



Literature Resources for Clinical Research

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Introduction to the Principles & Practices of Clinical Research (IPPCR), National Institutes of Health (NIH) , 2/5/08



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>

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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)

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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



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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*



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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



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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



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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*



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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

- JHU Report, 7/01



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PubMed/MEDLINE – cont'd

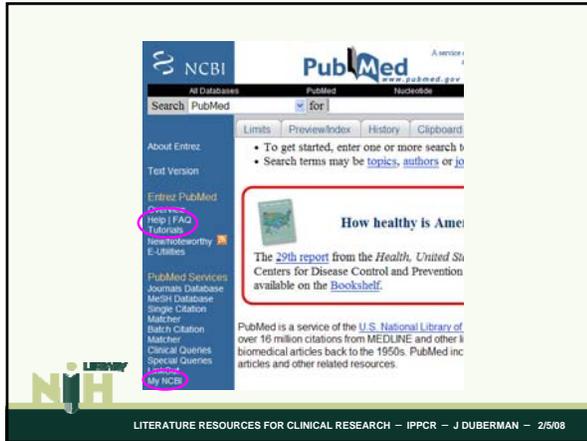
- **Understand PubMed to get comprehensive results**

- ★ ● **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





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



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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/>



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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>



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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/>



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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)



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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



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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.)



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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/>



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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/refinerearch.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)



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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://nmlm.gov/>
Regional Training classes - PubMed, ClinicalTrials.gov, & TOXNET classes
<http://nmlm.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

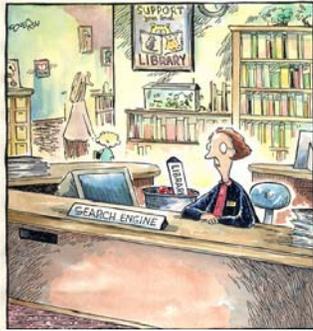


Search Quality – cont'd.

- 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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