Drug Information for Healthcare Practitioners

Paul L. Doering, MS
Distinguished Service Professor, Emeritus
College of Pharmacy
University of Florida
### Two Types of Informational Needs

1. **Reading to research a specific question**
   - **Example:** Does the dose of gatorcillin need to be reduced in a patient with renal impairment?

2. **Reading for current awareness**
   - **Example:** I wonder what new drugs the FDA has approved in the past few days?
Importance of Critical Evaluation of the Medical/Pharmaceutical Literature

- Healthcare is an ever-changing profession
- What was right yesterday is wrong today
- What is right today is wrong tomorrow
- New information is constantly being presented
- Yet, much of the literature is unreliable or misleading
Drug Information.....

Knowledge is of two kinds: we know a subject ourselves, or we know where we can find information upon it.”

Samuel Johnson 1775
Thursday, April 7, 2005, 12:30 pm-
phone call received from Health Reporter from local newspaper:

“Professor Doering, can I get your reaction to the removal of Bextra from the market?”

Doering: Oh? You mean Bextra was removed from the market?
A UF professor says he is not surprised by the move.

By DIANE CHUN
Sun medical writer

The painkiller Bextra, one of a class of drugs frequently prescribed for rheumatoid arthritis and osteoarthritis, has been pulled from the market by its manufacturer.

Pfizer Inc. announced Thursday that it has suspended sales at the request of the U.S. Food and Drug Administration. The government agency wants all drugs in the same class to carry the strongest possible warnings about increased risk of heart attack and stroke in long-term users.

"Today’s actions protect and advance the health of the millions of Americans who rely on these drugs every day," said Dr. Steven Galson, acting director of the FDA’s Center for Drug Evaluation and Research.

Galson said the tough new labeling will “highlight the major risks of these products, which are gastrointestinal bleeding and cardiovascular adverse events.”

The news about Bextra did not surprise Paul Doering, distinguished service professor at the University of Florida and co-director of the UF Drug Information and Pharmacy Resource Center.

“In all candor, the whole category of COX-2 inhibitors was (in my opinion) overrated in terms of their uniqueness,” Doering said Thursday.

“They are no stronger than Motrin, Aleve or any other non-steroidal anti-inflammatory drug,” he said. “It’s just that you could take doses of them without upsetting your stomach. Yes, they spared the stomach upset, but at what price?”

Bextra was approved by the FDA in November 2001, making it the most recent of the COX-2 (cyclooxygenase-2) inhibitors to be marketed. Pfizer, which makes Bextra, also manufactures Celebrex, the first of this class of painkillers developed to treat arthritis.

The FDA has asked Pfizer to add a boxed warning label to Celebrex, but for now, the drug will remain on pharmacy shelves. Agency officials have concluded that the drug’s benefits still outweigh any risk to patients.

According to Doering, when a new drug comes on the market, its true nature won’t be known for three to five years.

“Since Bextra has been approved in late 2001, this gray cloud has been forming over it, and the FDA had increasing concerns,” he said. “I guess they finally said, ‘We are going to pull the plug on this drug.’”

Vioxx, manufactured by Merck, was introduced in 1999 and voluntarily taken off the market in September after a study showed it increased the risk of heart attacks and strokes in patients who took it on a long-term basis.

When Vioxx was withdrawn, many people turned to Celebrex or Bextra, both widely marketed prescription non-steroidal anti-inflammatory drugs.

Pfizer advised Bextra users to consult with their doctor about appropriate treatment options. The company said that the FDA cited a risk of serious, sometimes fatal, skin reaction experienced by some Bextra users.

“This looks like strike two (against that class of drugs),” Doering said.

Pfizer said it “respectfully disagrees” with the FDA’s conclusion that Bextra was too risky to continue selling, and pledged further discussions with the agency about the possibility of returning it to the market.

The Associated Press contributed to this report.
## Sources of Information

<table>
<thead>
<tr>
<th>Sources of Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>“The Literature”</td>
</tr>
<tr>
<td>The Internet</td>
</tr>
<tr>
<td>The News</td>
</tr>
<tr>
<td>Manufacturers</td>
</tr>
<tr>
<td>Professional associations</td>
</tr>
<tr>
<td>Governmental sources</td>
</tr>
<tr>
<td>Networking</td>
</tr>
</tbody>
</table>
High salt consumption not dangerous, new European study finds, but U.S. experts disagree

May 03, 2011 | By Thomas H. Maugh II, Los Angeles Times

Low levels of salt consumption are associated with a higher rate of cardiovascular disease and deaths, European researchers reported Tuesday, but U.S. experts promptly criticized the study, which contradicts the prevailing dietary wisdom. "This study might need to be taken with a grain of salt," Dr. Peter Briss of the Centers for Disease Control and Prevention told the New York Times. Dr. Ralph Sacco of the University of Miami, president of the American Heart Assn., also criticized the study's design and conclusions, noting that the association would continue to stand by its guideline that Americans should consume no more than 1,500 milligrams of salt per day, well below the current average of about 3,500 mg per day. He argued that a vast amount of literature supports the current recommendation and that one study is not sufficient to make any changes in the guidelines.
Sodium won't kill you? Scientists shake up what we know about salt

Posted by Neil Katz  Leave Comment

(CBS) It's been common wisdom for years. Too much sodium leads to high blood pressure which leads to heart disease and possibly death. But a new study out of Belgium might just shake up what we think we know about salt.

Scientists who studied several thousand subjects for eight years found that not only was low sodium intake not associated with improved health, the group that appeared to consume the least sodium had a 56 percent greater chance of death from heart attack or stroke than the group that was reaching for the salt shaker with every meal.

The study had some major caveats. Researchers only tested sodium levels in participants' urine two times - once...
Low-Salt Diet Ineffective, Study Finds. Disagreement Abounds.

By GINA KOLATA
Published: May 3, 2011

A new study found that low-salt diets increase the risk of death from heart attacks and strokes and do not prevent high blood pressure, but the research’s limitations mean the debate over the effects of salt in the diet is far from over.

In fact, officials at the Centers for Disease Control and Prevention felt so strongly that the study was flawed that they criticized it in an interview, something they normally do not do.

Dr. Peter Briss, a medical director at the centers, said that the study was small; that its subjects were relatively young, with an average age of 40 at the start; and that with few cardiovascular events, it was hard to draw conclusions. And the study, Dr. Briss and others say, flies in the face of a body of evidence indicating that higher sodium consumption can increase the risk of cardiovascular disease.
Fatal and Nonfatal Outcomes, Incidence of Hypertension, and Blood Pressure Changes in Relation to Urinary Sodium Excretion

Kateryna Solovey-Krzemp, MD, PhD
Tatiana Kuznetsova, MD, PhD
Eugenia Tkachuk, MD
Valerie W. H. Jiang
Ilyes El-Gharali, MD, PhD
Kermit Brandt, MD, PhD
Nanette Atkinson, MD, PhD
Ingrid Edelmann, MD, PhD
Jana Filsinger, MD, PhD
Dietrich Hofmann, MD, PhD
Yuri Nikitin, MD, PhD
John A. Swann, MD, PhD
for the European Project on Genes in Hypertension (EPGEN) Investigators

Context. Elevated plasma renin activity, renal sodium excretion, and blood pressure have been associated with the risk of cardiovascular events. However, the role of sodium in cardiovascular risk is still uncertain. This study evaluated the relationship between urinary sodium excretion and cardiovascular outcomes in the European Project on Genes in Hypertension (EPGEN).

Design, Setting, and Participants. EPGEN included 12,806 participants from 10 countries in Europe, aged 40 to 69 years. The participants were randomly assigned to baseline and follow-up assessments.

Objective. The primary objective was to determine the relationship between urinary sodium excretion and cardiovascular outcomes in the EPGEN study.

Results. The primary outcomes were the incidence of nonfatal and fatal cardiovascular events, as well as the incidence of hypertension.

Conclusions. The findings from this study suggest that urinary sodium excretion is a strong predictor of cardiovascular outcomes, highlighting the importance of sodium reduction in the prevention of cardiovascular disease.

JAMA. 2011 May 4;305(17):1777-85.
The Latest Medical Journals
Searching the Literature

Search strategy
- determine references most likely to meet your needs
- balance all factors (e.g., depth, time)

The search
- general references, then indexing & abstracting services, then journal articles
Primary Literature

- Original Research
- Journal articles
- Meeting symposia
- Conference proceedings
- Newsletters including original research
The Secondary Literature

Indexing and Abstracting Services

Bibliographic databases

- MEDLINE
- IPA
- IDIS
- Current Contents
Indexing and Abstracting Services

Usefulness of titles & abstracts

Availability of the citations
Searching Databases

Limiting searches
- language, human, year, etc
- major topic
- subheadings (adverse effects)
- operators
- Boolean (and, or, not) and others (adj, with)

source (ie, journal)

publication type (eg, review)
ANTIQUES FROM THE EARLY DAYS OF DRUG INFORMATION

Paul L. Doering
Class of '72
YESTERDAY’S TECHNOLOGY BECOMES TODAY’S MUSEUM PIECE

Slide Rule

Calculating Machine
<table>
<thead>
<tr>
<th>Required appointment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive interview by the operator</td>
</tr>
<tr>
<td>Hooked up some weird equipment</td>
</tr>
<tr>
<td>Typed in a secret language</td>
</tr>
<tr>
<td>Stood around watching in awe</td>
</tr>
<tr>
<td>Answers looked like hieroglyphics</td>
</tr>
<tr>
<td>Leave scratching head</td>
</tr>
<tr>
<td>Sent a bill</td>
</tr>
</tbody>
</table>
Searching Pub Med


- PubMed tutorial

- Single Citation Matcher
  - Use when you have partial information about citation

- Field Searches
  - Use boolean operators or limit searches

- Type of Article
  - Review article, clinical guideline, meta analysis, clinical trial
The Tertiary Literature

General References

Textbooks → Electronic References
Tertiary Literature

General References

- Textbooks
- Handbooks
- Manuals

- Compendia
- Review Articles
- Fulltext Electronic Databases
Some Useful General References

- Drug Facts and Comparisons
- AHFS Drug Information 2011
- The Physician's Desk Reference (PDR)
- Handbook of Non-Prescription Drugs
- American Drug Index
### Some Other Useful General References

<table>
<thead>
<tr>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodman and Gillman's A Pharmacologic Basis of Therapeutics</td>
</tr>
<tr>
<td>Pharmacotherapy: A Pathophysiologic Approach</td>
</tr>
<tr>
<td>Martindale's Extrapharmacopoeia</td>
</tr>
<tr>
<td>Handbook of Injectable Drugs</td>
</tr>
<tr>
<td>Drug Interaction Facts by Facts and Comparisons</td>
</tr>
</tbody>
</table>
### Textbooks

#### Lag time
- What kind of information is timely enough?

#### Some available both printed and electronic
- How often are they updated?

#### Overview with consensus opinion
- May be someone else's opinion

#### Less expensive
- Subscription may cost $$$$
A Trio of Textbooks

DiPiro

Herfindal

Koda-Kimble
Electronic General References

- Micromedex
  - DRUGDEX
  - POISINDEX
  - Martindale’s

- Micromedex
- Up to Date
- Clinical Pharmacology
- Clinical Reference Library
- Facts, AHFS, etc

- Up to Date
- Clinical Reference Library
- Facts, AHFS, etc
What About Wikipedia?

- Originally thought to be a “bad choice”
- Contains up to date information
- Well referenced
- Reliability can be judged by the user
What About Wikipedia?

Thalidomide

From Wikipedia, the free encyclopedia

This article is about the drug. For the musical about a person with thalidomide disability, see Thalidomide!! A Musical.

Thalidomide ([θɛlɪdəmɪd]) was introduced as a sedative drug in the late 1950s. In 1961, it was withdrawn due to teratogenicity and neuropathy. There is now a growing clinical interest in thalidomide, and it is introduced as an immunomodulatory agent used primarily, combined with dexamethasone, to treat multiple myeloma. The drug is a potent teratogen in zebrafish, chickens, rabbits and primates including humans, severe birth defects may result if the drug is taken during pregnancy.

Thalidomide was sold in a number of countries across the world from 1957 until 1961 when it was withdrawn from the market after being found to be a cause of birth defects in what has been called "one of the biggest medical tragedies of modern times." It is not known exactly how many worldwide victims of the drug there have been, although estimates range from 10,000 to 20,000. Since then thalidomide has been found to be an effective treatment for a number of medical conditions and it is being prescribed again in a number of countries, although its use remains controversial, including its testing in the developing world. The thalidomide tragedy led to much stricter testing being required for drugs and pesticides before they can be licensed.
Drug Facts and Comparisons
www.factsandcomparisons.com/
Facts & Comparisons 4.0 is the electronic version

- Contains a menu of other products
- Nonprescription Drug Therapy included with eFacts
Clinical Pharmacology

- Never available as a textbook
  - Designed as a database

- Available in different platforms
  - CD-ROM, Intranet, Internet versions.

<table>
<thead>
<tr>
<th>Extensive menu of database options</th>
<th>Never available as a textbook</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Poisindex, Identidex, Drugdex, Martindale’s, Drug-REAX</td>
<td>• Originally on microfiche</td>
</tr>
</tbody>
</table>
Micromedex

Extremely comprehensive

Well-referenced

Extremely expensive

Only updated quarterly
  • New monographs and updates available from website
Physicians Desk Reference

www.PDR.net
Electronic Textbooks

- **Stat!Ref**
  - AHFS
  - USPDI
  - Medical textbooks

- **Natural Medicines Comprehensive Database**

- **MD Consult**
Journal Articles

Peer Review

Supplements may not be peer reviewed

Types of Articles

reviews, original articles, case reports, letters, editorials
The Internet

World Wide Web
or Wild Wild West

Evaluating web sites

• accountability
• authorship
• attribution
• disclosure & ownership
• currency
• editorial oversight
Governmental Resources

US Government

- FDA, CDC, NIH, NCI
  - www.xxx.gov
  - except cancer.gov

PubMed is provided by the National Library of Medicine

Dailymed

Google "dailymed"

Drugs, Supplements, and Herbal Information

**Drugs**
Learn about your prescription drugs and over-the-counter medicines. Includes side effects, dosage, special precautions, and more.

*Browse by generic or brand name*

A B C D E F G H I J K L M N O P Q R S T U V W X Y Z 0-9

For FDA approved labels included in drug packages, see [DailyMed](http://www.fda.gov/).

**Herbs and Supplements**
Browse dietary supplements and herbal remedies to learn about their effectiveness, usual dosage, and drug interactions.

**Related Topics**
- AIDS Medicines
- Antibiotics
- Antidepressants
- Blood Pressure Medicines
- Blood Thinners
- Cancer Alternative Therapies
FDA Adds New Safety Warnings To Statins.

Coverage of the FDA’s decision to add warnings to the labels of statins was widespread and presented the warnings as acknowledging a serious danger, while repeating that statins are still useful and effective medications. **ABC World News** (2/28, story 6, 1:30, Sawyer) reported, “Today, the FDA announced it will slap new safety warnings on the packages” of statins, “including a warning about confusion and memory loss.” ABC’s Dr. Richard Besser said, “The warnings will include the side of memory loss, confusion, a rise in blood sugar, which can lead to diabetes, and drug interaction causing muscle damage.”

**NBC Nightly News** (2/28, story 8, 1:15, Williams) reported that the "FDA has issued new warnings that" statins "are not, of course, without their risks." Chief Science Correspondent Robert Bazell, said, "There's no doubt that statins save lives...and experts emphasize people should not stop taking them without talking to their doctor, but the experts say these latest warnings might make some doctors
FDA Slaps Merck on Skipped Januvia Study
2 hours ago
In a warning letter, the FDA upbraided Merck & Co. for failing to conduct a promised animal study of pancreatitis risk associated with its diabetes drug sitagliptin (Januvia, Janumet).

Family Tree Helps Define Risk of Sudden Death
3 hours ago CME/CME
It may be easier to treat...

DSM-5 Critics Pump Up the Volume
4 hours ago
With crunch time looming for the ongoing revision of the psychiatry profession's diagnostic manual, critics hoping to stop what they see as destructive changes are taking their campaign to the consumer media.

Leukemia Survival Up with Gleevec

Antibodies in Spinal Fluid Post-Stroke Puzzling
February 29, 2012
Patients with acute stroke were more likely than those with other conditions to have antibodies in their cerebrospinal fluid, researchers found.

Resources (from Industry)
Email Updates

Welcome to the U.S. Food & Drug Administration (FDA) free e-mail subscription service. When you subscribe to this service, you will receive an e-mail message each time there is an update on the FDA page(s) you select.

To subscribe to this service or update your subscriber preferences, please enter your e-mail address below. You may change your subscriber preferences or cancel your subscription at any time.

We have a strict privacy policy. FDA does not collect personally identifiable information other than your e-mail address which is needed in order to provide the service. FDA will not use or share your e-mail address for any other purpose. The GovDelivery service FDA employs to provide this e-mail subscription service is not a government entity. Information you provide may be made available to GovDelivery and other non-governmental parties.

Subscription Type  Email

Email Address

Submit  Cancel

Your contact information is used to deliver requested updates or to access your subscriber preferences.
Summary

Many references available

Successful healthcare practice demands a critical evaluation of the primary literature
  • But you must be able to find it first

You will use all levels of information
  • Therefore, it is important to understand the value and limitations of each level
Go gators!