

Literature Resources for Clinical Research

February 5, 2008

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**Introduction to the Principles & Practices of Clinical
Research (IPPCR), National Institutes of Health**

Johns Hopkins University (JHU) 2001 Asthma Study

- * **Healthy volunteer died after being administered hexamethonium by inhalation**
- * **PI didn't find potential toxicity despite**
 - *“standard PubMed search” &*
 - *consulting “standard current editions of textbooks of pharmacology & pulmonary medicine”*

+ JHU Report, 7/01: *Report of Internal Investigation into the Death of a Volunteer Research Subject*, Johns Hopkins University, 7/01, http://www.hopkinsmedicine.org/press/2001/JULY/report_of_internal_investigation.htm

+ also see: J Savulescu and M Spriggs, *The Hexamethonium Asthma Study and the Death of a Normal Volunteer in Research*, *J. Med. Ethics*, 2002; 28;3-4 , <http://jme.bmj.com/cgi/content/full/28/1/3>

JHU 2001 Asthma Study – results

- * JHU research oversight improved,

“requiring investigators to collaborate with a librarian and a pharmacist to strengthen literature searches... to help search appropriate databases for potential side effects.”

Hopkins Response to FDA Observations, JHMI Office of Communications and Public Affairs, 9/7/01,

<http://www.hopkinsmedicine.org/press/2001/SEPTEMBER/010907A.htm>

- * **Guidelines established at JHU & elsewhere –**

Guidelines for Determining an Adequate and Comprehensive Literature Search of Drug and Device Safety for Use by Investigator and Institutional Review Boards, Institutional Review Board, Mount Sinai School of Medicine,

<http://www.mssm.edu/irb/pdfs/SearchGuidelines.pdf> (class handout)

Intro to Information Sources

* **How to distinguish between the many different information sources ?**

- *Various categories used when deciding where to search*
- *These are moving targets - frequent changes & blurring of categories*

- * **Classic** - proximity to source material
- * **Practical** - content & search capabilities
- * **Access** - readily available to you or to patients
- * **Familiarity** - sources you know about
- * **Purpose** - what you're searching for

Intro to Information Sources – cont'd

* **Proximity to Source Material**

- *original publications & data*
- *bibliographic databases & indexing/abstracting services*
- *reviews & reference works, textbooks*

* **Content & Search Capabilities**

- *subjects covered, in what degree of comprehensiveness*
- *full text of articles vs. titles & keywords, possibly with abstracts*
- *search technology & interface: structured indexing terms, thesaurus, wildcards, Boolean logic*

Intro to Information Sources – cont'd

* **Sources readily available to you or to patients**

- *online vs. paper*
- *items in your collection vs. items to be ordered*
- *free vs. fee*
 - + Patients more likely to know of info from free sources

* **Familiar Sources**

- *Sources you know about, & know how to search*
- *Sources you've heard about*
 - + Keeping up with changing info landscape

Intro to Information Sources – cont'd

- * **Basic Question: the purpose of your search – what are you searching for, and why?**

- *focus here is on searching for **adverse effects** & for **protocol development***

- *particular relevance to textbook chapters:*

- * 3 - Researching Bioethical Questions

- * 8 - Unanticipated Risk in Clinical Research

- * 16 - Design & Conduct of Observational Studies & Clinical Trials

- * 24 - Writing a Protocol

PubMed/MEDLINE

US National Library of Medicine (NLM) database
references to more than 16 million articles published in 5000
biomedical journals

- * *medicine, nursing, dentistry, veterinary medicine, allied health & pre-clinical sciences*
- * *currently includes references to articles from 1949 to present*
- * *free online – www.pubmed.gov ; NIH staff should click “PubMed@NIH” at the NIH Library web site:
<http://nihlibrary.nih.gov>*
- * *bibliographic database with author-provided abstracts*
- * *added indexing terms from MeSH (Medical Subject Headings) thesaurus*

PubMed/MEDLINE – cont'd

* JHU internal investigation found different PubMed results depending on the terms searched

- *possibly due in part to limited coverage of older material & classification changes over time*

<u>Terms searched</u>		<u># Results</u>	<u># Useful</u>
hexamethonium inhalation lung injury	=>	0 hits	
hexamethonium inhalation	=>	42 hits	0
hexamethonium lung	=>	not reported	3
hexamethonium lung toxicity	=>	4 hits	0
hexamethonium lung hypersensitivity	=>	16 hits	3
hexamethonium lung fibrosis	=>	3 hits	2

PubMed/MEDLINE – cont'd

- * **Understand PubMed to get comprehensive results**
 - **Search Aids available by clicking PubMed sidebar:**
 - + **“Help”** - online book
 - + **“Tutorial”** - web-based & interactive
 - **Distance Education Program Resources available at**
http://www.nlm.nih.gov/bsd/dist_edu.html

- * **Focus on:**
 - **MeSH** - added subject headings which often change over time
 - **Limits** - not always obvious - “clinical trial” limits don't include all observational studies
 - **My NCBI** - can be used to get updates - could be important while trial in progress

- To get started, enter one or more search terms
- Search terms may be [topics](#), [authors](#) or [journal titles](#)



How healthy is America?

The [29th report](#) from the *Health, United States, and Global Trends* is available on the [Bookshelf](#).

PubMed is a service of the [U.S. National Library of Medicine](#) containing over 16 million citations from MEDLINE and other biomedical articles back to the 1950s. PubMed includes full-text articles and other related resources.

More Information Sources

- * **Multiple information sources usually necessary for comprehensive searches**
 - *Different sources have areas of specialization but may overlap*
 - *Some sources are only available from commercial vendors*
 - * check your library/organization for institutional subscriptions
 - *Examples of some information sources follow; see websites for tutorials & more information*
 - * different versions of these sources may be available with varying coverage and capabilities
 - * many other sources may also be important for a given search

More Information Sources

- * **Embase™** – pharmacological & biomedical literature
 - key clinical medicine database, European based
 - Includes all of PubMed & additional material, but with different indexing; often useful for
 - drug side effects/interactions,
 - toxicology,
 - biotechnology,
 - medical devices,
 - health policy/management,
 - public/occupational/environmental health, &
 - alternative/complementary medicine – www.embase.com

More Information Sources – cont'd

- * **Micromedex®** – summaries & detailed monographs for drugs, diseases, alternative medicine, toxicological managements, reproductive risks & emergency care -

<http://www.micromedex.com/products/hcs/>

- “had lung toxicity as the first side effect of hexamethonium”
(JHU Report, 7/01)

- * **BIOSIS Previews®** – biological, biomedical & life science research - traditional, experimental & interdisciplinary subjects & technical notes/letters - includes *Biological Abstracts®* - <http://scientific.thomson.com/products/bp/>

More Information Sources – cont'd

* **Cited Reference Searching Capability:**

- **Web of Science®** – includes Science Citation Index® & Social Sciences Citation Index®, multidisciplinary indexes to the journal literature of the sciences & the social sciences - <http://scientific.thomson.com/products/wos/>

* **useful for conference coverage**

- **Scopus®** – scientific, technical, medical, and social science literature from 14,000 journals - includes patents & Scirus websearch engine - <http://www.scopus.com>

More Information Sources – cont'd

- * **Cochrane Library** – Regularly updated collection of evidence based medicine reviews & effectiveness of health care interventions for practitioners/policy makers - <http://www.cochrane.org/>
- * **Guidelines.gov** - evidence-based guideline clearinghouse
www.guidelines.gov
- * **Clinical trials:**
 - ClinicalTrials.gov** - NIH clinical trials list, www.clinicaltrials.gov
 - CenterWatch Clinical Trials Listing Service™**,
<http://www.centerwatch.com/>

More Information Sources – cont'd

- * **TOXNET** - cluster of databases covering toxicology, hazardous chemicals, environmental health & related areas – National Library of Medicine (NLM) - <http://toxnet.nlm.nih.gov> & <http://www.nlm.nih.gov/pubs/factsheets/toxnetfs.html>
- * **Texts & References** – either in print or online:
 - **NCBI Bookshelf** – free online books - <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Books>
 - Hexamethonium toxicity wasn't mentioned in the last 4 editions of Goodman & Gillman, or in the current edition of Fishman's Pulmonary Medicine – but was included in a previous edition of Fishman's text (JHU Report, 7/01)

More Information Sources – cont'd

Specialized sources

- * **Older information** – PubMed/Medline now covers back to 1949; earlier information is available in print sources
 - ***key hexamethonium toxicity article - British Heart J., 1954***
 - ***phrase “hexamethonium lung” in titles of two other articles from 1956 and 1962***
 - ***Cited reference searching could find more recent articles which refer to these older articles***
 - * *1966 and all that--when is a literature search done?, F McLellan, The Lancet, August 25, 2001, v358 i9282 p646 – discusses literature searches related to JHU incident*

More Information Sources – cont'd

Specialized sources

- * Regulatory information – **MedWatch** - post-marketing surveillance from pharmaceutical companies, required by FDA
<http://www.fda.gov/medwatch/index.html> (text pp. 397-399)
- * Engineering databases - **Inspec® & Compendex®** - information on medical devices
- * Others:
 - **patent literature**
 - **drug pipeline (drugs in development) databases**
 - **chemistry databases (Chemical Abstracts, etc.)**

More Information Sources – cont'd

Free full text & web information - increasing amount

- * **PubMed/MEDLINE** – can limit to items with links to free full text
- * **PubMed Central (PMC)** – free digital archive of biomedical and life sciences journal literature, NIH - <http://www.pubmedcentral.nih.gov/>
- * **BioMed Central** – open access publisher - <http://www.biomedcentral.com/>
- * **MedlinePlus** – consumer health information, NLM - <http://medlineplus.gov/>
- * **Directory of Open Access Journals** – many are full text searchable - <http://www.doaj.org/>

More Information Sources – cont'd

Free full text and web info – cont'd

- * **Google, Google Scholar & other web resources** – access to increasing amounts of information, some in full text –

www.google.com , <http://scholar.google.com/> , www.yahoo.com

- ***search most effectively with advanced search features:***

<http://www.google.com/intl/en/help/refinesearch.html>

<http://search.yahoo.com/web/advanced?ei=UTF-8>

- **JHU PI found first evidence of hexamethonium pulmonary toxicity on the internet**
- **Google and Yahoo found a hexamethonium toxicity site, but other search engines didn't** (JHU Report, 7/01)

More Information Sources – cont'd

Free full text and web info – cont'd

- * **Google, Google Scholar & other web resources – cont'd**
 - Why is the information provided?
 - What is the business model - who pays?
 - Incentives for accuracy and completeness?

 - Promising technology - increasingly powerful capabilities
 - Cautions include possible
 - * *inconsistent results,*
 - * *lack of search documentation*
 - * *lack of confidentiality*

Conducting Searches – Guidelines

Guidelines for Determining an Adequate and Comprehensive Literature Search of Drug and Device Safety for Use by Investigator and Institutional Review Boards

- Institutional Review Board, Mount Sinai School of Medicine,
<http://www.mssm.edu/irb/pdfs/SearchGuidelines.pdf> **(class handout)**

- * *includes* **overview,**
search log,
summary & bibliography forms
- * *Appendix contains* **process model,**
lists of sources, &
search technique suggestions

Conducting Searches – Guidelines

Responsible Literature Searching Guidelines, Health Sciences
Library System, University of Pittsburgh, (class handout)

- * *An overview with specific suggestions*
- * *Similar guidelines available from Weill Cornell Medical College, as part of a tutorial:*

- ***Tutorial on Responsible Literature Searching from Weill Cornell Medical College*** –

<http://library2.med.cornell.edu/Tutorials/RLS/>

Selected Additional Resources

Responsible Literature Searching for Research: A Self-Paced Interactive Program, CB Wessel, MedEdPORTAL, 2005, ID 162 - tutorial

<http://www.aamc.org/mededportal> (search for course title)

National Network of Medical Libraries - <http://nnlm.gov/>

Regional Training classes - PubMed, ClinicalTrials.gov, & TOXNET classes

<http://nnlm.gov/ntcc/index.html>

* JA Boorkman, JT Huber, & FW Roper, *Introduction to Reference Sources in the Health Sciences*, 4th Ed., 2004

* PM Malone, KL Kier, J Stanovich, *Drug Information: A Guide for Pharmacists*, 3rd Ed., 2006

* B Snow, *Drug Information – A Guide to Current Resources*, 2nd Ed., 1999

Search Quality

- * How do you know if you can trust your search results?
- * When is a search complete?
- * Difficult questions - best answered by
 - **experience**
 - **following guidelines & suggestions mentioned above**
 - **verifying your strategy & results**

Search Quality – cont'd.

* Tips for checking search quality

- *results include relevant articles that you already know about*

- *You understand **how the search engine works, what it searches, & what assumptions it makes:***

* plurals and/or alternate spellings automatically included?

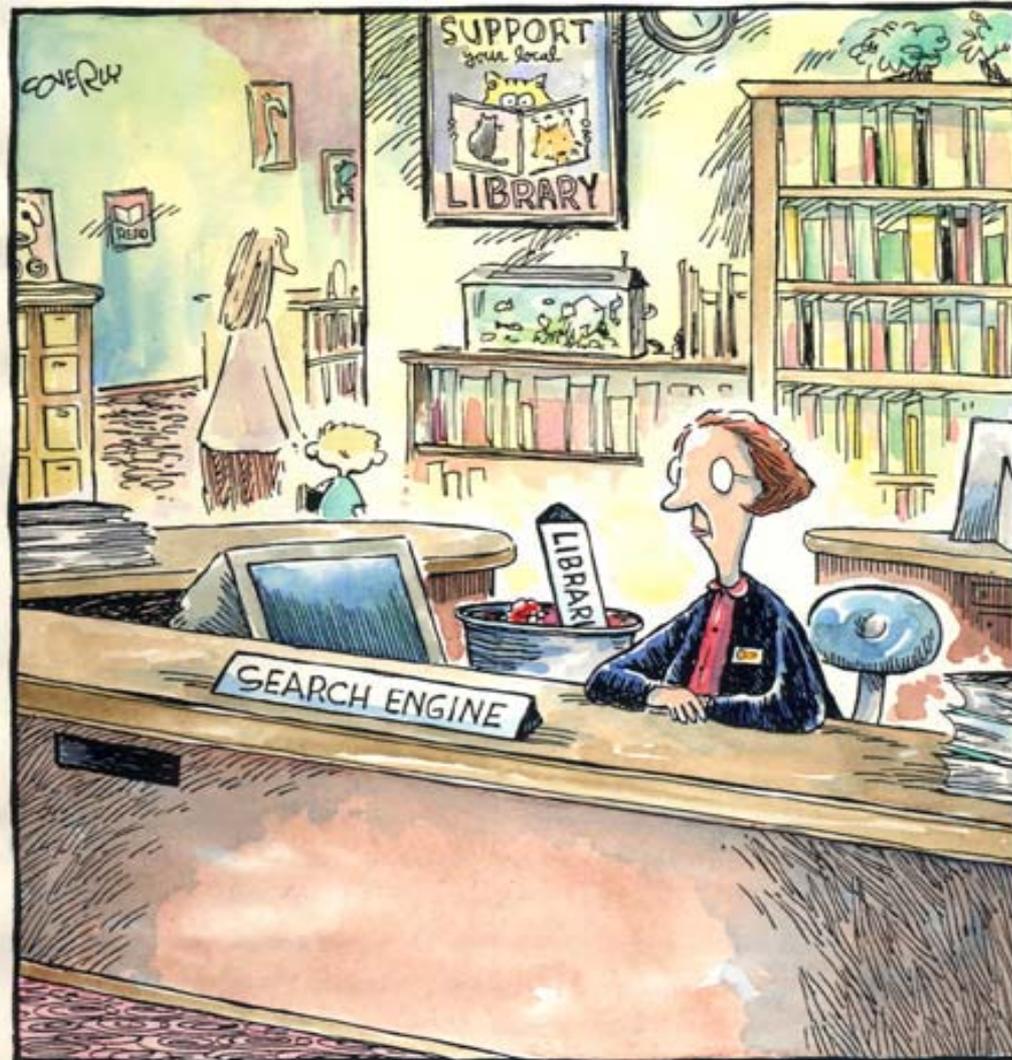
* search terms automatically “OR”ed with each other?

* Google results may be inconsistent, & many of its assumptions & relevancy rankings aren't disclosed

- *different searchers & searches yield no new relevant results*

- *you've set up **methods to identify and remove duplicates & to automatically get updates***

Ask Your Research Librarian!



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