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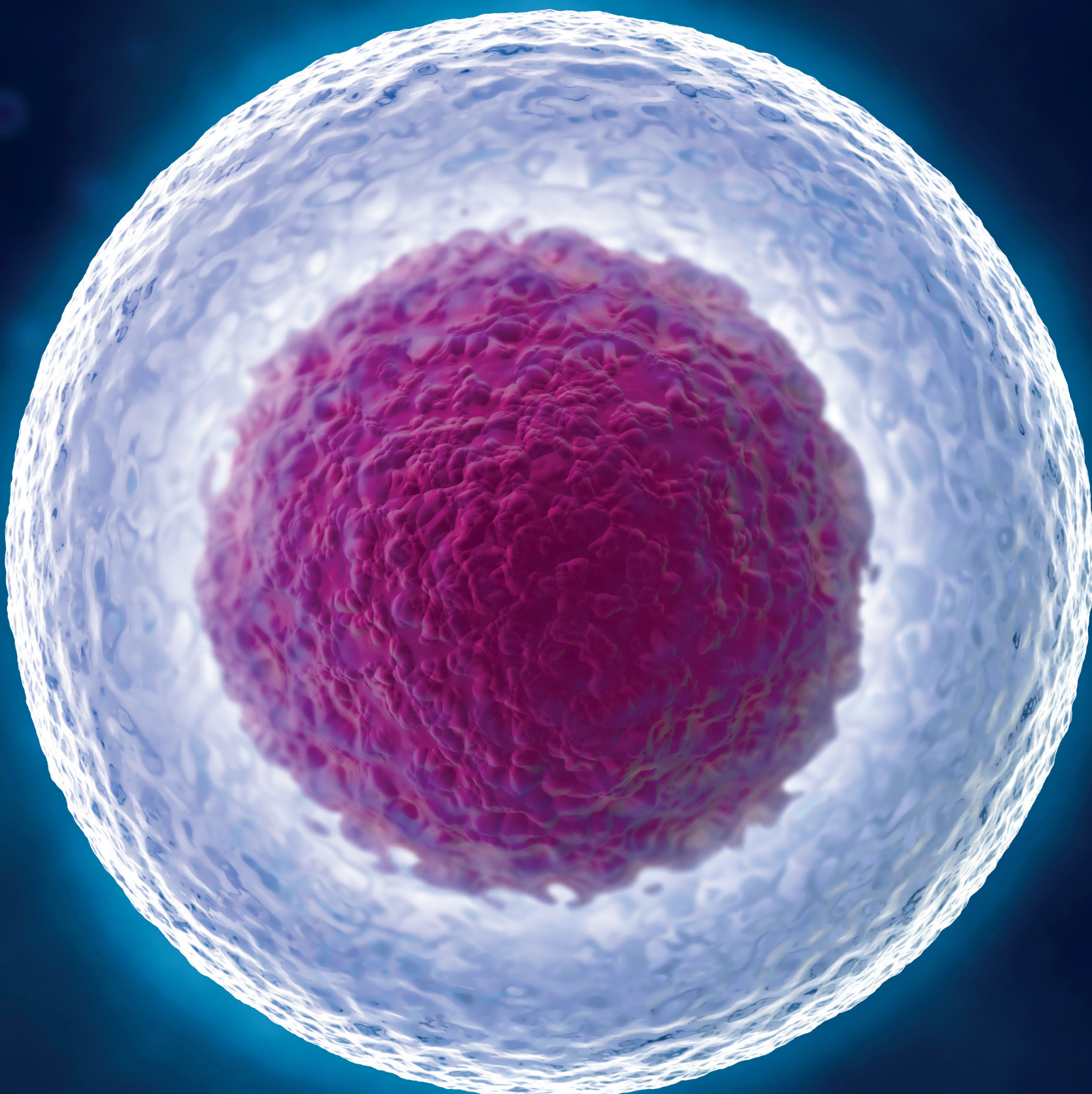

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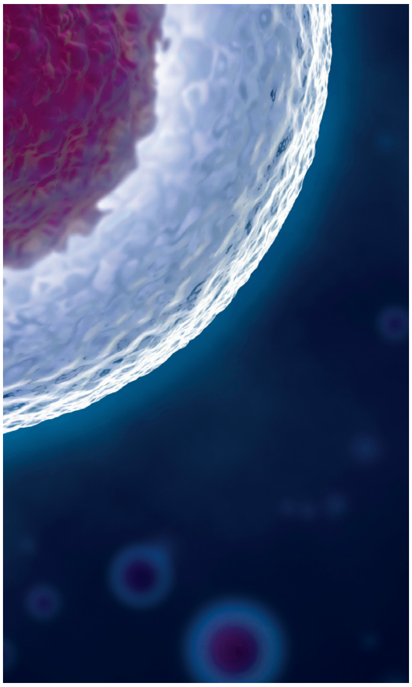

ON THE COVER: Individual cells may hold a key in finding a cure for cancer. See article on Page 5.

Contributors To This Issue

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By the Numbers

Beyond propaganda and rhetoric, numbers tell the real story

A 2009 COMPARISON of regular cigarettes and fire-safe cigarettes by the Harvard School of Public Health revealed that FSCs produced 13.9 percent more naphthalene and 11.4 percent more carbon monoxide than regular cigarettes. A key ingredient in moth balls, naphthalene may cause headaches, nausea, vomiting and diarrhea when exposures are high and concentrated enough. FSCs employ fire-safe paper, which is made with ethylene vinyl acetate copolymer emulsion adhesive — essentially carpet glue — linked to mouth and throat sores, asthma and bronchitis. Thirty states, including Michigan, have passed laws requiring that all cigarettes be fire-safe.

For more information go to www.firesafecigarettes.org/assets/files/HarvardStudy.pdf.

ACCORDING TO A U.S. Environmental Protection Agency report released in November 2009, new cars and light-duty trucks have increased fuel efficiency while decreasing carbon dioxide emissions for each of the past five years. In 2008, average fuel economy was 21 mpg, which rose to 21.1 mpg in 2009. Average CO2 emissions decreased 8 percent, or 39 grams per mile, and average fuel economy increased 9 percent, or 1.8 mpg, since 2004. The report asserts that the recent trend returns CO2 emissions and fuel economy to levels not seen since the early 1980s.

For more information go to www.epa.gov/otaq/fetrends.htm.

THE WORLD HEALTH Organization's 2009 AIDS Update reports that new HIV infections were reduced 17 percent over the past eight years. Sub-Saharan African infections decreased by 400,000, a 15 percent reduction; East Asia infections decreased 25 percent; and infections in South and South East Asia decreased 10 percent over the same time period. Report data reveals that more people infected with HIV are living longer due to antiretroviral therapy, and that AIDS-related deaths have declined by more than 10 percent over the past five years. The report's writers believe that the increased availability of treatment has saved approximately 2.9 million lives, and that more than 200,000 new infections have been prevented since 2001. Additionally, WHO reports that AIDS-related deaths in Botswana —where treatment coverage has risen to 80 percent —have declined 50 percent over the past five years.

For more information go to www.who.int/mediacentre/news/releases/2009/hiv_aids_20091124/en/index.html.

IN ITS ANNUAL "Toxics Release Inventory" report from December 2009, the U.S. Environmental Protection Agency revealed that environmental releases of toxic chemicals fell 6 percent in 2008, the last year for which a data set is available. The decrease lowers to 3.86 billion pounds the level of toxic chemicals released into the environment. The TRI monitors 650 chemicals from more than 21,000 sources, including manufacturing and metal mining facilities, electric utilities and commercial hazardous waste sites. Additional information from the report includes a total 14 percent decrease in air releases. Releases to surface water increased 3 percent, partially attributed by the EPA to a coal ash spill in Tennessee. Releases to land were up slightly, by 0.1 percent, between 2007 and 2008.

For more information go to http://www.epa.gov/tri.

Field Trips

Summer Camps for Children of All Ages!

THE DETROIT SCIENCE Center invites young people to “Get Geeked About Summer” through summer day camps. Programs are aimed at children from preschool through 12th grade, and include Science Splash!, Eekstein’s Great Comet Ride, Puzzles of Planet Earth, Crime Scene Science and more. Day camps feature all the amenities of the Detroit Science Center — theaters, planetarium, stage shows, hands-on exhibits and outdoor activities.

Detroit Science Center. Five-day camps are $150 for members, $165 for nonmembers; three-day camps are $90 for members, $100 for nonmembers; two-day camps are $60 for members, $65 for nonmembers; preschool/kindergarten camps are $75 for members, $85 for nonmembers. Camp hours are Monday through Friday from 9 a.m. to 4 p.m.; extended hours (with an additional fee for service) are 8 a.m. to 5:30 p.m.

For more information and a camp brochure, visit www.detroitsciencecenter.org or call 313-577-8400, option 5.

THE ALDEN B. Dow Museum of Science and Art in Midland presents I Spy Summer Fun day camps for children and youth. Science camps include Find Your Way: Orienteering and Geocaching, Don’t Be Under the Weather, Insane for Insects, The Science of Art and Cooking, and more. The museum also offers a wide variety of camps in art, history, music and theater, along with some courses for adults. Participants may choose full-day camps or mix and match half-day camps.

Alden B. Dow Museum of Science and Art. Prices vary, and scholarships are available; contact the museum for more information. Camps run Monday through Friday; full-day camps are from 9 a.m. to 4 p.m.; half-day camps are from 9 a.m. to noon and 1 p.m. to 4 p.m.

For more information and a camp brochure, visit www.mcfta.org or call 800-523-7649.

IMPRESSION 5 IN Lansing features hands-on Learn About Basic Science (LABS) camps for children and youth. Young children (ages 3 to 5) can participate in half-day camps such as Bugs! Bugs! Bugs!, Space Explorers, Recyclable Art and more. Older children (ages 5 to 15) can choose full-day camps such as Mummies and Mysteries, Survivor Science, Techno City, Jedi Academy and Gamestar Mechanic, among others. Weeklong camps run throughout the summer, and special one-day courses are offered from Aug. 30 to Sept. 3.

Impression 5 Science Center. Full-day camps are $180 for members, $220 for nonmembers; half-day camps (for ages 3 to 5) are $90 for members, $110 for nonmembers. Camp hours are Monday through Friday from 9 a.m. to 4 p.m. Call for information on half-day camps and extended hours.

For a listing of courses, visit www.impression5.org or call 517-485-8116, ext. 32.

CRANBROOK INSTITUTE OF Science invites children ages 4 to 14 to explore science and history through summer camps. Beginner Explorer Camps introduce young children (ages 4 to 5) to basic science topics through nature hikes, experiments and use of simple machines. Science Explorer Camps engage elementary students (grades 1 to 5) in learning about science through planetarium shows, experiments with electricity and ecosystem exploration. Students in grades 5 to 8 can choose from a variety of specialized camps, including Crime Scene Explorer, Physics Explorer, Outdoor Explorer and Ecology Explorer.

Cranbrook Institute of Science. Half-day camps (ages 4 to 5) are $215 for members, $240 for nonmembers; full-day camps (grades 1 to 8) are $315 for members, $350 for nonmembers. Camp hours are Monday through Friday from 9:30 a.m. to 4 p.m.; half-day camps run from 9:30 a.m. to 1 p.m.; extended hours (with an additional fee for service) are 7:30 a.m. to 6 p.m.

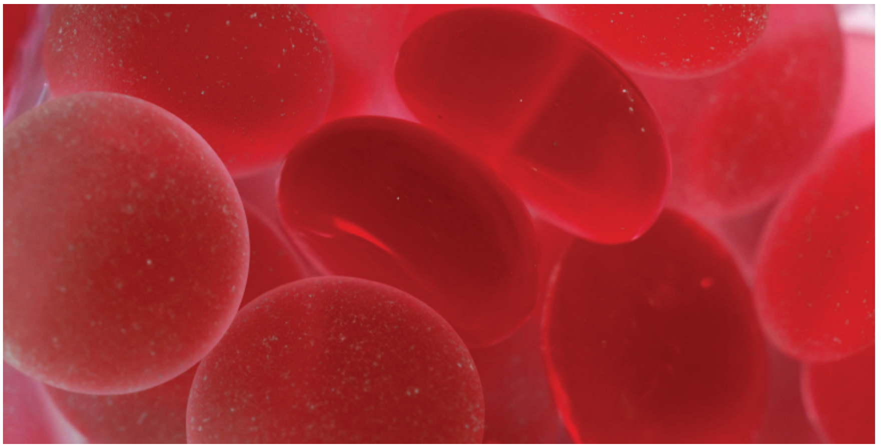
For more information and a camp brochure, visit www.science.cranbrook.edu or call 248-645-3210.

ANN ARBOR HANDS-ON Museum features Summer ScienceWorks Labs designed specifically for field trip groups. Groups gain admission to the museum as well as participation in a ScienceWorks Lab. Preschool labs include Music and Movement and All About Our Senses. Elementary (K through 5) labs include Slime Time, Bubbles, Circuit Masters and more. All labs reinforce science concepts learned in school.

Ann Arbor Hands-On Museum. ScienceWorks Labs are offered June 21 to Aug. 20. Labs can accommodate 15 to 30 students, or up to 60 participants when two labs are held concurrently. Groups of 20 or more: $8 per child (includes lab and museum admission) and special discounts for adults and teachers.

For more information, call 734-995-5439.

By John Fitzgerald Szczubelek



DATA FROM THE National Cancer Institute shows that death rates from cancer in Michigan, like those of the United States, are trending slightly downward.[1] Yet, only two Michigan counties are reported to have met objectives set by the Centers for Disease Control for reducing cancer mortality.[2] Diet, exercise, heredity and exposure to pathogens continue to be identified as major causes.[3] While efforts to address such risk factors are of great importance, new research from the University of Michigan is seeking a potential cure for cancer that focuses on the life and death of individual cancer cells.

Yvonne L. Kapila, an associate professor at the University of Michigan Department of Periodontics and Oral Medicine, is the senior and corresponding co-author of "Receptor-Interacting Protein Shuttles Between Cell Death and Survival Signaling Pathways."[4] Her work at U of M includes her present research as well as teaching in the University's dental school and treating patients at a community dental clinic. Her husband, Dr. Sunil Kapila, is chairman of the Department of Orthodontics and Pediatric Dentistry at U of M.

The object of Yvonne Kapila's research is to find a finely targeted treatment for cancer that harnesses an understanding of how the receptor-interacting protein (RIP) works at the cellular level to kill cancer cells. The present study of RIP is an outgrowth of her doctoral and postdoctoral work at the University of California-San Francisco.

While exploring the effects of periodontal disease on gum and bone tissues, Kapila studied the extracellular matrix (ECM) of which these tissues are partly comprised. She describes the ECM as "the stuff cells live in."

ECM serves many functions, including providing support and anchorage for cells, separating tissues from one another, and regulating communication between cells. Kapila cites collagen as a relatively well-known protein in the ECM, due to its prevalence in the human body and use in cosmetic surgery.

According to Kapila, collagen and other "ubiquitous proteins" formerly were regarded as the "amorphous ground substance" surrounding cells, but now, "the relationship between ECM and cells has taken on greater significance. This reflects a more modern and holistic view of how the body works."

Kapila's present research at the University of Michigan further explores the interplay between cells and the ECM, particularly with respect to the natural life and death cycles of cells. The hope is that by mapping out these processes, treatments can be developed to kill undesirable cancer cells without harming healthy cells.

Necrosis is cell death caused by trauma or injury. When a cell dies as part of a natural regenerative process, it is called programmed cell death or apoptosis. As Kapila explained, apoptosis results in the elimination of cells, but serves constructive purposes as well: "The interproximal spaces between the digits in a human hand are a product of apoptosis. Without apoptosis, the formation of the digits and other portions of the limbs would be incomplete. In fact, disruptions of apoptosis probably account for conditions in which there is webbing of the hands and feet."

In an average adult, billions of cells die each day through apoptosis. Since the 1990s, research concerning apoptosis has increased markedly and is revealing implications for an extensive variety of diseases, with cancer at the top of the list.

Kapila's latest research seeks a way to induce apoptosis in cancer cells through the introduction of a receptor-interacting protein. The key to making this happen lies in the process by which cells adhere to and separate from the ECM. Generally, cells must adhere to the ECM to survive. When a cell separates from the ECM and dies, this is called anoikis.

As Kapila explained, some cells are not susceptible to anoikis: "Blood cells that fight infection move freely as part of the body's immune system. Likewise, cancer cells are able to attach and disconnect from the ECM. This attribute is part of what allows cancer cells to spread and metastasize so easily. This gives them quite an advantage over other cells

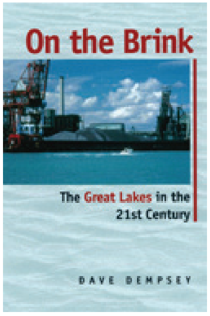
continued on page 11

1 "State Cancer Profiles," National Cancer Institute, www.statecancerprofiles.cancer.gov/cgi-bin/quickprofiles/profile.pl?26&001 (accessed April 21, 2010).

2 Id.

3 "Risk Factors," National Cancer Institute, Oct. 4, 2006, http://www.cancer.gov/cancertopics/wyntk/cancer/page4 (accessed April 21, 2010).

4 Pachiyappan Kamarajan, Julius Bunek, Yong Lin, Gabriel Nunez, and Yvonne L. Kapila, Molecular Biology of the Cell, Vol. 21, Issue 3, 481-488, February 1, 2010.



On the Brink (2004)
by Dave Dempsey
Reviewed by Claire Forman

NO SINGLE LOCATION in the state of Michigan is more than 85 miles from the shores of one of the Great Lakes. One of Earth's most valuable natural resources, the Great Lakes are not only habitats for abundant wildlife and foliage, but have provided humanity with food, drinking water, transportation and recreation for centuries. In fact, humanity's survival is as much a part of Great Lakes history as that of the salmon and the trout.

It is with this perspective in mind that we must consider the work of Dave Dempsey, recent recipient of the 2009 Michigan Author Award, presented by the Michigan Library Association for "his outstanding contributions to literature." While not his most recent work, "On the Brink" (2004) is perhaps the best representation of his worldview. A historical account of the Great Lakes region and those impacted by the glory of the inland seas, "On the Brink" presents insights into the development of environmental policy in the United States and Canada. For nearly two centuries, the two nations have tackled environmental issues that threatened the viability of these precious waterways. This book claims there will be an impending environmental disaster if Great Lakes region inhabitants do not change their behaviors.

Following George Santayana's adage "Those who do not understand history are doomed to repeat it," Dempsey asks readers to recognize the natural beauty that surrounds us and urges for proscribed steps toward preserving it. Dempsey's analyses, however, fail to provide readers with a better understanding of what must truly change if the Great Lakes are to be saved. Bad environmental policy is the true culprit in the Great Lakes story, and Dempsey was part of this tale for nearly three decades.

Dempsey served as an environmental regulator and adviser to Gov. James Blanchard for six years (1983 to 1989), and as program director at the nonprofit Clean Water Action. In 1994, Dempsey was named policy director for the Michigan Environmental Council, where he worked until 1999. Dempsey was also appointed a member of the Great Lakes Fishery Commission by President Bill Clinton and served from 1994 to 2001. Dempsey is currently on the board of directors for the Alliance for the Great Lakes and works as communications director for Conservation Minnesota in Minneapolis, Minn.

The prologue of "On the Brink" outlines a fictional story of a family 50 years in the future. On a vacation in the Port Huron region, the family takes advantage of all the modern technology available to them, reading about the history of the Great Lakes on monitors while staring at empty lakebeds. The fictional short story closes with a sensationalized and somewhat misguided message that leads us to believe the Great Lakes ecosystem is disappearing before our very eyes.

Dempsey's recommendation for curbing environmental threats to the Great Lakes presents a contradiction. He concludes that having "independent fact-finding commissioners with the ability to assess the effectiveness of existing programs, anticipate future problems, and sound the call for important changes" is the ideal solution for addressing environmental problems in the Great Lakes states, pointing to Canada as a model worthy of replication.

Such commissioners or boards, however, would only create additional layers of government bureaucracy and not be accountable to voters.

Dempsey further notes that the history of the Great Lakes has proven that "government can misspend as well as spend wisely" and that "it is not government but the people who elect and support government who will decide the fate of the Great Lakes." How will the people be able to "decide the fate of the Great Lakes" if they are not in fact electing the individuals charged with overseeing the future of the lakes?

Furthermore, Dempsey cites instances where existing boards and commissions ignored the public interest to maintain the favor of those who appointed them to office — the state and federal legislatures. Therefore, it cannot be reasonably expected that new commissions and boards would in fact support the public interest.

To determine future conservation steps, one must answer an age-old question as it pertains to environmental policy: What is the role of government? Dempsey, however, does not directly address this question. His conclusions only leave the reader more confused about what he believes to be the proper course of action.

For example, in the case of fish population decline, it seems Dempsey would advocate greater degrees of regulation to mitigate overfishing. Yet, in the same instance he calls the government "incompetent" and therefore incapable of properly addressing environmental issues.

In Chapter 3, Dempsey applauds the efforts of the Canadian government to protect portions of the Niagara landscape and southern Ontario timberlands in the late 19th century by establishing a series of public parks. However, in Chapter 10 he expresses little faith in government's ability to spend wisely to protect lake resources. It would seem that the success of government-based environmental protection is as consistent as Dempsey's analyses. ■

ON THE BRINK: A CHAPTER BLOW-BY-BLOW

Chapter 1, "Dreams of Wealth and Glory," recounts the discovery of the Great Lakes region by French and English settlers. Dempsey acknowledges that the local fur trade only flourished because the luxurious indulgences of the royal European classes created a high demand for the furs. According to Dempsey, this use of natural resources led to the utilization of the Great Lakes as a "tool rather than a home."

In Chapter 2, "Failing the Fish," Dempsey explains how poor government oversight and special interest groups led to a steep decline of the fish population in the first half of the 20th century due to overfishing and parasitic wildlife. Nearly 50 years passed while federal and local governments in the United States and Canada deliberated about the most effective method of regulating commercial fishing. Meanwhile, invasive species like the lamprey virtually destroyed the fishing industry by feeding on native fish species. Dempsey highlights "government incompetency," but fails to explore the possibility that private ownership of fishing waters could give anglers an incentive to explore environmentally friendly ways of eliminating the invasive species and maintaining their revenue source: the native fish. This method has been used successfully along the Yellowstone River Valley near Livingston, Mont., where spring creeks begin and end on private property. Owners charge fees for fly-fishermen who come from around the world in search of trout, and have taken steps to protect these assets, such as limiting livestock grazing along the banks and protecting other wildlife in the area. The state-owned Spring Creek in Lewiston, Mont., on the other hand, has free access but is crowded and offers a reduced fish population.

Chapter 3, "Protecting a New Home," recounts the region's settlement. However, Dempsey laments the fact that technological progress after the Civil War enabled settlers to grow more crops in the previously uninhabitable swampland of southern Michigan. Dempsey also explains in stunning detail the decades-long advocacy projects sponsored by local residents in the Lake Michigan dunes regions of Illinois and Indiana. Unfortunately, this portion of Great Lakes history provides a warning to us all about how special interest groups can manipulate government action to serve the privileged few.

Chapters 4 and 5, "Degradation" and "Indignation," respectively, expose the problem of pollution. Undoubtedly, decades of dumping sewage and industrial waste into the lakes and rivers of the Great Lakes region caused countless outbreaks of disease among humans and wildlife. This problem, however, is a result of a tragedy of the commons. This term describes the overuse and abuse that result from a lack of private ownership. In the most basic sense, if no one owns it, then no one will take responsibility for it.

The waters of the Great Lakes are no exception. As Dempsey points out in these chapters, government solutions to the contamination of public waterways only provided short-term fixes to long-term problems that still plague the region. While pollution significantly decreased after grassroots activists petitioned for government intervention in the early to mid-20th century, millions of taxpayer dollars are spent each year maintaining the waterways and public lands along the shoreline when many of the taxpayers do not in fact live along the water's edge.

Chapter 6, "Manipulating the Lakes," maps man's efforts to "improve" the appearance of the lakes. Highly critical of these initiatives, Dempsey explains that while many canal and dam projects were either explored or even begun, few actually materialized. The Erie and Welland canals, as well as the St. Lawrence Seaway, however, have become hallmarks of navigable ingenuity and industrial design. These manmade wonders unfortunately gave way to the unforeseen introduction of non-native predatory wildlife. Private efforts to restore fish populations to their original state often remedied the problem in the interests of maintaining the commercial fishing industry.

In Chapter 7, "The Comeback," Dempsey gives a very thorough examination of the conservation movement in the mid-20th century and its impact on the Great Lakes, paying particular attention to the region's DDT and pesticide contamination. With ecosystem recovery, however, came an onslaught of increased government regulation that has severely damaged human prosperity in recent decades.

In Chapter 8, "Losing the Lakes," Dempsey criticizes a plethora of government inaction. He gives case evidence for scenarios in which the federal, state or Great Lakes board authorities were aware of potential threats to the Great Lakes ecosystem but did nothing to mitigate risk and curb environmental destruction. In some instances, government acted, but was ineffective.

Chapter 9, "A Future in Peril," discusses the future risks facing the Great Lakes. Dempsey cites population growth, global warming leading to dropping water levels, increased pesticide use, exporting the water to drought-ridden areas in the western United States, increased commercial shipping and invasive species as prime examples of looming threats. ■

RISK ASSESSMENT: PART IV

This is the fourth and final MichiganScience article on risk assessment. These articles have been designed to acquaint and provide the reader with information that will allow him or her to understand and evaluate potential risks to human health resulting from exposure to chemicals, including drugs. In other words, this series on risk assessment was not designed to present the reader with an in-depth treatise on the complexities of risk assessment, but rather to provide a high level overview of the process. The hope was that enough information would be presented so that the reader, when faced with having to understand and make decisions relative to risk, would have the basic tools necessary to make an informed decision.

BY DR. ROBERT MEEKS

In the first three articles, we discussed the four basic steps in a risk assessment:

- Hazard Identification
- Dose-Response Relationships
- Exposure Assessment
- Risk Characterization

In the last article, we provided examples of a risk characterization for both a threshold chemical and a non-threshold chemical (i.e. carcinogen) and discussed the uncertainties in the whole process. An expanded view of the risk assessment process would include a provision for additional data to enhance the overall process or to reduce the uncertainties in the final risk assessment number (see Figure 1). Also shown in Figure 1 is risk management, which is the focus of this article. The entirety of the process outlined in Figure 1 is in essence the process of risk analysis.

A risk assessment simply cannot draw a distinct line between safe and unsafe. Safety is by its nature an inverse relationship of hazard. If the concept of safety is meant to simply mean the absence of risk resulting from exposure to chemicals, then this is nearly impossible to prove, because to do so requires proof that risk does not exist. Please recall from the earlier articles that it was pointed out that everything has a hazard or is toxic. It is best summed up, to paraphrase Paracelsus, as, "The dose makes the poison."

We can divide chemicals into three broad categories:

- The enormous number of naturally occurring chemicals that reach us primarily through food.
- Industrial chemical products that are produced for specific purposes.
- Industrial pollutants — chemical byproducts of fuel use, of the chemical industry and of most other types of manufacturing (Rodericks).

If the goal is to be absolutely safe, or without risk, from these products, especially industrial chemicals or the polluting byproducts, then a wholesale banning would be necessary. This would require turning the calendar back 200 years or more (Rodericks).[1] Therefore, the process of risk assessment is necessary to understand scientifically what the risk is from exposure from these sources and what is an acceptable level of exposure that would be without appreciable risk.

Once the scientific process is complete and the risks and uncertainties identified, decisions need to be made on how to manage the risk. This is perhaps the thorniest step in the overall process in the risk assessment paradigm. The risk assessor or those charged with protecting public health must make management decisions based on an evaluation of public health, economic, social and political consequences of a regulatory action. They must weigh competing priorities of individual freedoms, groups of individuals (i.e. the population as a whole), environmental groups, industry, etc. That is to say, judgments of acceptability of risky activities are not just a matter of numbers but draw on judicial, regulatory and political mechanisms through which societal choices are made and enforced. Some fundamental factors that must be considered in the management process are voluntariness, equity, procedural legitimacy, treatment of uncertainty and perceptions.

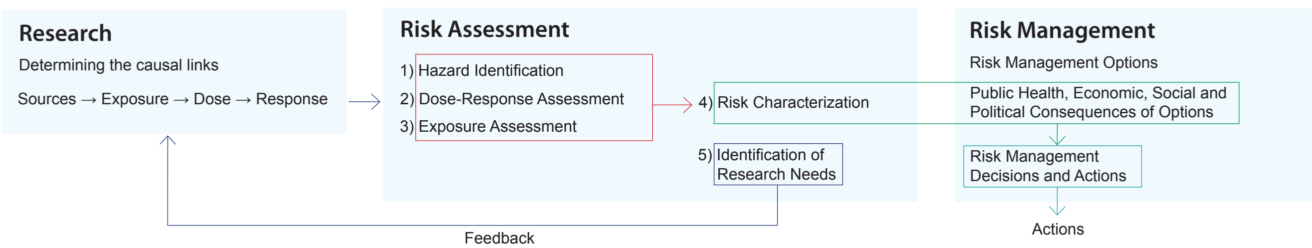
Voluntary vs. involuntary exposure is one key determinant is assessing risk acceptability. In a society that values individual liberties, the risk an individual is willing to take may be higher than a quantitatively similar risk that is imposed on an individual by another party. As a classic example, an individual can smoke cigarettes in the privacy of his or her home, creating a health risk for him or herself, and yet be forbidden to smoke in public, where this individual would impose a much smaller risk (via secondhand smoke inhalation) on others.

A second consideration in the management of risk concerns the fairness and equity of the distribution of risks and benefits. The concept of equity of risk is complicated by the fact that a risk management analysis that appears to be fair and equitable may turn out to be inequitable (though not perhaps unfair). This is very akin to the famous utilitarian dictum: "The needs of the many outweigh the needs of one."

Legal acceptability of risk is based on the answer to a fundamental question posed by society, regulators and industry, which is: How can disputes over risk be adjudicated and policy decisions made in the absence of adequate scientific information and knowledge about causal mechanisms? A critical issue, therefore, is "proof" in cases where it is not clear whether a risk is being imposed or where the magnitude of the suspected risk created by an exposure is highly uncertain. This will be discussed further below.

Uncertainties in the risk assessment process have been discussed in previous articles in this series. Uncertainty in the risk assessment process simply cannot be eliminated, and risk assessment and risk management cannot be clearly separated for uncertain risks. The decision of when to stop collecting data and to act is a risk management problem (Figure 1), while

Figure 1: Risk Analysis



expressing the uncertainty at the time of transition from research to management is part of the risk assessment process.

Individual perception of risk cannot be ignored, but often these perceptions regarding risk are changeable, unreliable and overly sensitive to impressions. Many times, an individual's perception of risk is influenced by special interest groups that have an agenda and can make broad statements that may be true on the surface but are devoid of the fundamental concepts of dose and response. In other words, they may neglect to state that while a material is hazardous, the level at which exposure takes place may be in the range at which no appreciable risk occurs (i.e., exposure is devoid of risk or is at a level to which an individual may be exposed for some duration of time without an impact on health). Therefore, a risk may be perceived as large when in reality the risk to human health is negligible.

So how does one approach the task of risk management? There is great propensity on the part of regulatory agencies and those who practice public policy to require numerical standards for judging what risks are acceptable. For non-cancer-causing chemicals, numerical thresholds are of great value. They reduce ambiguity and debate for the most part. The reason for this is that it is far easier to compare numbers than to evaluate the complexity of social decision processes.

One common approach to the risk management decision process is to conduct a cost-risk-benefit analysis when chronic health risks of an activity are known (Rodericks). The common practice in this approach is to evaluate risk control measures in the terms of dollars spent per statistical life saved. Balancing the costs against the benefits of risk control measures is clearly necessary for an efficient allocation of resources. To implement fully the cost-risk-benefit analysis approach, it is essential to develop more realistic measurements of the benefits from risk reduction than the conventional one of expected number of statistical lives saved. When risks are uncertain, a different set of issues must be confronted that essentially centers on the high costs of risk research, costs of risk control and uncertain benefits of possible risk reductions resulting from control measures.

It should be clear from the above discussion that one of the most challenging areas in statutory interpretation of risk assessment and risk management is the problem of setting cutoff levels or acceptable levels of exposure for risk regulators. The consistency and effectiveness of risk management decision-making might be enhanced if agencies had a systematic approach for determining whether specific risks are "de minimis" — that is, too trivial to warrant an expenditure of resources to assess or control them.[1]

Determining a de minimis risk level is essentially a pragmatic decision tool for distinguishing between trivial and nontrivial risks. In general, the de minimis approach is accomplished by establishing a risk cutoff level greater than zero. If a hazard is greater than the de minimis level, it becomes the object of possible regulation, up to and including a ban on the use of the chemical. If, however, the level falls below the de minimis level, it is excluded from further consideration. Ideally, a de minimis risk level would distinguish between small risks that are more costly to regulate than to tolerate and large risks that are more costly to tolerate than to regulate.

The de minimis approach is certainly consistent with current health and safety statutes and with regulatory agency efforts to establish insignificant risk levels in the evaluation of suspected hazardous chemicals. The fact that they are labeled insignificant risk levels rather than de minimis levels is not important. The logic underlying both is the same. For an example of this approach, let's refer back to the third article in this series, in which we evaluated chemical X and discovered that it had a reproductive effect with a NOEL or BMDL of 100 mg/kg/day. We applied a 100-fold uncertainty factor to the NOEL or BMDL and established an RfD of 1 mg/kg/day. The RfD established for this reproductive effect could, in essence, be considered the de minimis level below which there is an insignificant risk of a reproductive effect in women if exposed below this level for a lifetime.

On the other hand, how would we handle a non-threshold chemical (i.e., a carcinogen)? Some argue, as stated in previous articles in this series, that there is no safe level of exposure to a carcinogen (i.e., the no-threshold hypothesis). What is true is that under the no-threshold hypothesis any exposure to a carcinogen increases the probability of cancer occurring, but it does not mean that any exposure to a carcinogen will cause cancer. Short of banning all carcinogens, if the above were true, regulators take the position that the "safe level" for exposure to a carcinogen is defined as the dose or exposure that produces no more than a specified and very low level of excess lifetime risk (generally 1/1 million or one excess cancer in 1 million people exposed, which is sometimes expressed as 10-6). What does this mean? If we assume there are 300 million people in the United States, for example, exposed daily for their full lifetime to a concentration of a carcinogen that caused risk, then the number of extra cancer cases created over a 70-year lifespan would be:

(300 million people) x (1/1 million extra lifetime risk per person) = 300 extra cancer cases during a lifetime or an average of 300 ÷ 70 = four to five extra cases per year for an average lifespan of 70 years. Since the actual number of cases associated with 10-6 risk is probably lower than but certainly not more than the four to give extra cases per year, it would appear that a 10-6 risk level is an appropriate definition of protective of human health and that exposure below a level of one in a 1 million extra lifetime risk could be the de minimis level.

THE PRECAUTIONARY PRINCIPLE

While the above approach seems reasonable to manage risk even with

1 The term "de minimis" is derived from the Latin maxim "De minimis non curat lex," which means, "The law does not concern itself with trifles."

the uncertainties that are ever-present in the risk assessment process, there is a significant movement to manage risks in a much different approach, which is the use of the precautionary principle. The precautionary principle, as it relates to environmental hazards, was proposed in January of 1998 at the Wingspread Conference held at the headquarters of the Johnson Foundation in Racine, Wis. At the conclusion of the three-day conference, a diverse group of scientists, philosophers, lawyers and environmental activists issued a statement calling for governments, corporations and scientists to adopt the "precautionary principle":

> "When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent [e.g. chemical manufacturer] of an activity, rather than the public, should bear the burden of proof [of a lack of harm]."

The precautionary principle is an extrapolation of the motto "better safe than sorry." While there is precaution involved in traditional risk assessment (note the 100-fold uncertainty factor used in the first de minimis risk calculation above), the precautionary principle is meant to address situations with higher degrees of scientific uncertainty about how and whether particular harms might be caused. The principle is intended for cases concerning potentially irreparable harm, such as birth defects or species loss.

Because the precautionary principle is applied in instances where scientific evidence and causality are not "fully established," critics observe that the principle may be invoked based on less-than-plausible risks and used to ban, rather than reduce exposure to, a process or product. The European Commission, which implements legislation passed by the European Union, "stresses that the precautionary principle may only be invoked in the event of a potential risk and that it can never justify arbitrary decisions. Hence, the precautionary principle may only be invoked when the three preliminary conditions are met — identification of potentially adverse effects, evaluation of the scientific data available and the extent of scientific uncertainty" (European Commission Communication).

In summary, this four-part MichiganScience series on risk assessment has attempted to provide the reader with a high level overview of the process of assessing risk to human health and the environment resulting from chemical exposures. It has tried to convey the complexities of the process and the uncertainties associated with this process, as well as to provide some insights into the most complex part of the process: risk management. This is by no means the complete picture. After these processes are complete comes the task of trying to communicate the risk to the general public, so they can understand and accept the safe exposure levels that are set. ■

The four articles of Dr. Meeks' risk assessment series for MichiganScience are published together at www.MichiganScience.org/12811.

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Just the Facts

continued from page 5

and complicates prospects for treatment."

Kapila said that current knowledge does not provide a full explanation as to why cancer cells are different, but one theory is that they have "mutated due to exposure to toxins or other causes."

When cells adhere to the ECM, more is occurring than a mere structural connection. The attachment initiates "intracellular signaling pathways" that Kapila said allow the communication of instructions to the cell.

"The cell receives multiple signals, some of which tell it to live, and others which tell it to die," she said. "The RIP is involved in both cases. When it interacts with a cell death protein called FAS, the cell dies, and when it binds with a protein called FAK, the cell is told to survive and eventually duplicate a copy of itself. When we understand the particulars of this process, we will be that much closer."

To date, Kapila's team has modified RIP mechanisms experimentally in animal studies to attack squamous cancer cells. Squamous cell carcinoma may occur in many body parts including the skin, lips, mouth, esophagus, bladder, prostate, lung and cervix. It is the second most common form of skin cancer, and is caused by sun exposure.

This makes the present research both relevant and potentially useful. Early indications are that RIP mechanisms can trigger apoptosis in squamous cancer cells without harming normal cells. Kapila is pleased by the results, but cautions that the research is far from complete.

"We are a long way from saying that RIP can be used safely in humans," she said. "Ideally, one would hope to inject RIP in a carrier material and achieve the desired outcome. But on its own, RIP would not be able to distinguish a cancer cell from a good cell. More research has to be done to see which portions of RIP are suited for each cell function." ■

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