to identify patients who received a CT scan and to review the indication and results of the CT scan and laboratory tests. The indication for the CT scan will be collected as stated on the CT request form. The results will be collected from the written report which is done by a Registrar in Radiology and reviewed by a Consultant. All data pertaining to CT scans and laboratory test will be collected using the online PACS and NHLS systems respectively. All collected data will be entered into a data collection sheet (Appendix A). The indications for CT scan on the data collection sheet are based on current FIDSSA guidelines.

Data analysis

Data will be captured from the data collection sheets and entered onto an electronic spreadsheet using Microsoft excel.

Categorical data will be described using percentages. Continuous variables will be described using means and standard deviations for parametric normally distributed data and means and ranges for all other data.

Subgroup analysis of CT positive and CT negative patients will be performed. Comparisons between the groups will be performed using the unpaired t-test for parametric data with normal distribution. If the distribution is not normal, Mann-Whitney will be used. For comparison of categorical data, Fisher's exact or Chi-squared tests will be used.

ETHICS

Permission to conduct the study will be obtained from the superintendent of Charlotte Maxeke Johannesburg Academic Hospital, as well as the Head of Department of Emergency Medicine, once provisional ethics has been obtained from the Human Research Ethics Committee of the University of the Witwatersrand. Each patient will receive a study number. A separate document will be used to keep a record of study and file numbers. All data will be kept in a password protected file, separate from the data collection sheets to ensure anonymity of the data.

FUNDING

Budget is R500 for stationary and printing of data collection sheets. Any incidental cost will be borne by the researcher

TIMING

	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul
Literature review												
Preparing protocol												
Protocol assessment												
Ethics application												
Collecting data												
Data analysis												
Writing up												

LIMITATIONS

Inclusion into the study requires an admission diagnosis of suspected meningitis. Patients eligible, but admitted with an alternative diagnosis will thus be missed.

Indications for CT scan will be taken from the CT request form and clinical notes. This is based on subjective clinical findings and might not illustrate the exact clinical picture.

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Appendix A: Data collection sheet

Date: _____ Study number: _____

Age: _____ Gender: _____

CT scan indication:

Altered mental state: ☐

GCS>/=10 ☐ GCS< 10 ☐ GCS not specified ☐

Focal neurological lesion: ☐

Isolated to cranial nerves? Yes ☐ No ☐

Papilledema ☐

Unexplained seizures ☐

Ventriculoperitoneal shunt ☐

Other: ☐ _____

CT scan result:

Negative ☐

Space occupying lesion with mass effect ☐

Space occupying lesion without mass effect ☐

Raised intracranial pressure with no space occupying lesion ☐

Meningeal enhancement ☐

Other ☐ _____

Lumbar Puncture result:

Not Done ☐

Bacterial: ☐

Organism: _____

Viral: ☐

Cryptococcus: ☐

TB: ☐

Protein: _____

Glucose: _____

ADA: _____

Blood culture:

Positive Negative ☐ Not done ☐

Organism: _____

HIV status:

Positive ☐ Negative ☐ Not done ☐

CD4 count _____

Appendix B

To: **Prof Motara (H.O.D, CMJAH Emergency Department)**

I am an Emergency Medicine registrar registered as a student for the masters in medicine (MMed) degree in emergency medicine at the University of the Witwatersrand. I hereby request permission to carry out a research study, which is a part requirement of my MMed degree. My proposed research study is entitled: **The Role of Head CT prior to lumbar puncture in patients with suspected meningitis in a Johannesburg Emergency Department** (see attached protocol proposal).

If granted permission, this retrospective audit of patient records (files) will be based on patients that have presented to the Charlotte Maxeke Johannesburg Academic Hospital Emergency Department (area 165) with a diagnosis of suspected meningitis. At all times, patient anonymity and confidentiality will be respected. There will be no risks or side effects involved. The study will need to include 280 patients that had presented over approximately 24 months before the initiation of data collection. I will need to make use of patient records (files) to collect the necessary data. There will be no major expense involved. All minor expenses for the study will be borne by me. While undertaking this study I will ensure that my work and patient responsibilities will not be compromised.

Yours Sincerely

Dr Lana Cronje — Date 29·12·2017

I hereby grant / ~~do not grant~~ permission to Dr L Cronje to carry out the research study as outlined above, pending ethics approval.

Remarks _____

H.O.D Emergency Department — Date 29.12.2017

Appendix C



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. N. Mzila
Office of the Clinical Director
Email:Nolwazi.Mzila@gauteng.gov.za
Tell: (011): 488-4812
15 December 2017

Dear Dr. L. Cronje

STUDY TITTLE: The Role of Head CT Prior To Lumbar Puncture in Patients with Suspected Meningitis in a Johannesburg Emergency Department.

Permission to conduct the above mentioned study is provisional approved. Your study can only commence once Ethics approval is obtained. Please forward a copy of your Ethics Clearance Certificate as soon as the study is approved by the Ethics Committee for the CEO's office to give you the final approval to conduct the study.

Supported / ~~not supported~~

pp
Dr. M.I. Mofokeng
Clinical Director
DATE: 19/12/207

Approved / ~~not approved~~

Ms. G. Bogoshi
Chief Executive Officer
DATE: 19/12/2017

Lana Cronje Protocol

6 messages

Lana Cronje <cronje.lana@gmail.com> Thu, Nov 2, 2017 at 10:07 PM
To: Alison Bentley <dralisonbentley@gmail.com>
Cc: "M.Moolla" <mmoolla@vodamail.co.za>, Feroza Motara <feroza.motara@wits.ac.za>

Dear Dr Bentley

I have made the recommended changes to my protocol as suggested at the previous DRAG meeting. These changes have been approved by my supervisors. Please find attached my edited protocol as well as a list of corrections for your review.

Kind regards

Lana Cronje

2 attachments

Lana Cronje- Corrections post drag.docx
18K

Protocol Lana post drag.docx
107K

Alison Bentley <dralisonbentley@gmail.com> Sun, Nov 12, 2017 at 11:07 PM
To: Lana Cronje <cronje.lana@gmail.com>

Hi Lana

Please could you send me the changes requested by the committee - you should have received a scanned in document. I don't have a copy of them and I honestly don't remember what you had to do.

Alison

[Quoted text hidden]

Alison Bentley <dralisonbentley@gmail.com> Mon, Nov 13, 2017 at 10:22 PM
To: Lana Cronje <cronje.lana@gmail.com>

Hi Lana

Your protocol looks fine and has fulfilled all the requirements described by the protocol committee. I have made comments on your two queries

Well done. please print this email and let me know if the PG office requires a formal letter to this effect.

Sincerely

Alison Bentley
Chair DRAG protocol committee October 2017

On Thu, Nov 2, 2017 at 10:07 PM, Lana Cronje <cronje.lana@gmail.com> wrote:
[Quoted text hidden]

APPENDIX 1: ETHICS CLEARANCE CERTIFICATE

R14/49 Dr L Cronje

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M180123

NAME: (Principal Investigator)	Dr L Cronje
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Emergency Medicine Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The role of head computed tomography prior to lumbar puncture in patients with suspected meningitis in a Johannesburg Emergency Department
DATE CONSIDERED:	26/01/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Professor F Motara and Dr M Moolla
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	09/03/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially reviewed in **January** and will therefore be due in the month of **January** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

2018/4/15
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX 2: TURN-IT-IN REPORT

1935836:Scanning_prior_to_lumbar_puncture.docx

ORIGINALITY REPORT

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