ENVIRONMENTAL CHEMISTRY

LECTURE 4

Introduction to environmental health risk assessment

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Lecture outline

- Introduction, definitions
- Risk assessment methodology
- Assessing risk for carcinogens
- Assessing risk for non-carcinogens
- Limitations of risk assessments

Introduction

- Do you think this small stream dangerous?

Introduction

- What type of risk illustrated in this cartoon?

Malaysia

Why high cancer rates?

"Almost 20% of the population would suffer from at least one form of cancer, the first National Cancer Registry report revealed today."
Due to:

- Contaminated food & water
- Polluted environment
- Lifestyle

Malaysia's cancer rates alarming

July 5, 2003 NST

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By Annie Freeda Cruez
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KUALA LUMPUR, Fri. — Almost 20 per cent of the population would suffer from at least one form of cancer, the first National Cancer Registry report revealed today.

It also said one in 5.5 Malaysians risked getting cancer during their lifetime.

Food, the environment or lifestyle could be the cause.

According to the report, the most frequent cancers in men were leukaemia as well as cancers of the lung, nasopharynx, colon, rectum and prostate.

In women the most frequent occurring cancers were leukaemia as well as cancers of the breast, cervix, colon, ovary and lung.

The risk of cervical cancer in Malaysians was higher compared to Western nations and other parts of Asia, the report added.

Health Minister Datuk Chua Jui Meng, who said he was shocked by the findings, added that Malaysia had the world's highest rate of nasopharyngeal (nose) cancer for females and second highest rate for males.

The second highest country for nasopharyngeal cancer among both sexes is Hong Kong.

"Malaysian Indian men had the highest rate of laryngeal cancer in Asia," he told reporters after launching the report and first NCR scientific meeting at Grand Seasons Hotel here.

He said one of four Malaysian Chinese risked getting cancer, followed by Malaysian Indians (one in five) and Malays (one in seven).

Cancers in which the Chinese had the highest incidences included breast cancer, lung cancer and nasopharyngeal cancer.

Indians were at high risk of mouth, larynx, oesophagus and tongue cancer.

Malays were at risk for thyroid cancer, lymphatic leukaemia and lymphoma.

In Peninsula Malaysia last year, a total of 26,089 cancers were diagnosed in 11,815 males and 14,274 females.

"However, an estimated 10,656 cases were not registered," Chua added. Based on these figures, the annual incidence of cancer in Malaysia was expected to be some 40,000.

Those aged 40-64 comprised the largest group of registered cancer cases (52.5 per cent). Those aged 65 and above comprised 21[illegible] per cent of registered cancer cases.

"We are trying to ascertain whether the alarming finding of cancer among Malaysians is due to food, environment, lifestyle in workplace and at home or some other reasons," he added.

The clinical cancer research unit had been directed to prepare a Cabinet paper on the findings and to formulate strategies to prevent the disease.

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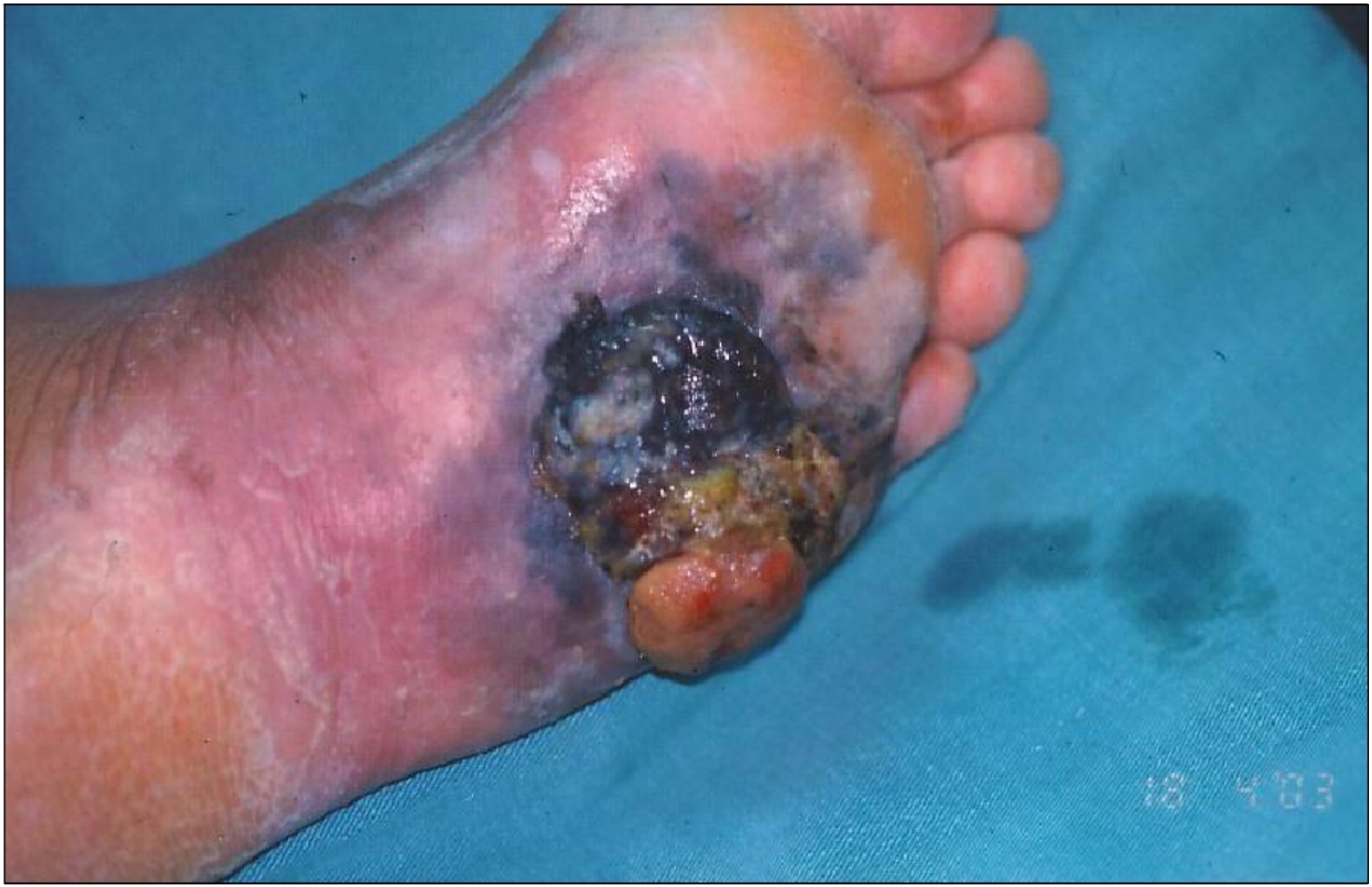


The greatest risk?

Ramai lelaki mandul

Pencemaran alam sekitar dan pemakanan jejas kesuburan

LONDON: Satu penyelidikan terbaru mendakwa masalah kemandulan yang lebih dikaitkan dengan wanita kini sebaliknya terbukti lebih ketara di kalangan lelaki.

Malah, kajian Persatuan Reproduksi dan Embriologi Eropah (ESHRE) membabitkan data daripada 24 negara Eropah menyatakan masalah tidak subur itu akan menjadi satu masalah utama di kalangan lelaki berbanding wanita, lapor Perbadanan Penyiaran Britain (BBC).

Pada masa ini, tahap tidak subur atau kemandulan lelaki dan wanita adalah sama - masing-masing 40 peratus kes kemandulan dikaitkan dengan lelaki dan wanita dan 20 peratus lain datangnya dari kedua-dua ibu dan bapa terbabit.

Namun, kajian terbaru Eropah itu sebaliknya mendapati untuk keperluan rawatan kesuburan seperti kaedah persenyawaan benih luar rahim (IVF) bagi tujuan membantu masalah ketidaksuburan di kalangan lelaki terus meningkat secara mendadak.

Antara faktor utama kekurangan sperma itu dikaitkan dengan pencemaran kepada bahan toksin.

Kajian itu menunjukkan penggunaan suntikan sperma intra-cytoplasmic (ICSI) yang mana satu sel sperma disuntik ke dalam telur menerusi proses IVF meningkat kepada 52 peratus pada 2002 berbanding 43 peratus pada 1997.

Malah, ada sejumlah lebih 122,000 kitaran ICSI dan hampir 113,000 IVF pada 2002, kata penyelidik Eropah itu dalam mesyuarat tahunan mereka di Copenhagen, semalam.

"Ketika ini, kita sendiri tidak tahu mengapa penggunaan kaedah ICSI itu sebegitu ketara. Mungkin banyak faktor yang terbabit," kata penyelia jawatankuasa kajian itu, Dr Anders Nyboe Anderson.

"Kita menyaksikan semakin kurangnya kes kemandulan disebabkan masalah saluran tiub kesuburan wanita yang tersumbat, mungkin disebabkan amalan seks selamat berikutan risiko Sindrom Kurang Daya Tahan Melawan penyakit (Aids) sejak 15 tahun lalu.

"Sebaliknya apa yang ketara adalah masalah kemandulan di kalangan lelaki. Ini mungkin disebabkan faktor alam sekitar seperti keadaan bumi yang semakin tercemar dan menjejaskan aspek kitaran makanan yang memberi kesan kepada tahap kesuburan seorang lelaki itu," katanya.

Katanya, klinik kesuburan swasta lebih gemar menggunakan teknik ICSI berbanding IVF bagi meningkatkan kejayaan bagi rawatan kali pertama biarpun dua sekalk itu berpeluang menghasilkan bayi.

Dr Anderson berkata, teori lain adalah lelaki, seperti juga wanita semakin berminat memulakan kehidupan berkeluarga pada usia lanjut ketika tahap kesuburannya pula menurun.

Katanya, semakin ramai lelaki berusia 50-65 tahun mendapatkan rawatan di klinik kesuburan dengan mereka berusia lebih 40 tahun mewakili satu perempat daripada kumpulan yang mendapat rujukan.

Dalam penyelidikan lain, sekumpulan saintis Kanada pula mendapati kerosakan DNA di dalam sperma lelaki itu meningkat mengikut umur seseorang itu.

Tahap kerosakan itu lebih ketara di kalangan lelaki lebih 40 tahun berbanding usia muda dan lelaki 45 tahun mempunyai kerosakan dua kali ganda berbanding mereka di bawah 30 tahun. – Agensi

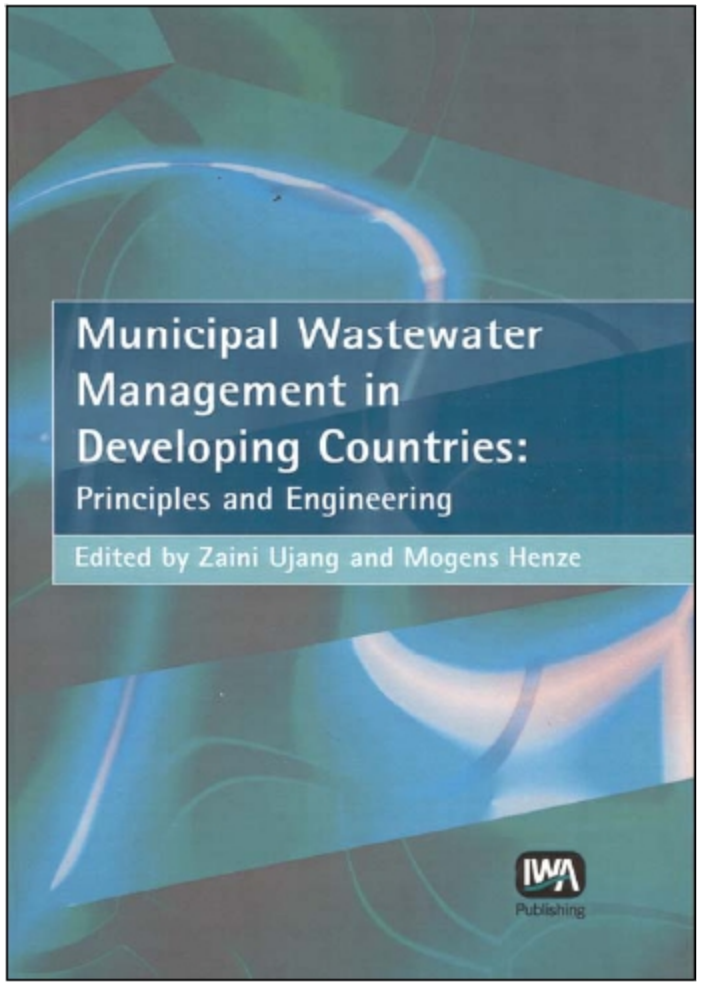
Chronological scientific issues

Target water pollutants, and technology options

Era	Pollutants	Solutions
1800s	Pathogenic bacteria	Sewer system
1900s	BOD, COD	Biological wastewater plants
1950s	Heavy metals, biodegradable substances	Treatment at source
1970s	Eutrophication	N and P control
1980s	Trace substances, carcinogens, flavor, taste	Activated carbon, membrane technology
1990s	CO_2, NH_4, N_2O, CFCs, NO_x, SO_x	Energy saving, photosyntetic bacteria, biotechnology, MBR
2000s	Endocrine disrupting chemicals (EDCs), eco-hazard	Membrane technology

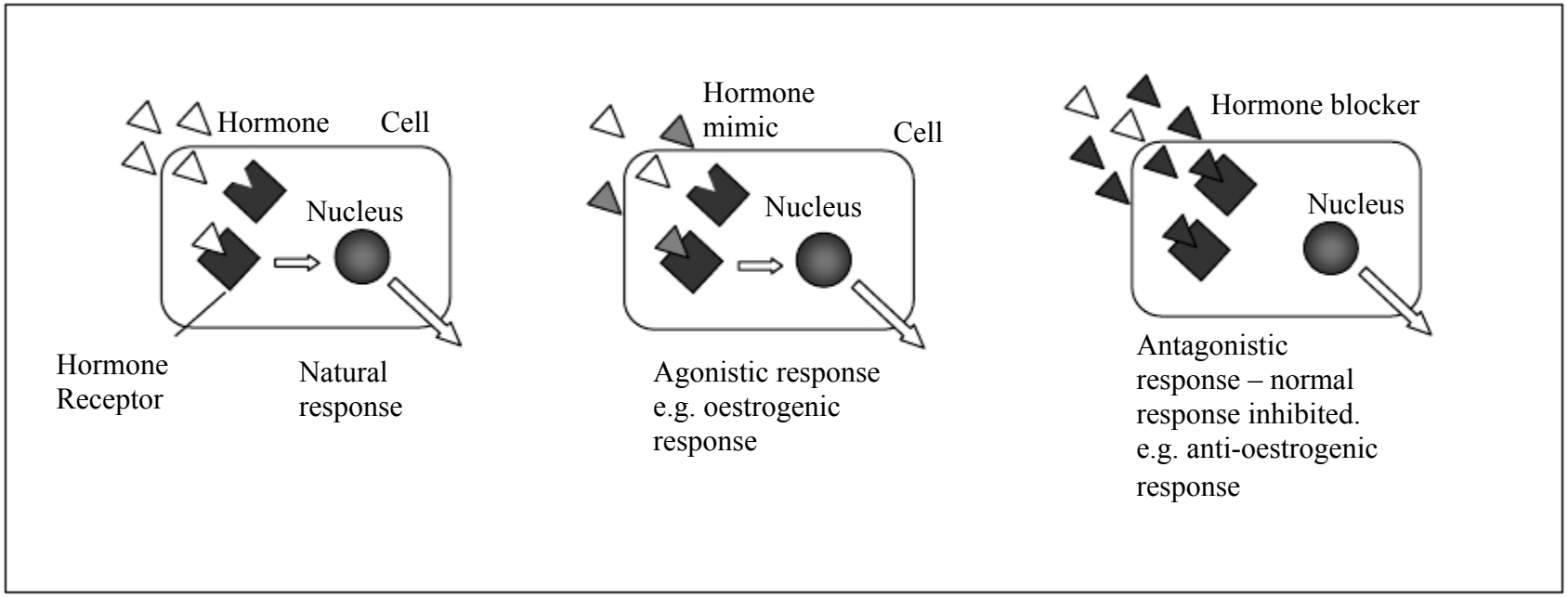
Municipal wastewater management for developing countries

Z. Ujang & M. Henze (2006)
IWA Publishing, London



Endocrine disrupting chemicals (EDCs)

How endocrine disruptors interfere with the normal functioning of the endocrine system?



What is EDCs?

- Exogenous substance (Ozaki, 2004)
- Cause adverse health effects (Ikejima *et al*., 2005, Jiang *et al*., 2005)
- Natural EDCs are most potent & have biological activity (Jiang *et al*., 2005)
- May lead to early death (Zhang & Zhou, 2005)
- Effects are not seen until adulthood (Aquatic Toxicology)
- Disruption of sex hormones (Stuart *et al., 2005)*
- Other hormones can also be affected (Liu *et al.,* 2005, Jiang *et al.,* 2005)

EDC in perspective

- Hazardous organic chemicals
- More than 38,000 types
- Disruption in endocrine system in animals & human being
- Examples: Bisphenol A (BPA), 17β-estradiol (E2), Nonylphenol (NP), Dioxins, PCBs etc.
- Exposure via water medium most common due to contaminated water sources, sewage effluents

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Sources of EDCs	Treatment Techniques
Household products Detergents, surfactants, breakdown products Industrial chemicals and metals Fungicides Insecticides	Adsorption (Zhang & Zhou, 2005) - GAC - Chitin - Chitosan - Ion exchange resin - Carbonaceous adsorbent Preliminary trials with ferrate (VI) & electrochemical oxidation (Jiang *et al., 2005)* Nanofiltration (Yoon *et al*., 2005, Kimura *et al*., 2004) Ultrafiltration (Yoon *et al*., 2005, Reverse Osmosis (Kimura *et al*., 2004, LPROM (Ozaki, 2004, Ikejima *et al*., 2005)

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EDC Compounds	Abbrev.	MF	MW	pK_a
17β-estradiol	E2	$C_{18}H_{24}O_2$	272.38	10.27
Bisphenol A	BPA	$C_{15}H_{16}O_2$	228.29	9.73
Nonylphenol	NP	$C_{15}H_{24}O$	220.35	10.14
Diethyl phthalate	DEP	$C_{12}H_{14}O_4$	222.24	-
2,4-dichlorophenol	2,4-DCP	$C_6H_4Cl_2O$	163.00	8.05

Risk in reality

- People take risks all the time
- Many risks are taken voluntarily, but others are not under our immediate control
- Involuntarily harm – government established and enforced “safe” levels for drinking water quality, air quality, food quality etc which known or potential risks to human health and safety
- Risk assessment and decision analysis methods are among the policy now used to address difficult or complex environmental problems

Definitions

- Risk involves a chance of injury or loss (death)

Risk = probability of a specific undesired consequence

- Risk levels vary by many orders of magnitude

Risk = probability of undesired consequence x size of loss

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Risk of death from various activities (US)

Cause of death	No. each year	Odds of death from this cause	Lifetime risk of death from this cause
Disease (all)	2,000,000	1 in 1.1	9.1×10^{-1}
Heart disease	770,000	1 in 2.7	3.7×10^{-1}
Cancer (all kinds)	480,000	1 in 4.4	2.3×10^{-1}
Accidents (all kinds)	95,000	1 in 22	4.5 x x 10^{-2}
Diabetes	37,000	1 in 57	1.8×10^{-2}
Suicide	31,000	1 in 68	1.5×10^{-2}
Drowning	5900	1 in 360	2.7×10^{-3}
Fire	4800	1 in 440	2.3×10^{-3}
Asthma	4000	1 in 530	1.9×10^{-3}

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… Risk of death from various activities (US)

Cause of death	No. each year	Odds of death from this cause	Lifetime risk of death from this cause
Viral hepatitis	1000	1 in 2100	4.8×10^{-4}
Electrocution	850	1 in 2500	4.0×10^{-4}
Car-train accident	570	1 in 3700	2.7×10^{-4}
Appendicitis	510	1 in 4100	2.4×10^{-4}
Pregnancy etc	470	1 in 4500	2.2×10^{-4}
Lightning	78	1 in 27,000	3.7×10^{-5}
Flood	58	1 in 36,000	2.8×10^{-5}
Tornado	58	1 in 36,000	2.8×10^{-5}
Fireworks	8	1 in 260,000	3.8×10^{-6}

Degree of risk

The risk of a nuclear power plant accident might be viewed differently for a plant located in a sparsely populated rural area as compared to one near a major urban center.

Or

An investment in the stock market might be considered riskier if the amount invested were $100,000 as compared to $1000

Perception of risk

People's mind: Risk depends on factors other than probability and size of loss:

- How well the risk is understood
- How well the people can control their exposure to the risk
- How equitably the exposure is distributed across the population at risk
- etc

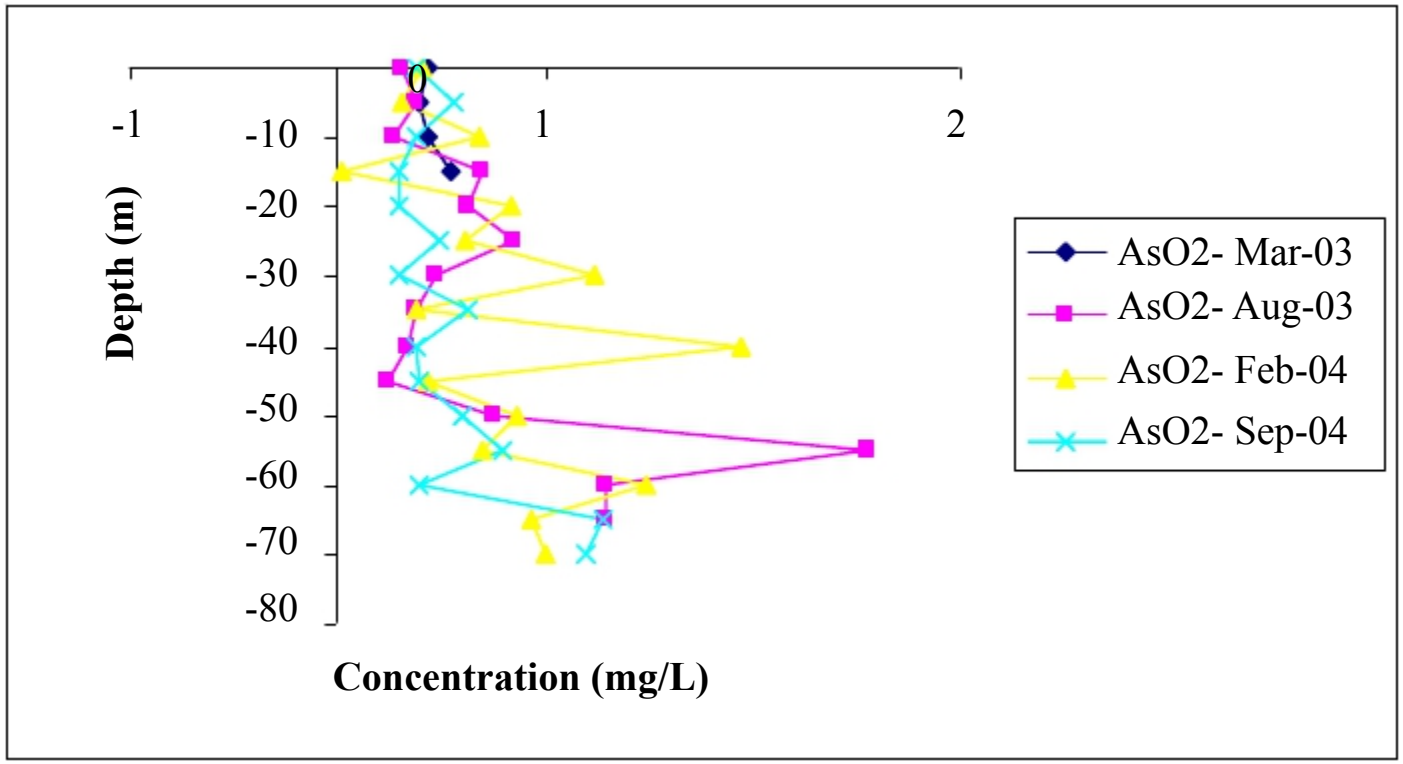
Risk to swim, drink in polluted lake?

WARNING SIGNPOST:

"Lake water contains high level of arsenic. Public is strongly advised not to fish, swim and bathe in the lake or to use lake water for drinking or other purposes"

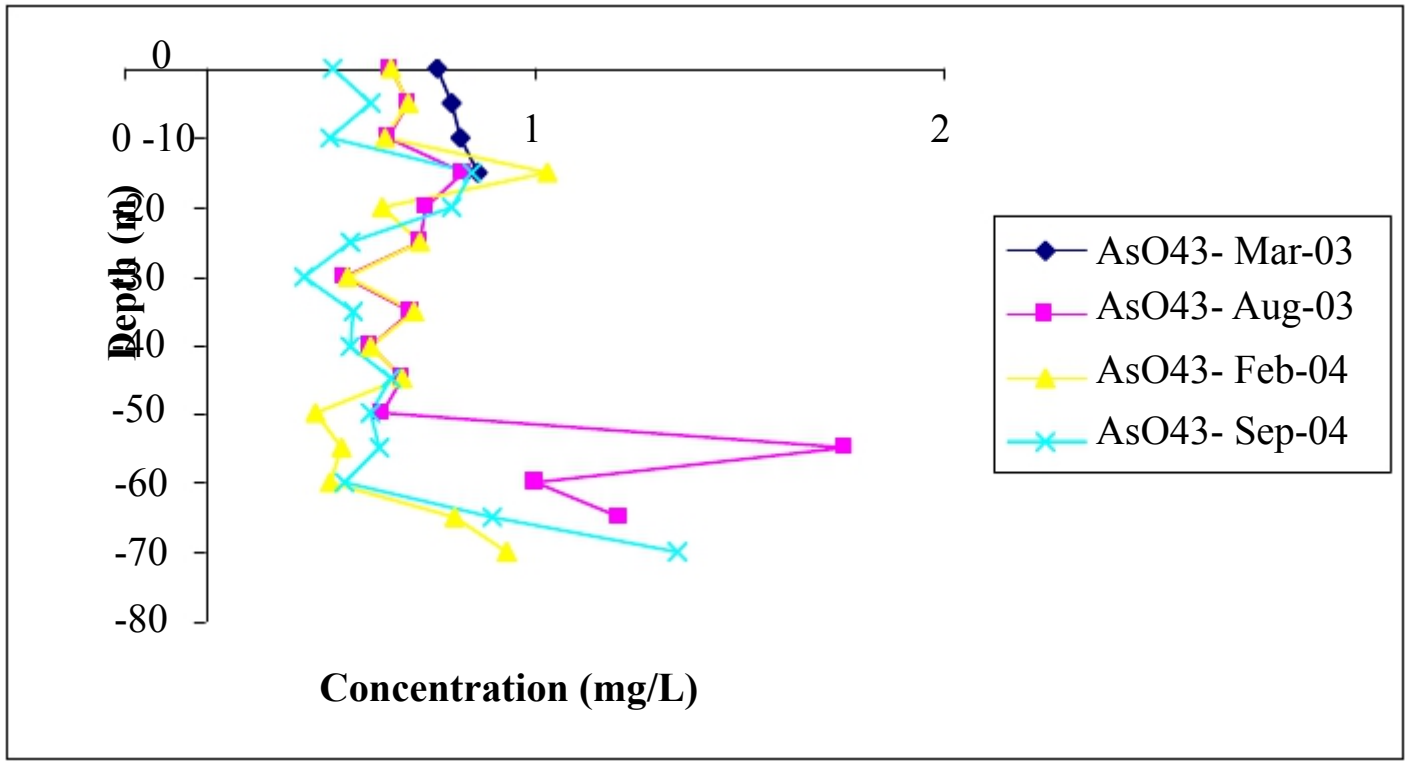
Results and discussion (cont.)

- Arsenite



Results and discussion (cont.)

- Arsenate



Risk and standards

- Public policy – identify safe levels of the most common contaminants in air and water
- Environmental Quality Act 1974: National-health based environmental quality standards (latest trend is "ecosystem health")
- Many chemicals have been identified as hazardous or toxic
- Contaminants concentrations below the standards are generally to be free of known health risk although this is not always the case
- Waste disposal sites, disused mining pools, etc.
- Risk assessment and management helps to prioritize problems and identify solutions in the face of limited resources and capability to respond to a potentially massive problems.

Focus of risk assessment

- Focus: Assess and reduce risk to human health
- Two categories of human health:
  - *Carcinogens*
  - *Non-carcinogens*
- Damage to particular organs or tissue such as liver, kidney or nerves

How safe is safe?

- Almost no zero risk!
- Eliminating risk, e.g. shutting down factory, abolishing dams, remediating all contaminated soils etc., is technically difficult or prohibitively expensive
- Solution: Minimize the risk to an acceptable levels of risk
- People are willing to accept a higher level of risk in activities over which they
  - *have direct control (skiing) or*
  - *from which they derive a direct benefits (take air planes)*

  compared to risks that are imposed involuntarily or that confer no direct benefits

How safe is safe?

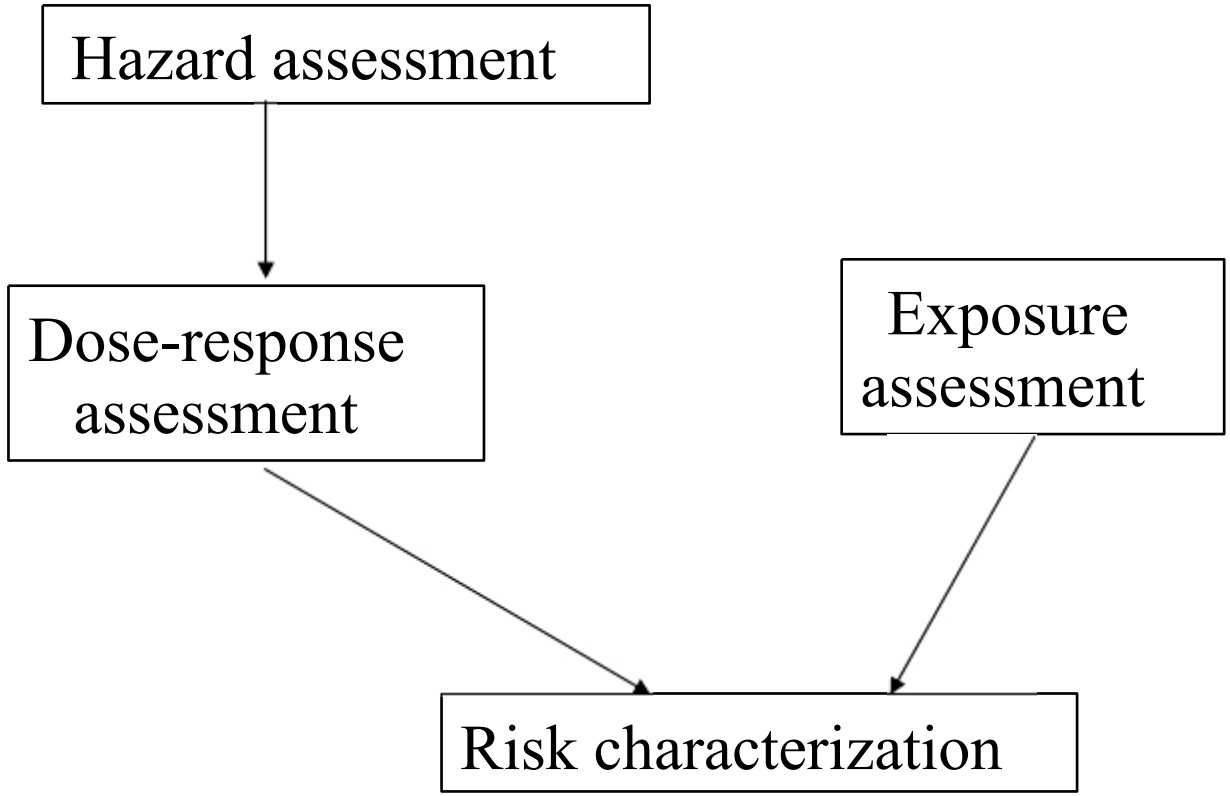
- Numerical criteria has been endorsed to assess whether a particular exposure to chemicals in the environment poses an acceptable or unacceptable risk to public health:
  - *Food Act 1983 - Drinking water quality*
  - *Environmental Quality Act 1974 – Hazardous waste*
  - *Environmental Quality Act 1974 – Stream water quality*

- Criteria for acceptability are different for carcinogenic and non-carcinogenic chemicals.
  - *For carcinogens, a one in a million chance (10^{-6} probability) of an additional human cancer over a 70-year lifetime is the level of risk considered acceptable*

Risk assessment methodology

- Hazard assessment
- Development of dose-response relationship
- Exposure assessment
- Risk characterization

Elements of risk assessment



Hazard assessment

- To determine whether there is any potential problem (observable increase in some illness or health condition) from exposure to a given chemical
- Use all available data from laboratory studies, animal studies and epidemiological studies
- Outcome: Evaluation and description of the nature and severity of any effects that might be caused by exposure to a particular chemical

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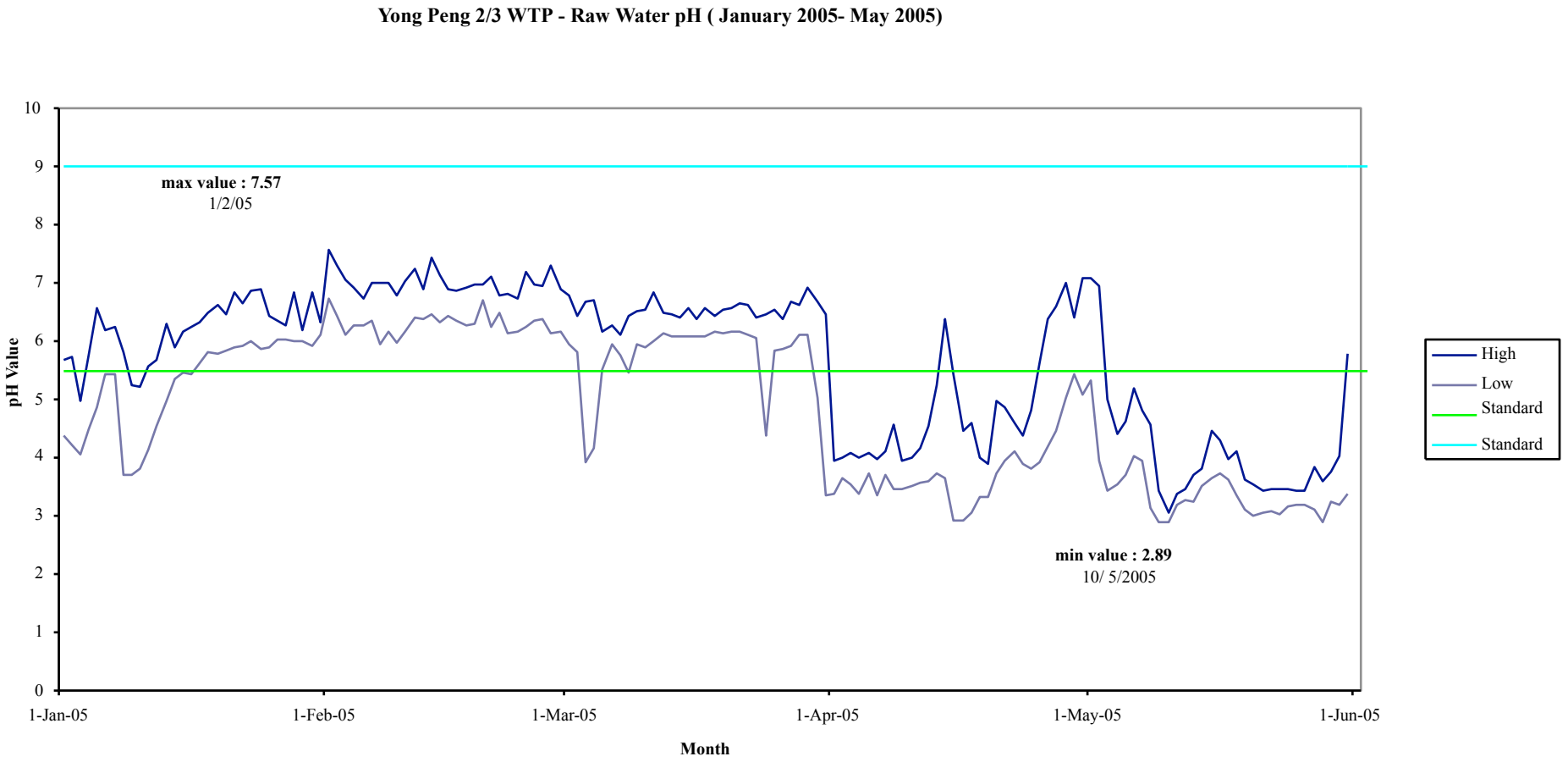
Is low pH dangerous as drinking water?



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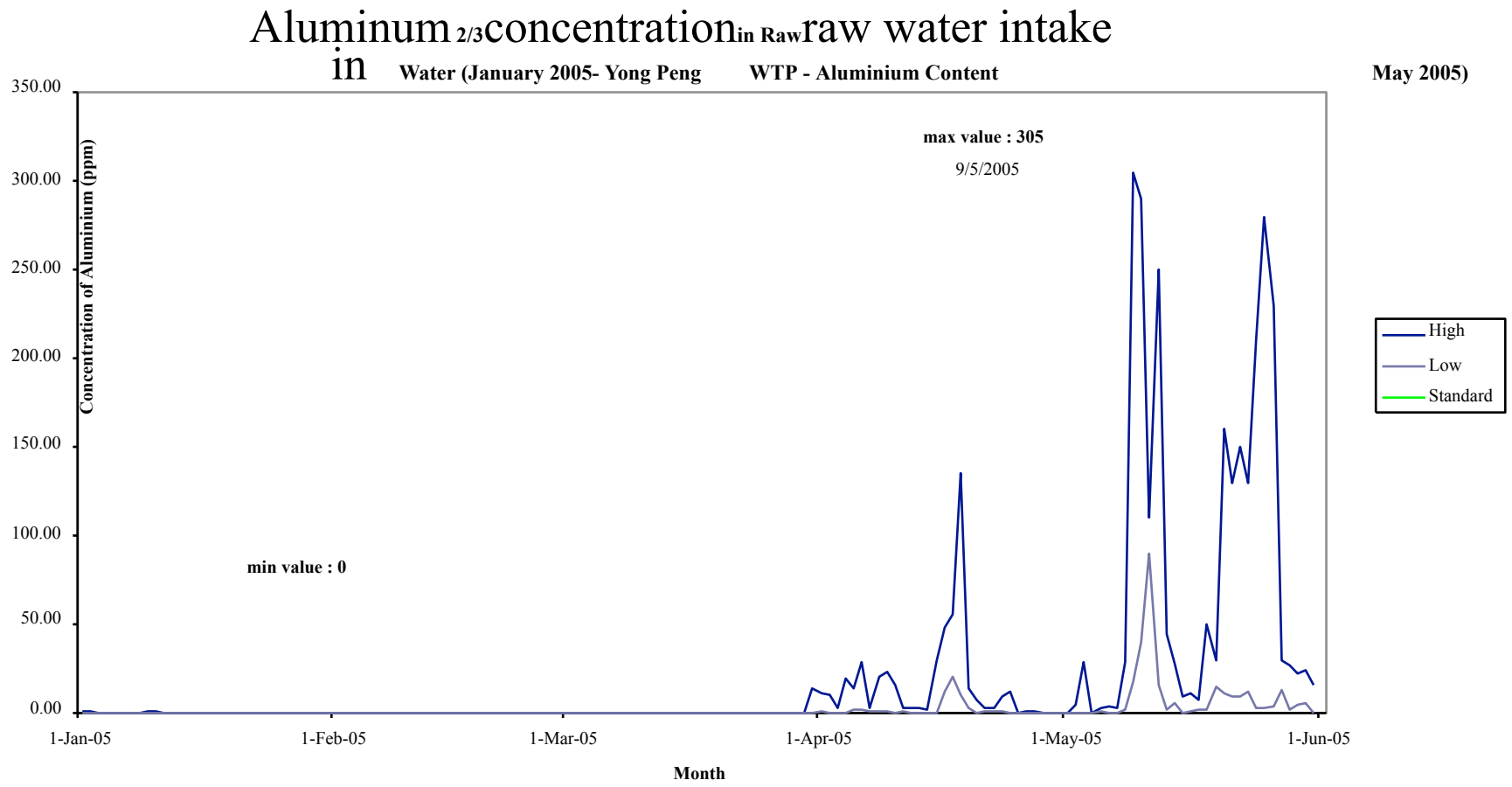
Is high aluminum dangerous as drinking water?



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Guidelines for Drinking-water Quality

Third Edition

Volume 1

Recommendations

WORLD HEALTH ORGANIZATION

Geneva

2004

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12.1 Acrylamide

Residual acrylamide monomer occurs in polyacrylamide coagulants used in the treatment of drinking-water. In general, the maximum authorized dose of polymer is 1 mg/litre. At a monomer content of 0.05%, this corresponds to a maximum theoretical concentration of 0.5 µg/litre of the monomer in water. Practical concentrations may be lower by a factor of 2–3. This applies to the anionic and non-ionic polyacrylamides, but residual levels from cationic polyacrylamides may be higher. Polyacrylamides are also used as grouting agents in the construction of drinking-water reservoirs and wells. Additional human exposure might result from food, owing to the use of polyacrylamide in food processing and the potential formation of acrylamide in foods cooked at high temperatures.

Guideline value	0.0005 mg/litre (0.5 µg/litre)
Occurrence	Concentrations of a few micrograms per litre have been detected in tap water.
Basis of guideline derivation	Combined mammary, thyroid and uterine tumours observed in female rats in a drinking-water study, and using the linearized multistage model
Limit of detection	0.032 µg/litre by GC; 0.2 µg/litre by HPLC; 10 µg/litre by HPLC with UV detection
Treatment achievability	Conventional treatment processes do not remove acrylamide. Acrylamide concentrations in drinking-water are controlled by limiting either the acrylamide content of polyacrylamide flocculants or the dose used, or both.
Additional comments	Although the practical quantification level for acrylamide in most laboratories is above the guideline value (generally in the order of 1 µg/litre), concentrations in drinking-water can be controlled by product and dose specification.

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Toxicological review

Following ingestion, acrylamide is readily absorbed from the gastrointestinal tract and widely distributed in body fluids. Acrylamide can cross the placenta. It is neurotoxic, affects germ cells and impairs reproductive function. In mutagenicity assays, acrylamide was negative in the Ames test but induced gene mutations in mammalian cells and chromosomal aberrations *in vitro* and *in vivo*. In a long-term carcinogenicity study in rats exposed via drinking-water, acrylamide induced scrotal, thyroid and adrenal tumours in males and mammary, thyroid and uterine tumours in females. IARC has placed acrylamide in Group 2A. Recent data have shown that exposure to acrylamide from cooked food is much higher than previously thought. The significance of this new information for the risk assessment has not yet been determined.

History of guideline development

The 1958, 1963 and 1971 WHO *International Standards for Drinking-water* and the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, did not refer to acrylamide. The 1993 Guidelines established a guideline value of 0.0005 mg/litre associated with an upper-bound excess lifetime cancer risk of 10^{-5}, noting that although the practical quantification level for acrylamide is generally in the order of 0.001 mg/litre, concentrations in drinking-water can be controlled by product and dose specification.

Assessment date

The risk assessment was conducted in 2003.

Principal reference

WHO (2003) *Acrylamide in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality*. Geneva, World Health Organization (WHO/SDE/WSH/03.04/71).

12.8 Arsenic

Arsenic is widely distributed throughout the Earth's crust, most often as arsenic sulfide or as metal arsenates and arsenides. Arsenicals are used commercially and industrially, primarily as alloying agents in the manufacture of transistors, lasers and semiconductors. Arsenic is introduced into drinking-water sources primarily through the dissolution of naturally occurring minerals and ores. Except for individuals who are occupationally exposed to arsenic, the most important route of exposure is through the oral intake of food and beverages. There are a number of regions where arsenic may be present in drinking-water sources, particularly groundwater, at elevated concentrations. Arsenic in drinking-water is a significant cause of health effects in some areas, and arsenic is considered to be a high-priority substance for screening in drinking-water sources. Concentrations are often highly dependent on the depth to which the well is sunk.

Provisional guideline value	0.01 mg/litre The guideline value is designated as provisional in view of the scientific uncertainties.
Occurrence	Levels in natural waters generally rangey between 1 and 2 µg/litre, although concentrations may be elevated (up to 12 mg/litre) in areas containing natural sources.
Basis of guideline derivation	There remains considerable uncertainty over the actual risks at low concentrations, and available data on mode of action do not provide a biological basis for using either linear or non-linear extrapolation. In view of the significant uncertainties surrounding the risk assessment for arsenic carcinogenicity, the practical quantification limit in the region of 1–10 µg/litre and the practical difficulties in removing arsenic from drinking-water, the guideline value of 10 µg/litre is retained. In view of the scientific uncertainties, the guideline value is designated as provisional.

Previous 0.05 mg/l

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Toxicological review

Arsenic has not been demonstrated to be essential in humans. It is an important drinking-water contaminant, as it is one of the few substances shown to cause cancer in humans through consumption of drinking-water. There is overwhelming evidence from epidemiological studies that consumption of elevated levels of arsenic through drinking-water is causally related to the development of cancer at several sites, particularly skin, bladder and lung. In several parts of the world, arsenic-induced disease, including cancer, is a significant public health problem. Because trivalent inorganic arsenic has greater reactivity and toxicity than pentavalent inorganic arsenic, it is generally believed that the trivalent form is the carcinogen. However, there remain considerable uncertainty and controversy over both the mechanism of carcinogenicity and the shape of the dose–response curve at low intakes. Inorganic arsenic compounds are classified by IARC in Group 1 (carcinogenic to humans) on the basis of sufficient evidence for carcinogenicity in humans and limited evidence for carcinogenicity in animals.

History of guideline development

The 1958 WHO *International Standards for Drinking-water* recommended a maximum allowable concentration of 0.2 mg/litre for arsenic, based on health concerns. In the 1963 International Standards, this value was lowered to 0.05 mg/litre, which was retained as a tentative upper concentration limit in the 1971 International Standards. The guideline value of 0.05 mg/litre was also retained in the first edition of the *Guidelines for Drinking-water Quality*, published in 1984. A provisional guideline value for arsenic was set at the practical quantification limit of 0.01 mg/litre in the 1993 Guidelines, based on concern regarding its carcinogenicity in humans.

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Assessment date

The risk assessment was conducted in 2003.

Principal references

IPCS (2001) *Arsenic and arsenic compounds.* Geneva, World Health Organization, International Programme on Chemical Safety (Environmental Health Criteria 224).

WHO (2003) *Arsenic in drinking-water. Background document for preparation of WHO Guidelines for drinking-water quality.* Geneva, World Health Organization (WHO/SDE/WSH/03.04/75).

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Limit of detection	0.1 µg/litre by ICP/MS; 2 µg/litre by hydride generation AAS or FAAS
Treatment achievability	It is technically feasible to achieve arsenic concentrations of 5 µg/litre or lower using any of several possible treatment methods. However, this requires careful process optimization and control, and a more reasonable expectation is that 10 µg/litre should be achievable by conventional treatment, e.g., coagulation.
Additional comments	• A management guidance document on arsenic is available. • In many countries, this guideline value may not be attainable. Where this is the case, every effort should be made to keep concentrations as low as possible.

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12.17 Cadmium

Cadmium metal is used in the steel industry and in plastics. Cadmium compounds are widely used in batteries. Cadmium is released to the environment in wastewater, and diffuse pollution is caused by contamination from fertilizers and local air pollution. Contamination in drinking-water may also be caused by impurities in the zinc of galvanized pipes and solders and some metal fittings. Food is the main source of daily exposure to cadmium. The daily oral intake is 10–35 µg. Smoking is a significant additional source of cadmium exposure.

Guideline value	0.003 mg/litre
Occurrence	Levels in drinking-water usually less than 1 µg/litre
PTWI	7 µg/kg of body weight, on the basis that if levels of cadmium in the renal cortex are not to exceed 50 mg/kg, total intake of cadmium (assuming an absorption rate for dietary cadmium of 5% and a daily excretion rate of 0.005% of body burden) should not exceed 1 µg/kg of body weight per day
Limit of detection	0.01 µg/litre by ICP/MS; 2 µg/litre by FAAS
Treatment achievability	0.002 mg/litre should be achievable using coagulation or precipitation softening

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Guideline derivation	
• allocation to water	10% of PTWI
• weight	60-kg adult
• consumption	2 litres/day
Additional comments	• Although new information indicates that a proportion of the general population may be at increased risk for tubular dysfunction when exposed at the current PTWI, the risk estimates that can be made at present are imprecise. • It is recognized that the margin between the PTWI and the actual weekly intake of cadmium by the general population is small, less than 10-fold, and that this margin may be even smaller in smokers.

Toxicological review

Absorption of cadmium compounds is dependent on the solubility of the compounds. Cadmium accumulates primarily in the kidneys and has a long biological half-life in humans of 10–35 years. There is evidence that cadmium is carcinogenic by the inhalation route, and IARC has classified cadmium and cadmium compounds in Group 2A. However, there is no evidence of carcinogenicity by the oral route and no clear evidence for the genotoxicity of cadmium. The kidney is the main target organ for cadmium toxicity. The critical cadmium concentration in the renal cortex that would produce a 10% prevalence of low-molecular-weight proteinuria in the general population is about 200 mg/kg and would be reached after a daily dietary intake of about 175 µg per person for 50 years.

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History of guideline development

The 1958 WHO *International Standards for Drinking-water* did not refer to cadmium. The 1963 International Standards recommended a maximum allowable concentration of 0.01 mg/litre, based on health concerns. This value was retained in the 1971 International Standards as a tentative upper concentration limit, based on the lowest concentration that could be conveniently measured. In the first edition of the *Guidelines for Drinking-water Quality*, published in 1984, a guideline value of 0.005 mg/litre was recommended for cadmium in drinking-water. This value was lowered to 0.003 mg/litre in the 1993 Guidelines, based on the PTWI set by JECFA.

Assessment date

The risk assessment was conducted in 2003.

Principal references

JECFA (2000) *Summary and conclusions of the fifty-fifth meeting, Geneva, 6–15 June 2000*. Geneva, World Health Organization, Joint FAO/WHO Expert Committee on Food Additives.