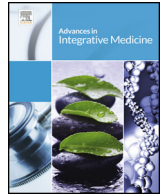




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Medical hypotheses: A clinician's guide to publication

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“The history of science has repeatedly shown that when hypotheses are proposed it is impossible to predict which will turn out to be revolutionary and which ridiculous. The only safe approach is to let all see the light and to let all be discussed, experimented upon, vindicated or destroyed. I hope the journal will provide a new battlefield open to all on which ideas can be tested and put through the fire” inaugural editorial by Medical Hypotheses founder David Horrobin.” [1]

1. Introduction

A medical hypothesis article has two main aims: to serve as a forum for theoretical work in medicine; and to facilitate the publication of potentially radical ideas. Medical hypotheses are particularly important in a field such as integrative medicine. Not only do traditional theoretical concepts found in complementary medicine warrant further examination and scholarship to fully understand and evaluate their mechanism of action, integrative medicine practitioners are often at the forefront of implementation of new scientific concepts in practice.

Although some journals – such as *Advances* – are beginning to incorporate medical hypotheses as an article type. There are generally few avenues for publishing medical hypotheses. However, for various reasons integrative medicine has been a difficult topic to publish in other journals with medical hypotheses sections, with some of the leading journals in this field actively discouraging articles from this field [2].

Sharing ideas with other clinicians and researchers around medical science is much better than hiding or patenting it. At *Advances* we hope that the medical hypothesis section will serve to stimulate debate, discussion and critical evaluation while appropriately acknowledging the originator of that idea. The reality

remains that integrative medicine practitioners – or indeed practitioners of any sort for that matter – rarely involve themselves in research [3].

These articles also serve an important role for developing the research agenda in integrative medicine. For example, the macrophage theory of depression – that inflammatory cytokines play a role in the aetiology of major depressive disorder – was originally put forward as a hypothesis article in the journal *Medical Hypotheses* (and incidentally, remains that journal's most cited article) [4]. Although the aetiology of sudden infant death syndrome (SIDS) is unknown, two of the leading suspected pathophysiological causes (infection and shock) were originally proposed as hypotheses in the same journal [5–7]. In fact, many of the leading current theories – many now proven correct – from the aetiology of Alzheimer's disease to the chronic effects of Zinc deficiency began in the guise of a medical hypothesis.

Such openness undoubtedly brings with it challenges, and can serve as an invitation to the ridiculous as much as the radical. A hypothesis is, by definition, unproven, and for every new hypothesis that proves to be correct there are many that do not. A drastic reorganisation of *Medical Hypotheses* editors and journal procedures (until then *Medical Hypotheses* had no peer review system) had to occur when it published several papers denying the existence of HIV/AIDS [8]. Complementary or alternative medicines are defined by exclusion (from mainstream practice) and by this very definition often lump promising and rational therapies with theories that test the very boundaries of rationality, ethics and (sometimes) even good taste. *Advances* will maintain a very open attitude to publishing radical hypotheses, but authors must also remember that extraordinary claims will also require an extraordinary argument.

A well-written, rigorous medical hypothesis can not only significantly inform evidence-based practice, but it can also help to drive the research agenda for integrative medicine. However, a poorly written and/or irrelevant medical hypothesis article can not only negatively influence treatment decision-making, but also lead to the hypothesis itself being dismissed regardless of its scientific value. Therefore it is essential that issues of quality and rigour are fully considered when developing medical hypothesis articles for publication. The whole process of designing, planning, conducting, analysing, writing and receiving feedback from journal editors can also be satisfying on a personal level and the clinician can develop new skills that may improve their clinical practice.

Scholarly writing, as done through publication of case reports, systematic reviews and case series as well as medical hypotheses

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articles can offer valuable learning experiences for clinicians, offering insights into their own practice that result in improved clinical care for their patients, obliging mental and practical discipline in reflective practice [9–12]. Peer-review can offer valuable feedback and provides insights to clinicians beyond their training or clinical practice experiences. In addition to professional benefits, clinicians partaking in scholarly writing activity can also help develop their fields.

Medical hypotheses articles are one of the few ways in which insights drawn from clinical experience that are 'common knowledge' can influence and inform the research agenda. Such clinician involvement is necessary, for example, to reflect the realities of clinical practice in the field or discipline that is being studied [13]. However, it is also important that clinicians engage with research in a meaningful and rigorous way. For a medical hypotheses article to appropriately inform evidence-based practice, not only must they be rational and logic, they must be presented in a scientifically rigorous manner as well. In this article we present the requirements of a medical hypothesis paper for publication in *Advances*.

2. What is a medical hypothesis paper?

A medical hypothesis paper invites integrative medicine authors to submit new and thought-provoking predictions based on scientific theories or findings. They are theoretical papers putting forth often radical, speculative and non-mainstream ideas, providing they are coherently expressed. Hypothesis papers go beyond summarising a body of work or the reporting of data – they are not 'review' articles. Nor are they an avenue for presenting primary data, although preliminary data may be useful to highlight the hypothesis being presented. Rather, a medical hypothesis paper provides a vessel for healthy debate and thoughtful speculation, which leads to the growth of research and therefore the growth of knowledge. The purpose of a hypothesis paper is to put forward an idea, whether it is a solution to an existing problem or building on top of what is already known, thereby bringing attention to it and inspiring its investigation. This radical thinking leads to advancements in research by adding creativity to a very methodical structure. Science may provide the answers but researchers provide the questions. A hypothesis paper is a means used to justify these questions and why they are important to answer.

3. How to lay out a hypothesis

A hypothesis must first be well argued and articulated and most importantly scientifically sound and logical. Though a hypothesis does not necessarily need to be supported by original data, it must be supported by ideas or data commonly accepted by the scientific community. A hypothesis must also be original and represent a conceptual advancement for its field. Basically, a hypothesis should be logically organised, accounting for at least some known facts which have measurable consequences that are in principle, observable.

A medical hypothesis paper for integrative medicine should be able to cover or answer these three main questions: What is already known about this subject/topic/area? What does the proposed theory add to the current knowledge? How can this hypothesis be tested? When structuring a hypothesis paper, keep in mind that the paper must tell a story and be captivating to its audience. It should progress in a logical sense, the reader must be able to understand the story and where it may be headed even without any knowledge in the area.

The focus of a hypothesis paper is to establish an argument – it is not the recitation of simple facts or findings. Hypotheses are

developed in two main ways, by deductive reasoning or by inductive reasoning [14]:

Deductive reasoning follows a linear approach which builds from top to bottom, starting with the observation of established facts leading to a theory (e.g. heat has been shown to dilate blood vessels which cause a decrease blood pressure. The sun emits heat. *Therefore* being in the sun decreases blood pressure). This reasoning is logical and a direct line can be seen from the first two facts to the conclusion, making the hypothesis a strong hypothesis. Deductive reasoning always makes for a stronger argument as it is usually based on facts which draw a conclusion, if the facts are correct than so is the conclusion.

Inductive reasoning on the other hand builds from the ground up, with a logic that generalises from a typically raw and limited set of observations. This pattern is of an explanatory hypothesis, where the theory attempts to predict or estimate a fact (e.g. bleeding from superficial cuts was less severe higher up the mountain. It is much colder higher up the mountain. *Therefore* cold temperatures decrease bleeding from superficial cuts). This reasoning requires more supporting evidence as it is usually based on less established facts and is usually derived from general observations. Further explanation would need to be presented to prove how such a theory would be possible; by providing surrounding facts to support the argument. For the example above, one could support the argument by providing evidence of other similar correlation such as such applying a cold pack to a wound decreases bleeding or hypothermia has been shown to decrease blood flow which can decrease bleeding and relating these to the argument and back to the hypothesis.

It is important to identify which reasoning your hypothesis follows; understanding the type of hypothesis that is being presented, aids in establishing what structure to follow. If the argument follows deductive reasoning, it is important to establish the known facts and explain how the conclusion was derived by them. On the other hand if the argument follows inductive reasoning then it is important to use additional surrounding facts to better support the argument.

4. Dos and Don'ts of Medical Hypotheses writing

Few journals provide detailed guidelines on how to prepare a medical hypothesis for publication. However, former editorial board member of *Medical Hypotheses* William Bains wrote an article in that journal in which he summarised the main strengths and weaknesses of submissions made to that journal [15]. The following points proposed by Bains are things to keep in mind when putting together a hypothesis paper:

- A long list of examples which are consistent with the hypothesis being presented, are not considered evidence that the hypothesis is true; example of evidence that is not consistent with the 'mainstream' (alternative) hypothesis makes for a better argument for the presented hypothesis as being more plausible.
- Ignoring or omitting well established facts that are not consistent with the presented hypothesis is considered poor etiquette and can discredit the article.
- The argument alone that 'x is correlated with y and therefore x is linked to y' does not make a strong argument unless further evidence is provided. Correlation rarely implies causation itself, though it can often uncover fruitful relationships that warrant further examination.
- Overcrowding the paper with detailed references is unnecessary and draws away from the main points being made. Only what is considered truly relevant from the reference should be mentioned in order to further contribute to the paper without the need to describe unnecessary detail.

- Avoid misleading statements when referencing other papers. The true outcome of the referenced paper is what is important, not the individual's interpretation of said paper.
- Evidence that the problem based around the hypothesis is real makes for a stronger argument. A theory may have more weight if it is a proposed solution to a well established problem.
- The hypothesis must have some implications which relate to the real world and these implications must be testable. Additionally, seeing as a medical hypothesis is being proposed, it should have at least some implications and be relevant to the practice of medicine.

5. Article structure

A hypothesis paper for integrative medicine should be concise yet comprehensive and understandable. The length of the paper should reflect the relevant content, meaning if the content provided only covers 2–3 points the length of the paper should reflect that coverage and not reflect the coverage of a paper with 4–6 points. Even though no official word limits exist, a well written hypothesis paper should not be longer than 3000 words; if above this word count often authors will be asked to further condense their work where appropriate.

5.1. Title

Preferably the title should include the word “Hypothesis” or a word identifying the paper as being a hypothesis paper such as ‘The potential mechanism of ...’ or ‘The hypothetical pathogenesis...’ while also describing the topic which will be discussed and at least hit at what the hypothesis might be.

5.2. Abstract

The abstract should encompass the overall paper on a smaller scale, containing explicit details of the hypothesis being proposed, the main points of supporting evidence and the most relevant and important implications to its field. Ideally the abstract should include: a small introduction to the topic, followed by the clearly defined hypothesis and main points supporting the hypothesis, finishing with the impact this discovery would have on the medical field or practice.

5.3. Introduction/background

This section should introduce the scientific area to be addressed, it should be concise and supported by appropriate references. The introduction should set the scene for the hypothesis; it should not be an attempt to review the evidence in detail.

5.4. The hypothesis

After introducing the background to the field, the hypothesis should be explained in explicit detail. Clearly covering how and why this hypothesis is different from current thinking, how did the idea evolve and why is it important; keeping in mind that the scientific logic behind the hypothesis should be clearly evident and coherent.

5.5. Evaluation of the hypothesis

The evaluation of the hypothesis should be in the light of known and published data or information. This section usually entails the evaluation of both the evidence in support and the evidence against (if available) the proposed hypothesis. A just hypothesis should have implications and make predictions; these predictions should be open

to further experimentation or observation which could confirm or refuse the hypothesis. This part is crucial in justifying a hypothesis; the argument provided here should be logical and coherent.

5.6. Empirical/preliminary data (optional)

The inclusion of extensive new data is not usually accepted in hypothesis papers; however, on occasion, pilot data may be included if it is truly necessary to support the proposed hypothesis and if the data is unlikely to be published in its own right. Authors are usually allowed to indicate their own pilot data in brief description if it is necessary. This should not be mistaken as an opportunity to present or attempt to publish ones work.

5.7. Discussion

Typically, a quick summary of the paper can be included at the begging of the discussion followed by the impact or implications that this hypothesis will have in its field if proved correct. The importance of the proposed hypothesis will need to be explicitly stated, along with suggestions on how the hypothesis may be tested and how it may impact on current practice if confirmed. Additionally, the author could also discuss future research directions in this section.

6. Writing style

A hypothesis paper, like all other research articles, must be written in an academic or scholarly tone. Usually, when writing a hypothesis paper the language used should be comprehensible to a wide audience in bioscience and medicine, including those who may not be specialists in that particular field. Often, clarity and concision of the presentation are key requirements when putting together a hypothesis paper. Subdivision of the paper should be guided by the author as no one structure will suit the presentation of different hypotheses; however, the author should bear in mind that the use of headings are usually beneficial as they usually enhance the reader's comprehension. References, as a general rule, should be limited to those that have a direct bearing on the understanding of the hypothesis.

7. Peer review

Providing a submission is well-written, is scientifically sound and well-argued *Advances* will publish hypothesis papers on any aspect of medicine, providing the hypothesis either suggests a solution to a particularly important problem or suggests an idea with fairly wide relevance (and therefore impact). It therefore remains the responsibility of the authors to argue the case for their hypothesis. Any medical hypothesis paper submitted to *Advances* will be peer reviewed, but this is not to block the publication of new or challenging ideas.

For this reason, peer review will be used as a tool to determine what readers may think of the article, and whether the hypothesis itself is written convincingly. A good hypothesis paper should be able to convince at least one informed reader that your hypothesis is right. If reviewers are able to point out glaring gaps or errors in your argument, or if they cannot understand your argument at all, then there is either something wrong with the hypothesis or there is something wrong with your description of the hypothesis. In either case, your paper will need revision, and this – not blocking potentially unpopular or radical ideas – is the point of peer review.

As a guide for potential authors, the following factors and criteria will be considered during the peer review process: Is the hypothesis important to medical science? Is the hypothesis original? How clearly has the hypothesis been described? Are the methods suggested for testing the hypothesis valid and

reliable? Are the proposed conclusions and interpretation sound, reliable and rational? Is the paper technically well written (in terms of grammar and scientific communication)? Are the figures and tables, if any are used at all, original? Are original references appropriately cited to support statements in the hypothesis? Additional specific comments may be put forward by reviewers that will also require addressing.

8. Summary

'A medical hypothesis submission should explain something that needs explaining, it should take account of what is already known, and should lay out a clear, logical and compelling argument for the hypothesis. Medical hypotheses are of particular importance to integrative medicine as often integrative medicine practitioners are the forefront of the implementation of new scientific concepts in practice. In order for a hypothesis to warrant further examination it must convince its audience that the argument being presented is valid and that the hypothesis is testable. The paper must tell a story, be supported by facts, provide new insight into its field and ultimately have implications and be relevant to the practice of medicine.

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