Michigan Society for Medical Research

BioFocus

A Newsletter Exploring Science & Biomedical Research Issues For School Educators

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Our Mission

The Michigan Society for Medical Research (MISMR) is a nonprofit educational organization that supports biomedical research and testing and the judicious use of animals in research, education and testing in the interests of human and animal welfare. Established in 1981, MISMR is made up of the state's leading research universities, teaching hospitals, pharmaceutical companies, voluntary health organizations and hundreds of scientists, educators and students who understand and support the importance of animal research and testing in advancing health care and treatment.

MISMR Educational Projects & Activities

Annual Essay Contest

Every year MISMR sponsors an essay contest open to all Michigan high school students. Students from well over 500 schools in the state have annually participated in the contest to address the benefits of biomedical research. Prizes are awarded.

Speakers Bureau

MISMR volunteers visit K–12 schools and civic community groups through out Michigan each year to educate the public about biomedical research and to dispel commonly held myths.

The Animal Research Minute

A daily radio editorial broadcast to more than 3,500 stations nation wide, The Animal Research Minute discusses the humane and responsible use of animals in research that are leading to human and animal health improvements. **CLICK>www.FBResearch.org**

www.mismr.org

Medical Devices

Better Health Through Engineering & Biology

By Alan P. Brown, PhD, DABT
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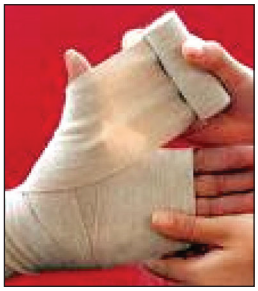

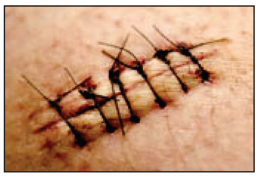

The use of medical devices has improved the health and welfare of every American (and most populations in the world) from birth throughout an individual's lifetime. What are medical devices and how have we benefited from them? How has biomedical research, including the ethical use of animals provided invaluable information for developing and testing medical devices? This article will provide a brief overview regarding these topics.

Medical devices encompass an extremely broad category of items, such as bandages, crutches and wheel chairs, sutures, needles and syringes, catheters, contact lenses and lens care solutions, orthopedic implants, dental fillings, pacemakers, thermometers, glucose meters, surgical tools and instruments, respirators, infusion pumps that deliver drugs, and equipment that monitor and measure blood pressure and heart rate. Based on this brief, but diverse list, it is evident that medical devices are used by nearly everyone, and have improved human health and welfare, irrespective of age or medical condition.

Medical devices in the United States are regulated by the US Food and Drug Administration, which is responsible for assuring they are safe, effective, and manufactured to standards that assure fitness for use. Similarly, governmental agencies in Europe, Japan, and elsewhere have regulatory authority regarding the use of medical devices in their respective countries. Depending upon the device and intended use, they are placed into various categories, with requirements for approval dependent upon their categorization. For example, safety and efficacy testing of bandages and contact lenses will be different from what are needed for an artificial knee.

It is important to test medical devices, and the materials that they are constructed with, for potential risks when in contact with the body. Devices are evaluated for biocompatibility to determine that the following do not occur:

- **Direct injury to living tissue**
- **Inflammatory and adverse immunologic/allergic responses**
- **Adverse systemic or delayed effects**

Potential risks can be due to the material components of the device, any impurities present, the parts of the body that interact with the device (such as skin, eyes, or bone),

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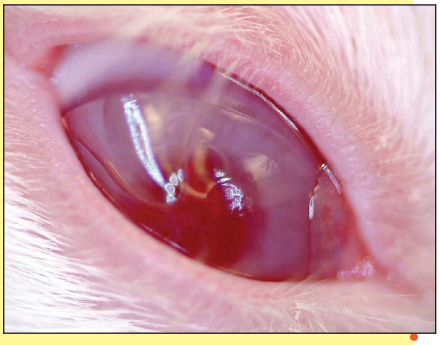

FIG. 1
Contact lens placed on the eye of a rabbit.

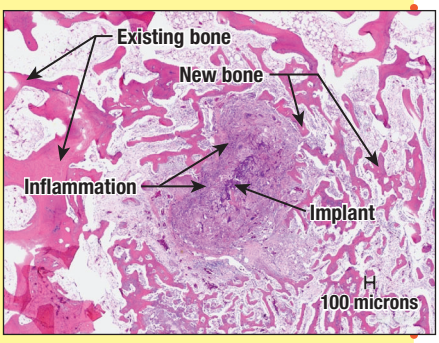

FIG. 2
This photomicrograph depicts a section of a rabbit's femur that was surgically implanted with a medical device. A section of the femur was fixed and stained with hematoxylin and eosin, and evaluated with a microscope by a pathologist to study the effects of the implant on local bone. The pathologist evaluated new bone formation, local inflammation, and changes in structure of the implanted device.

BioFocus

WE WANT TO HEAR FROM YOU!

We want to include your stories, comments or questions relating to animals in your classroom in upcoming editions of *BioFocus*. Please e-mail stories to: mismr@umich.edu

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Medical Devices... *Continued from page 1*

and the extent and duration of tissue contact. Although devices are typically comprised of inert, polymeric materials that do not act like drugs, adverse effects could occur due to impurities or breakdown products from the device.

Because of the very diverse nature of medical devices and their global use, international standards exist for testing. These standards help device manufacturers avoid redundant testing, especially with animals, and are based on current scientific knowledge. Safety or biocompatibility testing of medical devices is guided by the International Standard Organization (ISO) 10993: Biological Evaluation of Medical Devices documents. This group of 20 different documents provides guidance to manufacturers and regulatory agencies for classifying medical devices, the types of biological safety testing that should be conducted, and methods for conducting the tests.

First, medical devices are classified into one of 3 major categories, followed by a subcategory, which are the following:

1) **Surface contacting:** skin, mucosal membrane, and breached or compromised surfaces
2) **Externally communicating:** blood path indirect, tissue/bone/dentin, and circulating blood
3) **Implanted devices:** tissue/bone or blood

Next, the intended duration of contact between the device and the body is evaluated, which could be:

- **Less than 24 hours**
- **Prolonged** — 24 hours to 30 days
- **Permanent** — greater than 30 days

The required types of biocompatibility safety testing to be conducted are dependent upon the device classification and duration of tissue contact. Depending upon the study objectives, either a portion of the medical device or an extract of the device is tested in animal studies. Extraction is a process for producing a suitable liquid for testing, and evaluates whether potential leachable or extractable chemicals are present in the device which may be toxic.

Common biocompatibility studies in animals include tests in guinea pigs to determine whether a device or any extractable chemicals can provoke an allergic response in skin. Extracts prepared from devices are tested for potential systemic toxicity in mice, and for the potential to be irritating to rabbit skin. Additional irritation studies in animals (typically rabbits) may be conducted depending upon the site of tissue contact for the device in clinical use. For example, contact lenses can be placed on the rabbit eye for assessing potential irritation to the cornea, conjunctiva, and other ocular tissues *(See Fig. 1)*. Medical devices that have prolonged or permanent contact with human tissues are also evaluated in toxicology studies in rats. Portions of the medical device are surgically implanted under the skin of rats for 4, 13 or 26 weeks, followed by evaluation of potential systemic toxicity.

For devices that are surgically placed in tissues, implantation studies are commonly conducted in animals (typically rats or rabbits) to evaluate potential effects of the device on surrounding living tissue (muscle, bone or skin). Implantation studies in animals vary in length, depending upon the medical device, and how it will be used clinically. Some medical devices used in surgical procedures are designed to break down and be metabolized in a defined period of time. Animal studies can provide invaluable information regarding the length of time these materials may be present in the body. For example, sutures can be surgically placed in muscle of rats or rabbits for evaluating local tissue response and how long the sutures remain in the site. Materials used to make orthopedic implants, such as artificial joints, can be surgically implanted in the rabbit femur for evaluating the interaction between the device material and bone *(See Fig. 2)*.

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Fast Facts...

Definition of a Medical Device

The formal definition of a medical device is an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar article intended for use in the diagnosis of disease or other condition, or in the cure, mitigation, treatment or prevention of disease in man or other animals, or intended to affect the structure or function of the body of man or other animals, which does not achieve its primary intended purposes through chemical action within or on the body of man (or animal) and which is not dependent upon being metabolized for the achievement of its primary intended purpose.

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Animal studies are also important for assessing the efficacy of various medical devices, especially those intended for surgical procedures. Bone fractures are often treated with adhesives, surgical screws, and materials to stop bleeding. Surgical studies in animal models of bone fractures are important for assessing safety and efficacy of new devices prior to their use in human patients. These studies are often conducted in rabbits in which a defect in a long bone (tibia, femur, or fibula) is created by a veterinary surgeon, while the animal is under anesthesia, followed by implantation of a device designed to aid in the bone healing process. Following recovery from anesthesia, the animals are housed for various periods of time, after which healing of the bone fracture is assessed by radiography, micro-computed tomography, and/or microscopic evaluation of bone by a pathologist. These studies typically evaluate new bone formation, tissue healing, local inflammatory changes, and whether any adverse changes occur.

Orthopedic surgical screws.

In summary, medical devices comprise a diverse and important component of modern medicine, with benefits to nearly everyone. The ethical use of animals in research and testing of medical devices has played a major role in assuring their safety and efficacy.

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