Welcome to Searching

When you complete this section you should be able to:

1. Understand the general concepts of searching for alternatives.

2. Identify appropriate terminology or resources to consult for terminology.

3. Analyze a protocol to determine the information needed to conduct a literature search.

4. Develop a search strategy for the protocol.

5. Know other resources to consult

Introduction

Federal animal welfare regulations require that an investigator performing procedures that are painful or distressful to the animal provide assurance that no alternatives exist to the painful procedure. According to the USDA, Animal Care Policy 12 (http://www.aphis.usda.gov/ac/policy/policy12.pdf) "We believe that the performance of a database search remains the most effective and efficient method for demonstrating compliance with the requirement to consider alternatives to painful/distressful procedures." To provide this assurance, the investigator must provide, except in unique circumstances, a written narrative that describes the literature databases searched (e.g., Medline, EmBase, Biosis Previews, AGRICOLA, etc.), the keywords or strategy used to retrieve information, and a brief description of why alternatives are or are not available.

The first step in conducting a search is to have a clear understanding of the objectives and methods of the proposed study. Too often investigators ask for alternatives to very specific procedures without putting the procedure in the context of an experiment. To properly look for alternatives you have to know why the procedure is being performed and what the expected outcome is.

If an information specialist is being used to conduct the search, there should be direct communication between the investigator and the information provider. This avoids misinterpretation by third party participants. Once all pertinent information is at hand, the literature search strategy can be developed. It is convenient to conduct a search using the 3Rs as a guide. The first part of the search will examine the literature closely related to the proposed study for refinements to the proposed methods, methods or models that reduce the number of animals used, and to see if the proposed work duplicates previously published experiments (this is a requirement of the U.S. Animal Welfare Act (http://www.aphis.usda.gov/ac/awa.html#2143)). The terminology used in this part of the search will come from the area of study. Depending on the type of research, it might also be important to look for appropriate anesthetics, analgesics, methods of restraint, etc.

In the second part of the strategy, the remaining R--replacement--is considered. There may be some overlap with the first part of the search, in that alternative animal models may already be in hand. If not, then alternative animal and nonanimal models should be considered.

In the following tutorial, we will begin with a short introduction to the basic concepts involved in searching electronic databases. We will then discuss development of the search strategy and the terminology that may be useful. As a tie-in to this, we will list resources that can be consulted for appropriate terminology. This will lead us to consider how to analyze a research protocol to extract information and formulate questions that will guide our selection of terminology and development of the strategy. Based upon the protocol, we will choose appropriate databases and then execute the search.

General overview of searching concepts

Regardless of the database system used there are basic searching concepts that remain constant.

What is truncation?

Depending upon the database system being used, symbols such as the * or ? may be used at the end of a search term to retrieve many word variations to the original term.

Example of truncation at the end of the term:

> *train** will retrieve *train, training, trainer, trained, trainers, trainees, etc.*
> *behav?* will retrieve *behavior, behaviour, behaving, etc.*

Dangers of Truncation:

> Truncation can result in irrelevant retrieval of information. Be cautious when using truncation. For example if you truncate the word *rat** you will receive information containing words such as *rate, ratio, rations, ratification, etc.*

What about spelling?

When searching multiple databases, it is important to include American, British, and European spellings of English language words to ensure retrieval of all materials. This is especially important in the biomedical sciences.

Examples include:

> anesthesia, anasthesia, anaesthesia
> behavior, behaviour
> estrogen, oestrogen
> hematology, haematology
> pediatric, paediatric
> tumor, tumour

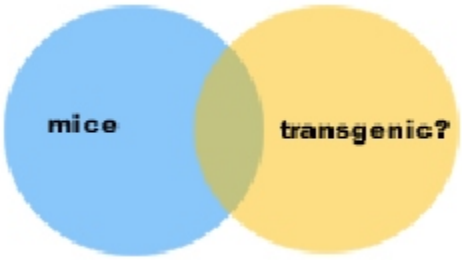
What is boolean logic?

The use of connecting words (operators) such as **AND**, **OR**, **NOT**, to either expand or narrow a search.

AND is used to find information containing both search terms linked by the operator. This is a way of narrowing your search results.

For example, to find information about the use of transgenic mice:

mice and transgenic?



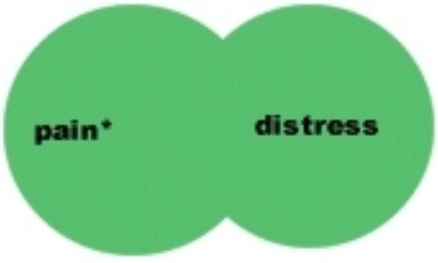
Each circle represents the set of documents containing one of the terms. The shaded area indicates the documents retrieved which include both terms--mice and transgenic?.

Truncation (the ?) is used to retrieve both transgenic and transgenics. It is used to retrieve various endings of the term.

OR is used to find information containing either one or both of the search terms. This is a way of expanding your search results.

For example, to find information referring to pain, distress or both terms:

pain? or distress?



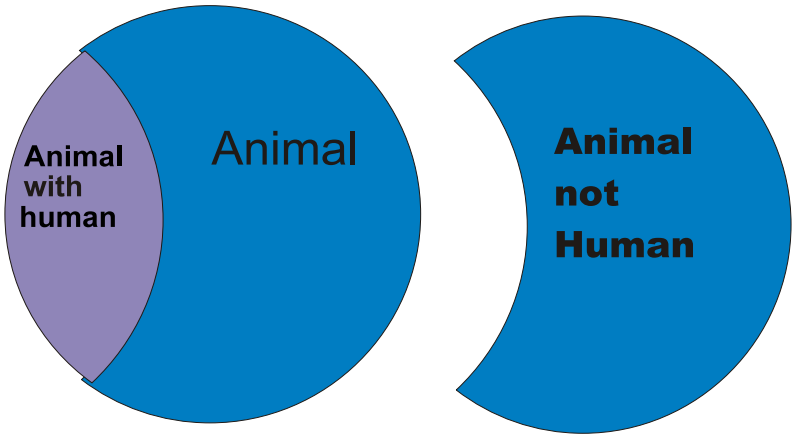
Each circle and the overlapping area represents the set of documents containing one or both of the terms. As a result this will find all documents that refer to the word pain?, all documents that refer to the word distress? and all documents that refer to both terms.

NOT is used to find information that does not contain a term. This is another way of narrowing the search. Be careful, however, because relevant information may be lost.

For example, to find only animal studies but not human studies:

animal? not human

This removes citations containing the word human, however, comparative studies of humans and animals will also be removed. **Use NOT with plenty of caution!**



A Few More Tips

★ Determine possible **synonyms** for each concept and decide where **truncation** should be used.

For example: heart, cardiac, cardiovascular, cardiopulmonary
blood collection, blood sampling, euthan? (euthanasia, euthanatize),
sacrifice? (sacrifice, sacrificed)
xylazine, rompun

★ Pay attention to **descriptors** or other **terminology** from **relevant citations** that might improve the search.

★ For new, recently developed, or rapidly changing technologies (for example, virtual simulators, laboratory equipment, transgenics), consider limiting the search by article **publication year**. This will weed out references to computer software/hardware that is obsolete, outdated transgenic techniques, etc.

★ If you are having difficulty in paring down the amount of information retrieved, consider **limiting** search terms to the **title**, or fields used to add indexing or thesaurus terms such as **descriptors**, **keywords**, or **identifiers**. However, be aware that while this will ensure a more targeted search it might exclude useful information.

For example: (dog or dogs or cani?)/ti,de,id
This will search the database for the terms dog, dogs, canine, canines, canid, canids, canis, etc. but only if they appear in the article title field, descriptors or identifiers fields.

The Alternatives Search Strategy

When preparing to conduct a literature search, certain information must be known. This can come from a protocol form or discussion with the investigator. As mentioned before, direct dialogue between the information specialist and the investigator is preferred to avoid any misinterpretation of the proposed research.

Information needed by information specialist or searcher

No matter how it is obtained, the information should include:

- ★ **Title of animal study protocol:** Providing the title of the protocol may provide some keywords.
- ★ **General area of study:** (e.g., drug testing, cardiology, toxicology, fetal alcohol syndrome, lipid metabolism, etc.)
- ★ **Type of protocol:** Is the proposed study a research, teaching, or testing protocol?
- ★ **Proposed animal species:** The animal model may be used as a keyword in the reduction and refinement phase of the search. At times the animal species is not initially used in the search in order to determine if the study can be done in alternate models. Is there a unique quality or usefulness about your chosen species that warrants its selection? Providing this may provide additional keywords or eliminate the need to search for other possible models being used.
- ★ **Describe your experimental protocol including objectives and endpoints:** This section should succinctly outline the scientific plan and direction of the experiment.
- ★ **Identify the systems or anatomy involved in the study** (e.g., lung, central nervous system, kidney, etc.)
- ★ **List any drugs or compounds used in procedures.** (e.g., anesthetics, analgesics, test compounds, etc.)
- ★ **Describe the methods and procedures using animals and the relevance to the study, paying particular attention to those procedures that may cause pain or distress to the animal.**
- ★ **List any potential alternatives** (3Rs of Reduction, Refinement and Replacement). (e.g., alternate models, modified techniques, housing modifications, modified restraint, in vitro methods, computer simulations, etc.)

Developing the search strategy

It is convenient to develop the search using the 3Rs as a guide. **Search strategies** for alternatives may be divided into **two phases**, **reduction and refinement**, and **replacement**.

Phase I: Reduction and refinement- citations pertinent to the field of study or the animal procedure

The first part of the search will examine the literature closely related to the proposed study for refinements to the proposed methods, information on methods or models that reduce the number of animals used, and to see if the proposed work duplicates previously published research. If the investigator has published previous literature this is a good time to read abstracts of his or her previous work and become familiar with terminology used to describe the study and to note what terms were used by database vendors to index the abstract. Upon completion of Phase I, the information specialist should have a basic understanding of the research area including: 1) the literature published in the particular field, 2) the techniques used, and 3) the commonly used species. The information specialist is now ready to search for possible replacement alternatives.

Phase II: Replacement- use of non-animal or alternative animal models.

In the second part of the strategy, the remaining R--replacement--is considered. There may be some overlap with the first part of the search, in that alternative animal models may already be in hand. If not, then alternative mammalian and nonmammalian models should be considered, as well as non-animal models. The following questions may be used to assist in the search for replacement alternatives:

- ★ Are there in vitro techniques that may reduce or replace the number of animals used (e.g., chorioallantoic membrane assay, use of primary cultured hepatocytes)?
- ★ Are there any alternative animal models (e.g., invertebrates, fish, protozoa, etc.)?
- ★ Have any computer simulations or statistical models been developed that relate to the study?

Terminology

Alternative Terms: Refine and Reduce

The phrase *animal testing alternatives* is used as an indexing term by AGRICOLA, MEDLINE, and other databases but fails to retrieve much useful information. Using the term *alternative?* as part of the strategy, especially for research protocols, is, by and large, useless.

In general, the terminology used in this part of the search will come from the area of study and from the literature describing a proposed technique or approach. For example, killing rats to obtain bone samples for determination of bacterial infections might be refined by using a noninvasive imaging method to detect lesions. This would also allow for a reduction in the number of animals. Important terms would be lesion, bone infection, (assess? or monitor? or diagnos?), imaging, etc.

Depending on the type of research, it might also be important to look for appropriate anesthetics, analgesics, methods of restraint, etc. Also remember to include both American and European spelling of words--for example, anesthesia, anaesthesia, anasthesia. It is also useful to determine that any anesthetics or analgesics that are going to be administered do not interfere with any of the physiological variables that are being measured.

Remember to consult with the database help screen for information on how to search phrases.

A sampling of other useful terms (? indicates truncated word stem) includes:

analgesi?
anestheti? anasthe? anaesthe?
tranquiliz? sedative
monitor? assess? diagnos?
restrain? immobil?
endpoint? biomarker?
advers?
train? (positive reinforce?)
animal welfare
assay? technique? method? proced?
environ? enrich? toy toys play?
behav? well-being
model?
statistic? (experimental design)
model models (animal model)
pain (control relief recogni? assess?)

For more information, see also Animal Welfare Information Center Scope Notes at

Terminology

Alternative Terms: Replacement

Below is a short list of useful terms.

model? or artificial or vitro or culture?
various lower phyla: fish or cephalopod?
simulat? or digital(n)imag? or interact? or virtual or mannequin? or assay?
model?
animal(n)testing(n)alternative?
environment?(n)enrich?
invertebrate?
bacteria
fish or cephalopod?
simulat?
software
video?
virtual(n)(surger? or reality)
mannequin? or manikin?
cadaver?
plastinat?
anesthe? or anasthe? or anaesthe?
anxiolytic
euthanasia
pain? distress?

When in doubt, check a thesaurus!!

AGRICOLA Thesaurus for Animal Use Alternatives
http://www.nal.usda.gov/awic/alternatives/altfact.htm

CAB Thesaurus allows the user to look up terms and their relationships, and access index terms through their synonyms.
http://194.203.77.66/

MeSH Browser (from Medline/PubMed) is designed to help quickly locate descriptors of possible interest and to show the hierarchy in which descriptors of interest appear.
http://www.nlm.nih.gov/mesh/MBrowser.html

Protocol Analysis

In this section, we will look at the analysis and search strategy development for two very different types of protocols. The research protocol examines the use of rats for developing osteomyelitis prevention strategies. In the training protocol, Dr. Stan Breager proposes to use pigs in his class on Advanced Trauma Life Support. **The training protocol is separate from this document.**

Analyze a protocol to determine the information needed to conduct a literature search.

In this section, an abridged version of a research protocol, containing crucial elements of the proposed activity, is presented. The protocol will be analyzed for relevant concepts that may allow for the implementation of the 3Rs—reduction of animal numbers, refinement of painful/distressful procedures, replacement with nonanimal/cell culture methods.

Protocol Title: Development of an animal model of acute osteomyelitis to test prevention strategies

Objective/Hypothesis

Contaminated trauma through open fractures due to high velocity missile wounds are common military combat injuries. An inexpensive method of prevention of acute, trauma-induced osteomyelitis would be useful in the field and hospital setting.

The environment of an open fracture can be manipulated in both a salutary and degratory fashion with respect to the establishment of acute osteomyelitis. In this study, two compounds will be tested for their abilities to effect the development of *Staphylococcus aureus* osteomyelitis in a rat model. L-fucose should decrease and arachidonic acid should increase the propensity toward infection in comparison with controls.

Materials and Methods

1. Animals. Albino Sprague-Dawley rats will be used.
2. Bacteria. Strain SMH of *Staphylococcus aureus*

Technical Methods

Pain Alleviation:

The rats will be anesthetized with a cocktail of 1.5 ml ketamine and 1.5 ml xylazine and 0.5 ml acepromazine given at a dosage of 0.5 to 0.7 ml/kg. If the plane of anesthesia is too light as determined by a positive toe pinch reflex, one half the original cocktail dose or isoflurane may be given. Yohimbine may be given to hasten recovery. Buprenorphine will be given up to 3x/day if the animal shows signs of pain.

Establishment of infection

The tibia is exposed and a wound is created in the bone with a dental burr. The wound is inoculated with *S. aureus* or *S. aureus* with L-fucose or arachidonic acid, allowed to incubate, and rinsed with sterile saline. The wound is sutured closed. The animals are killed at various times over several weeks, tibias removed, and examined to track development of osteomyelitic lesions.

DISCUSSION

The search strategy will be developed to find answers to questions posed by the protocol.

What are the main concepts to be considered in the search strategy?

- ★ animal models of osteomyelitis
- ★ in vitro models
- ★ noninvasive diagnostic techniques
- ★ confounding effects, if any, of anesthetics and related drugs

Protocol Analysis

The purpose of this protocol is to develop a model that can be used to test chemicals for their ability to prevent osteomyelitic lesions from developing in bones following trauma. The first question then is: Are there other animal models that may be more suitable for testing potential therapeutics or that more closely resemble the human condition? A corollary to this is: **Is there useful information on the proposed model that might allow the use of fewer animals or might reduce the pain suffered by the animals?** A different model might allow the investigator to use fewer animals or reduce pain, while refinements made to the proposed model, if available, might reduce animal pain or animal numbers.

The logical next question is: **Are there any in vitro methods that might allow for early screening of potential therapeutics**? While animals will have to be used at some point in the drug development scheme, a validated in vitro assay will allow the investigator to quickly screen numerous chemical moieties for therapeutic potential using few or no animals. Screening assays allow the testing of tens to thousands of compounds using cells grown in culture or tissues harvested from humanely killed animals.

In the proposed experimental design, animals will be killed at predetermined time points and examined for development of lesions. While this approach provides definitive assessment of the bones, noninvasive diagnostic techniques may be available that will provide equally definitive data. The third question then is: **Are noninvasive diagnostic techniques available?** This approach allows far fewer animals to be used over the course of the experiment.

Finally, it is always useful to determine if the anesthetics, analgesics, or compounds used to hasten recovery from a sedative (in this case, yohimbine) , might exert their own influence on the experimental outcomes. So our final question is: **Do the proposed anesthetics, analgesics, or α_2-adrenergic antagonist (yohimbine) pose a confounding influence on the outcome?**

Database Selection

Because we will be looking for biomedical (related to the research) and veterinary (related to the animals being used) information, we will include Medline, EmBase, Agricola, CAB, and Biosis.

Developing the Strategy

While we could certainly begin the search with any of our questions, a good place to start the search will be to look in the literature for information concerning the proposed experiment, in this case the use of arachidonic acid or L-fucose as agents to facilitate or inhibit the development of osteomyelitic lesions in rats. This allows us to determine if the experiment is duplicative (remember, unnecessary duplication is not allowed under the US Animal Welfare Act) and also to provide the investigator with any additional background information on the chosen model. This may give the investigator a better idea of the variablity to expect in the model and choose appropriate animal numbers. Terms for this part of the

search will come from the protocol. In this case, we will use the terms osteomyelitis, arachidonic acid, and L-fucose.

When developing any search strategy, it is always a good idea to keep different concepts separate as you create search sets. [A search set is a specific term or grouping of terms sent to the database as a query.] Separating concepts into discreet sets allows for flexibility in using terms as the strategy develops.

Figure 1 Separate concepts into discreet sets.

The Search Strategy

Set	Term Searched	Items
S1	OSTEOMYELIT?	37339
S2	L-FUCOSE OR ARACHIDONIC - ACID	128060
S3	S1 AND S2	27
S4	RD (unique items)	15

In Figure 1, osteomyelit? (The ? is a truncation mark used to retrieve word variations, e.g.-osteomyelitis, osteomyelitic, etc.) is Set 1 (S1) and has resulted in the retrieval of 37,339 citations containing our search term; L-Fucose or arachidonic acid is Set2 and has retrieved 128,060 citations. We can now combine these two sets to retrieve only those citations that contain both of our concepts. Combining Set 1 with Set 2 winnows the number of relevant citations to 27. Because we are searching in multiple databases, there will be some duplication of citations. Using a tool found in Dialog, we can remove the duplicates and end up with 15 unique citations that appear in Set 4. A few representative citations are in Figure 1a. **(Note: These can appear as pop-ups or internal links)**

In this case, it appears that the use of arachidonic acid in facilitating the establishment of disease is already an established protocol. However, this does not mean that the investigator is unnecessarily duplicating prior research. It may be justified by the need to establish or validate the model in this particular laboratory. This information might still prove useful to the investigator in properly designing the experiment. For the information specialist, the descriptors assigned to these citations allow us to become more familiar with the terminology that will allow us to pick appropriate search terms. This is especially important if the searcher is unfamiliar with the topic.

Figure 2 Developing the search strategy.

The Search Strategy

Set	Term Searched	Items
S5	ACUTE(3N)S1	2346
S6	STAPH? (W)AUREUS	168795
S7	S6 AND S5	489
S8	RD (unique items)	291
S9	TRAUMA? OR POSTTRAUMA?	448998
S10	S9 AND S6 AND S1	269
S11	RD (unique items)	174

The next phase of the search (Figure 2) will look for general information related to models of acute osteomyelitis. In this part of the search, we will not include the facilitating agents as we want to broaden the scope of the search. In this way, models using

a different approach will be retrieved. This might allow a more appropriate model to be uncovered in the literature or might provide other information that will allow the investigator to refine the proposed model. However, terms related to the type of osteomyelitis will be included. In this case, the investigator is interested in trauma-induced acute osteomyelitis caused by *Staphylococcal aureus (S. aureus)*. Again, we will add these new concepts to our strategy as discreet sets. Set 5 shows why this is useful. In Set 1 (see Figure 1), we searched for any information related to osteomyelitis and found 37,339 citations; in Set 5 we now want to limit our search to acute osteomyelitis. This is done by simply telling the database system to look at Set 1 and cull articles in which the word "acute" appears within 3 words of the term osteomyelitis. This will retrieve phrases such as, "acute osteomyelitis", "acute models of osteomyelitis", etc. We have now pared the relevant information to 2,346 citations. Because this particular research is interested in lesions caused by *S. aureus*, we add Set 6 and retrieve 168,795 citations. We now combine Set 5 and Set 6 to retrieve 489 citations that contain information on *S. aureus*-induced acute osteomyelitis. Removal of duplicate citations reduces this number to 291. In general, the information found includes a mix of both animal and a few in vitro models. Not surprisingly, articles on diagnostic techniques were also found. Remember, the purpose of this section is to retrieve information that will give background information on the proposed model or uncover better models. Sample citations are found in Figure 2a.

In the previous sets, we focused on general models of osteomyelitis, now we will narrow our focus to osteomyelitis caused by trauma or posttrauma events. We create Set 9 by searching the databases for the terms trauma or posttrauma. As before, the terms are truncated to allow retrieval of all variations of the words, eg.-traumatic, posttraumatic, etc. We now combine Set 9, our trauma terms, with Set 6 (S. Aureus) and Set 1 (Osteomyelitis). This will retrieve citations on S. Aureus and its implications in trauma-induced osteomyelitis (Set 10 and Set 11 (duplicates removed). Because we are trying to find information that might help refine the proposed model (and after a conversation with the investigator), we will allow the retrieval of citations that concern chronic models or acute hematogenous osteomyelitis (osteomyelitis caused by a blood-borne infection). Sample citations can be found in Figure 2b.

Figure 3 Developing the search strategy.

The Search Strategy

Set	Term Searched	Items
S12	VITRO OR CULTURE OR ISOLATE? (4N) (BONE OR TIBIA)	3554863
S13	S12 AND S1	2545
S14	S13 AND S6	696
S15	RD (unique items)	477
S16	S15 AND S9	27
S17	S15 AND ((VITRO OR CULTURE)/TI,DE,ID OR ISOLATE? (4N) (BONE OR TIBIA))	233

We are now ready to look for any in vitro or non-animal models that might be useful to the investigator (Figure 3). In this part of the search, we now use terminology to look for replacements to the animal model. Not surprisingly, animal models will still be retrieved but most of the citations will focus on minimal animal use (animals needed to harvest cells or tissue) or no animal use. The term "vitro" will look for *in vitro* techniques but we will also

include the term "culture" to retrieve tissue or cell culture methods. Finally, we will use various operators (see above) to look for methods using isolated bone or tibias (another culture technique). This string is found in Set 12.

As we did before, we narrow Set 12 by combining it with Set 1 (osteomyelitis) and find 2545 citations. We narrow again with Set 6 and find 696 citations; duplicate removal narrows this to 477. This is actually not a difficult number of titles to peruse (believe it or not) but we will see if any papers in this area include trauma (Set 9). Including Set 9 substantially narrows the field to 27 records (Set 16). However, none of these records were useful and generally included our search term "culture" in relation to cultures of *S. aureus* and not cell or tissue culture techniques. This is one of the pitfalls of this kind of searching.

To circumvent this, we will now introduce another searching feature that is available on many database systems. Using field limiters, we will now instruct the database to limit the terms "vitro" and "culture" to the title (ti) of the article, or the descriptors (de) or identifiers (id) added by the database vendor. This is another powerful tool that allows us to focus our search to a small subset of a topic. We will continue to allow the "isolated bone or tibia" search string to appear anywhere in a record, i.e., title, abstract, or descriptors. When we reexamine Set 15 (in vitro models of S. aureus-induced osteomyelitis-477 citations), we now reduce the number of records to 233 (Set 17). Sample citations are found in Figure 3a.

Figure 4 Developing the search strategy.

The Search Strategy

Set	Term Searched	Items
S18	(IMAG? OR MARKER? OR BIOMARKER? OR NONINVASIVE OR MRI OR TOMOGRAPH?) AND (DIAGNO? OR ASSESS?) AND S1 AND S6	75
S19	KETAMINE OR XYLAZINE OR ISOFLURANE ACEPROMAZINE OR BUPRENORPHINE OR YOHIMBINE	72600
S20	S1 AND S19	7
S21	S2 AND S19	234
S22	RD (unique items)	153

Now we can look for information on osteomyelitis diagnostic methods. The protocol calls for animals to be killed at various timepoints and necropsied. However, the use of imaging techniques or physiological biomarkers could lead to the use of fewer animals. In set 18, we use a variety of terms commonly used to index this literature. These include: imag? that will retrieve information on imaging, imaged or image; marker? and biomarker? to include plurals; noninvasive; MRI to pick up articles using the abbreviation for Magnetic Resonance Imaging (our term imag? will pick up the phrase); and tomograph? to retrieve information on various types of tomography. We will also include terms for the type of procedure being performed–in this case diagnostics. The terms will include the truncated form of diagno? to retrieve diagnostic, diagnostics, diagnose, etc. The term assess? is also used to retrieve articles using assess, assessment, assessed, etc. Finally, these are linked to our other concepts of osteomyelitis (S1) and S. aureus (S6) with the AND operator. This tells the databases that relevant citations must contain all of these concepts to be retrieved. This set retrieves 75 citations; sample citations can be found in Figure 4a.

In the last question to be examined, we will determine if any of the preanesthetics, anesthetics, analgesics or anesthetic antagonists might confound the expected outcome. The drugs are listed in Set 19 (S19) and are combined first with the osteomyelitis set (S1). Nothing useful was found in Set 20 (S20). Next we determine if the drugs might interact with the treatment drugs–arachidonic acid or L-fucose. The results are 153 citations in S22. Sample citations are found in Figure 4b.

In this tutorial, the number of sample citations is small. In reality, the information specialist would provide all pertinent citations to the investigator. By discussing the protocol with the investigator, the information provider can examine all the citations retrieved at each stage of the search, and download those that will be most useful to the investigator. **The idea is not to overwhelm the scientist with so much information as to render it useless, but to provide a good review of the literature on all aspects of the proposed experiment.**

In the final section of this module, we will look at the value of the search and how to interpret the results. But first, it's quiz time!!

QUIZ

1. Federal animal welfare regulations require investigators to search at least four databases for alternatives.

_____True _____False (Answer is false.)

2. Truncation allows for:

a. searching in multiple databases
b. retrieval of words sharing the same stem (Answer is b.)
c. storage of search results in an electronic trunk.

3. Using the boolean operator "OR" allows the searcher to expand the search results.

_____True _____False (Answer is true.)

4. Using the boolean operator "AND" allows the searcher to expand the search results.

_____True _____False (answer is false.)

5. Including the term "alternative?" in the search strategy will

a. always find useful information, especially for research protocols.
b. usually retrieve information unrelated to the 3Rs. (Answer is b.)
c. find information on the harmful effects of certain kinds of music.

6. In developing the search strategy, keeping concepts in discrete sets allows for greater flexibility in searching.

_____True _____False

Note to Consultant: THE ALTERNATIVE SEARCH: VALUE, USE AND INTERPRETATION OF RESULTS:
A training module in 2 sections.
This is also included as a separate file.

Figure 1a. Sample citations from Set 4

Arachidonic acid facilitates experimental chronic osteomyelitis in rats.
Rissing JP; Buxton TB; Fisher J; Harris R; Shockley RK
Infect Immun (UNITED STATES) Jul 1985 , 49 (1) p141-4
Arachidonic acid was used as a facilitating agent in experimental rat Staphylococcus aureus osteomyelitis and compared with the more commonly used agent, sodium morrhuate. The injection of arachidonic acid or sodium morrhuate and S. aureus into rat tibiae caused increased quantitative bacterial bone counts, gross bone pathology, roentgenographic changes, and weight loss. The doses required to produce these changes appeared to be lower for arachidonic acid.
Descriptors: *Arachidonic Acids--Toxicity--TO; *Osteomyelitis--Etiology--ET ; Disease Models, Animal; Osteomyelitis--Pathology--PA; Osteomyelitis --Radiography--RA; Rats; Sodium Morrhuate--Toxicity--TO; Staphylococcal Infections--Complications--CO; Staphylococcus aureus--Pathogenicity--PY; Tissue Culture

Study on experimental osteomyelitis in mice.
YOKOYAMA TAKASHI (1)
Tokyo Ika Daigaku Zasshi (Journal of Tokyo Medical College) , 1989 ,
VOL.47,NO.1 , PAGE.91-104 , FIG.6, TBL.10, REF.26
Abstract: Osteomyelitis, a representative refractory infectious disease in the field of orthopedics, is liable to develop into a prolonged and chronic disease. In order to investigate the pathogenesis of osteomyelitis, attempts have been made to produce experimental animal model of the purulent osteomyelitis, however ideal model has not been developed. The present paper reports that a mouse model of experimental osteomyelitis was established successfully by injection of Staphylococcus aureus with arachidonic acid as a sclerosing agent directly into the medullary cavity of the tibia of mice with a microsyringe. By injecting both 105.6 CFU of Staphylococcus aureus No.28 and 31.5ng of sodium salt of arachidonic acid, the optimal condition for the formation of osteomyelitis in this model, the localized purulent osteomyelitis which closely resemble the human disease radiologically and histologically was fully recognized. For the first 2 weeks, the mice received both of the agents showed a statistically higher amount of prostaglandin in the tibia compared with the group of the staphylococci alone. In the leukopenic mice due to cyclophosphamide, the osteomyelitis occured in 90% of the mice by an intramedullary inoculation of 104.2 CFU of Staphylococcus aureus without use of the sclerosing agent. The evaluation method of the osteomyelitis was contrived by the score expressing the lesion of the osteomyelitis numerically in terms of its radiological, bacteriological and histological appearance, and the relative severity which was calculated from each score of the three findings made it possible to evaluate the osteomyelitic lesion quantitatively. It was made possible to compare the rate of formation and the severity of the osteomyelitis among experimental groups with a high accuracy, especially through the three criteria for determining the formation of osteomyelitis, based on the soft X-ray findings and the relative severity.
Descriptors: mouse (animal); osteomyelitis; Staphylococcus aureus; experimental disease; X-ray inspection; vitamin F; polyene; aliphatic carboxylic acid; unsaturated carboxylic acid
Broader Descriptors: Myomorpha; Rodentia; Mammalia; Vertebrata; animal; inflammation; disease; infectious disease; bone disease; bone and joint disease; bone marrow disease; hematologic disease; Staphylococcus; Micrococcaceae; bacterium; microorganism; model; radiographic inspection; nondestructive inspection; inspection; fatty acid; carboxylic acid;

Figure 2a Sample citations from Set 8

The effect of wound environment on the incidence of acute osteomyelitis.
Evans RP; Nelson CL; Harrison BH
Clin Orthop (UNITED STATES) Jan 1993 , (286) p289-97.
A model was developed to identify and compare the local wound factors that induce acute osteomyelitis in a prospective, controlled investigation. When compared with wounds containing either virulent bacteria or dead bone, statistical analysis disclosed a significant increase in the incidence of osteomyelitis when virulent bacteria and dead bone were combined. The incidence of osteomyelitis in wounds containing an inoculated, hematoma-filled dead space was significantly less when compared with wounds containing dead bone and virulent bacteria. The incidence of osteomyelitis is significantly less when a nonvirulent strain of bacteria is substituted for a virulent strain. Although rigid internal fixation increased the incidence of osteomyelitis to 100% and long-term antibiotic therapy decreased the incidence, these changes were not statistically significant. These data allow the authors to predict the relative risk of osteomyelitis when these wound factors are present. The prevention of osteomyelitis depends on the clinical identification and modification of these local wound factors.
Descriptors: *Models, Biological; *Osteomyelitis--Physiopathology--PP; *Wounds and Injuries--Physiopathology--PP ; Acute Disease; Ceftriaxone--Therapeutic Use--TU; Osteomyelitis--Drug Therapy--DT; Osteomyelitis--Microbiology--MI; Prospective Studies; Rabbits ; Risk; Staphylococcus aureus--Pathogenicity--PY; Virulence; Wounds and Injuries--Microbiology--MI
CAS Registry No.: 73384-59-5 (Ceftriaxone)

A new model for posttraumatic osteomyelitis in rabbits.
Eerenberg JP; Patka P; Haarman HJ; Dwars BJ
Department of Surgery, Free University Hospital, Amsterdam, Holland.
J Invest Surg (UNITED STATES) Sep-Oct 1994 , 7 (5) p453-65 ,
A new animal model for posttraumatic osteomyelitis was designed. This model mimics the pathogenesis of the human disease more accurately than models presently available. Femora of New Zealand white rabbits were exposed at the greater trochanter and a stainless steel rod was inserted into the marrow cavity. A Staphylococcus aureus suspension was placed in and around a bone defect, which was drilled midshaft. The disease was evaluated by clinical observation and roentgenographic, hematologic, bacteriologic, and histologic parameters. Osteomyelitis developed in all 24 infected rabbits. None of the five rabbits receiving only an intramedullary rod developed an osteomyelitis. This model proves that an experimental posttraumatic osteomyelitis associated with a foreign body can be reliably induced, even when no infection-promoting chemical agents, small inoculum of bacteria, or minimal bone trauma is present.
Descriptors: *Disease Models, Animal; *Femur Neck--Injuries--IN; *Foreign Bodies --Complications--CO; *Osteomyelitis; *Prostheses and Implants--Adverse Effects--AE; *Staphylococcal Infections ; Bone Marrow--Injuries--IN; Bone Marrow--Microbiology--MI; Bone Marrow --Pathology--PA; Equipment Contamination; Femur Neck--Surgery--SU; Osteomyelitis--Etiology--ET; Osteomyelitis--Pathology--PA; Osteomyelitis --Radiography--RA; Rabbits; Reoperation; Staphylococcal Infections --Etiology--ET; Staphylococcal Infections--Pathology--PA; Staphylococcal Infections--Radiography--RA

Figure 2b. Sample citations from Set 11

Chronic staphylococcal osteomyelitis: a new experimental rat model
Spagnolo, N. Greco, F.; Rossi, A.; Ciolli, L.; Teti, A.; Posteraro, P.
Infection and immunity. Dec 1993. v. 61 (12) p. 5225-5230.
A rat model of chronic staphylococcal osteomyelitis was developed. Fibrin glue (5 microliters) and Staphylococcus aureus [2x10(6) CFU/5 microliters] were inoculated into the proximal metaphysis of the tibia. The rats were killed at intervals of between 1 and 6 months, and the tibias were removed. Induced lesions were evaluated by radiographic, macroscopic, and histological examinations and bacterial counts. Roentgenograms revealed osteomyelitis in more than 90% of the tibias. Gross bone pathology revealed skeletal deformation, new bone formation, abscesses, and draining skin fistulas in more than 80% of cases. Histological examination revealed osteomyelitis in more than 90% of cases, and bacterial counts were positive in 86% of cases. Only fibrin glue (5 microliters) was inoculated into controls. Controls showed no osteomyelitic lesions, and counts were negative in seven of eight control tibias. The main feature of this model is the use of fibrin glue instead of the sclerosing agents and foreign bodies used in other models. The model reproduces lesions similar to those of human posttraumatic osteomyelitis and can be reliably used in pathophysiological and therapeutic studies.
Descriptors: rats - disease models - staphylococcus aureus -
osteomyelitis ;
Section Headings: L110 LABORATORY AND EXPERIMENTAL ANIMALS

A new model for posttraumatic osteomyelitis in rabbits.
Eerenberg JP; Patka P; Haarman HJ; Dwars BJ
J Invest Surg (UNITED STATES) Sep-Oct 1994 , 7 (5) p453-65
A new animal model for posttraumatic osteomyelitis was designed. This model mimics the pathogenesis of the human disease more accurately than models presently available. Femora of New Zealand white rabbits were exposed at the greater trochanter and a stainless steel rod was inserted into the marrow cavity. A Staphylococcus aureus suspension was placed in and around a bone defect, which was drilled midshaft. The disease was evaluated by clinical observation and roentgenographic, hematologic, bacteriologic, and histologic parameters. Osteomyelitis developed in all 24 infected rabbits. None of the five rabbits receiving only an intramedullary rod developed an osteomyelitis. This model proves that an experimental posttraumatic osteomyelitis associated with a foreign body can be reliably induced, even when no infection-promoting chemical agents, small inoculum of bacteria, or minimal bone trauma is present.
Tags: Animal; Comparative Study; Female
Descriptors: *Disease Models, Animal; *Femur Neck--Injuries--IN; *Foreign Bodies --Complications--CO; *Osteomyelitis; *Prostheses and Implants--Adverse Effects--AE; *Staphylococcal Infections ; Bone Marrow--Injuries--IN; Bone Marrow--Microbiology--MI; Bone Marrow --Pathology--PA; Equipment Contamination; Femur Neck--Surgery--SU; Osteomyelitis--Etiology--ET; Osteomyelitis--Pathology--PA; Osteomyelitis --Radiography--RA; Rabbits; Reoperation; Staphylococcal Infections --Etiology--ET; Staphylococcal Infections--Pathology--PA; Staphylococcal Infections--Radiography--RA

Figure 3a. Sample citations from Set 17

Application of a rat osteomyelitis model to compare in vivo and in vitro the antibiotic efficacy against bacteria with high capacity to form biofilms.
Gracia E; Lacleriga A; Monzon M; Leiva J; Oteiza C; Amorena B
J Surg Res (UNITED STATES) Oct 1998 , 79 (2) p146-53 , ISSN
A rat experimental osteomyelitis model was used to study the efficiency of antibiotics on biofilm bacteria adhered to implants in relation to the efficiency obtained in vitro. In the osteomyelitis model, 10(4) bacteria of the strain variant used for the in vitro studies (a slime-producing variant of Staphylococcus aureus) were inoculated into the rat tibia at surgery, after implanting a stainless steel canula precolonized for 12 h with this strain. After 5 weeks, a 21-day antibiotic treatment was applied (using cefuroxime, vancomycin, or tobramycin). Subsequently, implant and tibia were studied for presence of bacteria. In this osteomyelitis model, cefuroxime inhibited bone colonization and reduced the number of bacteria in metal and bone at a higher degree ($P < 0.05$) than vancomycin and tobramycin (the latter antibiotic did not have this reduction effect). The in vitro assay was applied using three concentrations of each antibiotic (8, 100, and 500 microg/ml) and 6-, 24-, and 48-h biofilms. Bacterial viability was evaluated by ATP-bioluminescence after 24 h of antibiotic treatment. In this in vitro assay, cefuroxime significantly ($P < 0.05$) reduced in all cases the number of viable bacteria in biofilms, tobramycin did not affect viability, and vancomycin affected viability except at the lowest concentration used (8 microg/ml, i.e., 8x the minimal bactericidal concentration of this antibiotic) when facing the oldest (48 h) biofilm. These results demonstrate the usefulness of the osteomyelitis model applied in providing evidence for a close correlation between the in vitro and in vivo findings on the effect of three antibiotics under study.

Mechanisms of Staphylococcus aureus invasion of cultured osteoblasts
Ellington J.K.; Reilly S.S.; Ramp W.K.; Smeltzer M.S.; Kellam J.F.; Hudson M.C.
Microbial Pathogenesis (MICROB. PATHOG.) (United Kingdom) 1999, 26/6 (317-323)

Staphylococcus aureus is a bacterial pathogen causing approximately 80% of all cases of human osteomyelitis. This bacterium can adhere to and become internalized by osteoblasts and previous studies indicate that osteoblasts are active in the internalization process. In the current study, we examined the roles of microfilaments, microtubules and clathrin-dependent receptor-mediated endocytosis in the internalization of S. aureus by MC3T3-E1 mouse osteoblast cells. Microfilament and microtubule polymerization was inhibited with cytochalasin D and colchicine. Clathrin-coated pit formation was examined by using the transaminase inhibitor, monodanslycadaverine. The results of this study indicate that mouse osteoblasts utilize actin microfilaments, microtubules and clathrin-coated pits in the internalization of S. aureus; however, microfilaments seem to play the most significant role in the invasion process.

Figure 4a. Sample citations from Set 18

Excretion of urinary hydroxyproline in correlation with severity of induced osteomyelitis in rabbits
ABBAS H L.
JACTA PHYSIOL HUNG 78 (3). 1991. 235-239.
Osteomyelitis was induced artificially by injecting Staphylococcus aureus culture in the tibiae of young rabbits. Weekly estimations of hydroxyproline in urine were done for six weeks. It was found that the osteomyelitic rabbits excreted more hydroxyproline (about 96%) two weeks after the infection in comparison to the control animals and it continued to be very high (about 138%) six weeks after the infection. The results indicate that urinary hydroxyproline reflects degradation of collagen fibers in the bone, and may be an indicator of the severity of the disease.

(99m)Tc-E-selectin binding peptide for imaging acute osteomyelitis in a novel rat model.
Gratz,-S; Behe,-M; Boerman,-O-C; Kunze,-E; Schulz,-H; Eiffert,-H; O'Reilly,-T; Behr,-T-M; Angerstein,-C; Nebendahl,-K; Kauer,-F; Becker,-W. Nucl-Med-Commun. 2001 Sep; 22(9): 1003-13
Nuclear-medicine-communications
INTRODUCTION: In the present study, (99m)Tc-radiolabelled E-selectin binding peptide ((99m)Tc-IMP-178) was investigated for its potential to image acute pyogenic osteomyelitis in a new animal model. Intraindividual comparisons were performed using an irrelevant peptide ((99m)Tc-IMP-100) to demonstrate specificity. METHODS: An acute pyogenic osteomyelitis was induced by injecting 0.05 ml of 5% sodium morrhuate and 5x10(8) CFU of Staphylococcus aureus into the medullary cavity of the right tibia in 16 rats. Sixteen additional rats served as untreated controls. Whole-body imaging of pyogenic (n=4) and untreated (n=4) animals was performed continuously during the first 8 h (12 MBq i.v. of (99m)Tc-IMP-178 and (99m)Tc-IMP-100 for control), and one further single image was acquired after 16 h p.i. Tissue biodistribution studies were performed in 12 rats with an acute pyogenic osteomyelitis and in 12 untreated rats 1, 4 and 24 h after injection. Data of the histological/radiological and haematological investigations were obtained in all animals. RESULTS: Histopathologically, 15 of 16 treated rats (93%) developed an acute pyogenic osteomyelitis showing a major infiltration of the bone marrow by polymorphonuclear leukocytes as well as the formation of sequestra. Haematologically, the number of leukocytes increased by 100%, the lymphocytes by 11% and the granulocytes decreased by 39%. After i.v. injection, (99m)Tc-IMP-178 rapidly cleared from the body resulting in good scintigraphic target-to-background (T/B) ratios. The highest uptake of the tracer in the pyogenic bone was observed at 60 min p.i. (0.43+/-0.02% ID.g-1 for (99m)Tc-IMP-178 and 0.30+/-0.02% ID.g-1 for (99m)Tc-IMP-100), resulting in a higher osteomyelitis-to-healthy collateral ratio with T/B of 2.40+/-0.65 ((99m)Tc-IMP-178) compared with 1.85+/-0.48 ((99m)Tc-IMP-100). No adverse reactions were seen after injection of (99m)Tc-IMP-178. CONCLUSIONS: (99m)Tc-IMP-178 allows imaging of an acute osteomyelitic lesions, presumably by interaction of (99m)Tc-IMP-178 with activated upregulated vascular endothelium.
MJME: *Carrier-Proteins-metabolism; *E-Selectin-metabolism; *Osteomyelitis-radionuclide-imaging; *Technetium-diagnostic-use
MIME: Acute-Disease; Amino-Acid-Sequence; Disease-Models,-Animal; Molecular-Sequence-Data; Osteomyelitis-blood; Osteomyelitis-pathology; Rats-; Rats,-Wistar; Tissue-Distribution

Figure 4a (cont.). Sample citations from Set 18

Evaluation of serum biochemical markers of bone metabolism for early diagnosis of nonunion and infected nonunion fractures in rabbits.
Southwood,-L-L; Frisbie,-D-D; Kawcak,-C-E. Am-J-Vet-Res. 2003 Jun; 64(6): 727-35
OBJECTIVE: To evaluate the use of serum concentrations of biochemical markers of bone metabolism (osteocalcin [OC], bone-specific alkaline phosphatase [BS-ALP], and deoxypyridinoline [DPYR]) to compare healing in infected versus noninfected fractures and in fractures with normal repair versus delayed (nonunion) repair in rabbits. ANIMALS: 32 female 9- to 10-month-old New Zealand White rabbits. PROCEDURE: A femoral fracture defect was made in each rabbit. Rabbits were assigned to the following groups: the bone morphogenetic-2 gene treatment group with either noninfected nonunion or infected (ie, inoculation of defects with Staphylococcus aureus) nonunion fractures or the luciferase (control) gene treatment group with either noninfected nonunion or infected nonunion fractures. Serum samples were obtained before surgery (time 0) and 4, 8, 12, and 16 weeks after surgery. Callus formation and lysis grades were evaluated radiographically at 16 weeks. RESULTS: Serum OC and BS-ALP concentrations decreased from time 0 at 4 weeks, peaked at 8 weeks, and then decreased. Serum DPYR concentration peaked at 4 weeks and then decreased, independent of gene treatment group or fracture infection status. Compared with rabbits with noninfected fractures, those with infected fractures had lower serum OC and BS-ALP concentrations at 4 weeks, higher serum OC concentrations at 16 weeks, and higher serum DPYR concentrations at 4, 8, and 16 weeks. Combined serum OC, BS-ALP, and DPYR concentrations provided an accuracy of 96% for prediction of fracture infection status at 4 weeks. CONCLUSIONS AND CLINICAL RELEVANCE: Measurement of multiple serum biochemical markers of bone metabolism could be useful for clinical evaluation of fracture healing and early diagnosis of osteomyelitis.

Imaging experimental osteomyelitis using radiolabelled liposomes.
Awasthi,-V; Goins,-B; Klipper,-R; Loredo,-R; Korvick,-D; Phillips,-W-T. J-Nucl-Med. 1998 Jun; 39(6): 1089-94
We evaluated radiolabelled liposomes (liposomes labeled both with 99mTc and 111In) for the early detection of osteomyelitis in an experimental model. METHODS: Liposomes, containing 5% polyethylene glycol-distearoyl phosphatidylethanolamine with encapsulated glutathione and deferoxamine, were prepared and labeled with 99mTc and 111In by a previously described method. Acute osteomyelitis was induced in male New Zealand rabbits by intramedullary injection of sodium-morrhuate and Staphylococcus aureus in the tibial bone marrow. Serial imaging studies, consisting of radiolabelled liposome imaging (2-4 mCi 99mTc and 75-125 microCi 111In), 99mTc-methylene diphosphonate (MDP) (3-5 mCi) and 67Ga-citrate (500 microCi), were performed starting at the third day after injection. Each radionuclide study was separated by at least 2 days. The animals also underwent radiography of the lower extremities. The animals were then killed and the infected tibia was excised for histopathology. RESULTS: For interpreting relative efficacy of individual radiopharmaceuticals, only animals showing positive histopathological findings (n = 9) were considered. Radiographs (Days 12, 13) were conclusive for osteomyelitis in only 3 rabbits. Radiolabelled liposome imaging (Days 4-6) showed positivity in 8 cases and was equivocal in 1. Though the lesion could be delineated as early as 8 hr postinjection in the 99MTc window, the best target-to-nontarget ratio (T/NT) of 1.86 +/- 0.19 was obtained at 48 hr in the 111In window. Three-phase 99mTc-MDP scan (Day 7) was positive in only 5 rabbits with 3 hr T/NT of 1.6 +/- 0.23. Galium-67-citrate images (Days 9-11) were positive in 8 cases and equivocal in 1, the mean 48 hr T/NT being 1.74 +/- 0.24. These results show liposomes are better than 99mTc-MDP for imaging bone infection. Given the early localization and better quality of the images, radiolabelled liposomes also exhibited advantages over 67Ga-citrate for detection of acute osteomyelitis.
MJME: *Indium-Radioisotopes-diagnostic-use; *Osteomyelitis-radionuclide-imaging; *Technetium-diagnostic-use MIME: Acute-Disease; Citrates-diagnostic-use; Gallium-diagnostic-use; Liposomes-; Rabbits-; Radiopharmaceuticals-diagnostic-use; Sensitivity-and-Specificity; Technetium-Tc-99m-Exametazime-diagnostic-use; Technetium-Tc-99m-Medronate-diagnostic-use

Figure 4b. Sample citations from Set 22

Anesthesia-associated depression of peripheral node lymphocyte traffic and antibody production in sheep accompanied by elevations in arachidonic acid metabolites in efferent lymph
Spruck C.H.; Moore T.C. Transplantation Proceedings 1988 , 20/6 (1169-1174).
The present study extends earlier observations of prostaglandin Einf 2 (PGEinf 2) involvement in depression in lymphocyte traffic and accompanying alterations in immune response factors, including involvement of other arachidonic acid metabolites and changes in lymphocyte types and subtypes. Prior studies of arachidonic acid metabolites have involved the use of both barbiturate-halothane and ketamine-xylazine general anesthesias.
Drug Descriptors:* prostaglandin e2; *ketamine--pharmacology--pd; *xylazine--pharmacology--pd
Medical Descriptors: * anesthesia; *antibody production; *arachidonic acid metabolism; *lymph node sheep; nonhuman; intramuscular drug administration; priority journal; complication
CAS Registry Number: 363-24-6 (prostaglandin e2); 1867-66-9, 6740-88-1, 81771-21-3 (ketamine); 23076-35-9, 7361-61-7 (xylazine)

alpha- and beta- adrenergic stimulation of arachidonic acid metabolism in cells in culture
Levine L.; Moskowitz M.A. Proceedings of the National Academy of Sciences of the United States of America 1979, 76/12 (6632-6636)
Drug Descriptors: * alpha adrenergic receptor blocking agent; *alpha adrenergic receptor; * **arachidonic acid**; *beta adrenergic receptor; *bromocriptine; *dibenamine; * dihydroergotamine; *ergocryptine; *ergotamine; *noradrenalin; *phenoxybenzamine; *phentolamine; *phospholipid; *propranolol; *prostacyclin ; *prostaglandin; *prostaglandin d2; *prostaglandin e2; *prostaglandin f2 alpha; *thromboxane a2; *tolazoline; ***yohimbine**; colchicine; cycloheximide; cytochalasin b
Medical Descriptors: * kidney cell; *lymphoma kidney; in vitro study; animal experiment; dog; mouse; drug analysis; drug comparison
CAS Registry Number: 506-32-1, 6610-25-9, 7771-44-0 (arachidonic acid); 25614-03-3 (bromocriptine); 51-50-3, 55-43-6 (dibenamine); 511-12-6 (dihydroergotamine) ; 511-09-1 (ergocryptine); 113-15-5, 52949-35-6 (ergotamine); 1407-84-7, 51-41-2 (noradrenalin); 59-96-1, 63-92-3 (phenoxybenzamine); 50-60-2, 73-05-2 (phentolamine); 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6 (propranolol); 35121-78-9, 61849-14-7 (prostacyclin); 41598-07-6 (prostaglandin d2); 363-24-6 (prostaglandin e2); 551-11-1 (prostaglandin f2 alpha); 57576-52-0 (thromboxane a2); 59-97-2, 59-98-3 (tolazoline); 146-48-5, 65-19-0 (yohimbine); 64-86-8 (colchicine); 642-81-9, 66-81-9 (cycloheximide); 14930-96-2 (cytochalasin b)

A role for arachidonic acid in general anesthetic action.
Denson D D(a); Eaton D C. Society for Neuroscience Abstracts 21 (1-3): p 1833 1995
Registry Numbers: 506-32-1: ARACHIDONIC ACID; 6740-88-1: KETAMINE; 7440-09-7: POTASSIUM; 9001-84-7: PHOSPHOLIPASE A-2
Descriptors: ARACHIDONIC ACID; KETAMINE; POTASSIUM; PHOSPHOLIPASE A-2
Miscellaneous Terms: KETAMINE; MEETING ABSTRACT; MEETING POSTER; PHOSPHOLIPASE A-2; POTASSIUM CHANNEL

Other Resources to Consult

A Guide to Searching for Alternatives to the Use of Laboratory Animals
Dr. Krys Bottrill, FRAME (Fund for the Replacement of Animals in Medical Experiments)
http://www.frame-uk.demon.co.uk/guide/index.htm

Searching for 3Rs information -published literature sources
Information Managers in the Pharmaceutical Industry, July 2002
http://www.impi.org.uk/i3r_v2_jul2002.pdf

Allen, T. (Summer 1999). **On-line Databases: What is Available? What is Missing?** Animal Welfare Information Center Bulletin, Vol. 10 (1-2): 11-14.
http://www.nal.usda.gov/awic/newsletters/v10n1/10n1alle.htm

Kreger, M.D. (1999). **The literature search for alternatives.** In The Care and Feeding of an IACUC: The Organization and Management of an Institutional Animal Care and Use Committee, M.L. Podolsky and V.S. Lukas, eds., Boca Raton, FL: CRC Press:, pp. 139-152.

Kreger, M.D. (1997). **Why conduct literature searches for alternatives?** ASLAP Newsletter (American Society of Laboratory Animal Practitioners) 30(3):19-23.
http://www.nal.usda.gov/awic/alternatives/aslap.htm

Langley, G., C. Broadhead, K. Bottrill, R. Combes, R. Ewbank, P. Hawkins, R. Hubrecht, M. Jennings, C. Newman, S. Rowe, J, Southtree, M. Todd, and L. Ward (1999). **Accessing information on the reduction, refinement, and replacement of animal experiments.** ATLA-Alternatives to Laboratory Animals 27(2): 239-245.
NAL call number: Z7994 L3A5

Shevell, J.L. and M.L. James (1995). **Search for animal alternatives and the role of the Information Specialist.** Contemporary Topics in Laboratory Animal Science 34(3): 65-68.
NAL call number: SF405.5 A23

Smith, C. (1994). **AWIC tips for searching for alternatives to animal research and testing.** Lab Animal 23(3): 46-48.
http://www.nal.usda.gov/awic/alternatives/tips.htm

Stokes, W.S. and D.J.B. Jensen (1995). **Guidelines for institutional animal care and use committees: consideration of alternatives.** Contemporary Topics in Laboratory Animal Science 34 (3):51-55, 58-60.
NAL call number: SF405.5 A23

Snow, B. (July, 1990). **Online searching for alternatives to animal testing.** Online p.94-97.\
NAL call number: QA76.55 O6

Wood, M.W. and L.A. Hart (2001). **Searching for the 3Rs: Facilitating compliance in the bibliographic search for alternatives**. INSPEL 35(3): 191-198.
NAL call number: Z671 I15