APPLE PECTIN

. . . the number of children and grandchildren with cancer in their bones, with leukemia in their blood, or with poison in their lungs might seem statistically small to some, in comparison with natural health hazards, but this is not a natural health hazard--and it is not a statistical issue. The loss of even one human life, or the malformation of even one baby--who may be born long after we are gone--should be of concern to us all. Our children and grandchildren are not merely statistics toward which we can be indifferent.

-- President Kennedy, June, 1963

What is Apple Pectin?

Pectin is a structural heteropolysaccharide contained in the primary cell walls of terrestrial plants. It was first isolated and described in 1825 by Henri Braconnot.

It is produced commercially as a white to light brown powder, mainly extracted from citrus fruits, and is used in food as a gelling agent particularly in jams and jellies. It is also used in fillings, sweets, as a stabilizer in fruit juices and milk drinks and as a source of dietary fiber.

The pectin in apples is transformed into a soothing coating for the intestines by intestinal bacteria, which eases stomach cramps.

Pectin adds bulk to stools and is useful in combating diarrhea.

A study that appeared in the "Journal of the National Cancer Institute" hints that pectin may stop cancer spreading through the body, and that pectin binds certain carcinogenic compounds in the colon, speeding their elimination from the body.

A study published in the "Annals of Internal Medicine" showed that apple pectin helps to reduce blood sugar levels in diabetics.

Apple pectin reportedly helps retain cholesterol in the stomach, binding cholesterol to itself and carrying it through the digestive tract to be eliminated and is also reported to help the body rid itself of

. lead
. mercury
. and other heavy metals prevalent in modern water, food, and air.

Biology:

Naturally, pectin in the form of complex, insoluble protopectin is part of the non-woody parts of terrestrial plants. In the middle lamella between plant cells, pectin helps to bind cells together and regulates water in the plant.

The amount, structure and chemical composition of the pectin differs between plants, within a plant over time and in different parts of a plant. Hard parts contain more pectin than soft parts of a plant. During ripening, pectin is broken down by the enzymes pectinase and pectinesterase; in this process the fruit becomes softer as the middle lamella breaks down and cells become separated from each other. A similar process of cell separation caused by pectin breakdown occurs in the abscission zone of the petioles of deciduous plants at leaf fall.

Pectin is a natural part of human diet, but does not contribute significantly to nutrition. The daily intake of pectin from fruit and vegetables can be estimated to be around 5 g (assuming consumption of approximately 500 g fruit and vegetable per day).

In human digestion, pectin passes through the small intestine more or less intact. In the large intestine and colon, microorganisms degrade pectin and liberate short-chain fatty acids that have positive influence on health (prebiotic effect). Pectin is thus a soluble dietary fiber.

Consumption of pectin has been shown to reduce blood cholesterol levels. The mechanism appears to be an increase of viscosity in the intestinal tract, leading to a reduced absorption of cholesterol from bile or food.

Chemistry:

The characteristic structure of pectin is a linear chain of á-(1-4)-linked D-galacturonic acid that forms the pectin-backbone, a homogalacturonan.

Into this backbone, there are regions where galacturonic acid is replaced by (1-2)-linked L-rhamnose. From the rhamnose residues, sidechains of various neutral sugars branch off. This type of pectin is called rhamnogalacturonan I.

Up to every 25th galacturonic acid in the main chain is replaced with rhamnose. Some stretches consist of alternating galacturonic acid and rhamnose – "hairy regions", others with lower density of rhamnose – "smooth regions". The neutral sugars are mainly D-galactose, L-arabinose and D-xylose, the types and proportions of neutral sugars varying with the origin of pectin.

A third structural type of pectin is rhamnogalacturonan II, which is a less frequent complex, highly branched polysaccharide.

Isolated pectin has a molecular weight of typically 60 - 130 000 g/mol, varying with origin and extraction conditions.

In nature, around 80% of carboxyl groups of galacturonic acid are esterified with methanol. This proportion is decreased more or less during pectin extraction. The ratio of esterified to non-esterified galacturonic acid determines the behavior of pectin in food applications. This is why pectins are classified as high- vs. low-ester pectins – or in short HM vs. LM-pectins, with more or less than half of all the galacturonic acid esterified.

The non-esterified galacturonic acid units can be either free acids (carboxyl groups) or salts with sodium, potassium or calcium. The salts of partially esterified pectins are called pectinates, if the degree of esterification is below 5% the salts are called pectates, the insoluble acid form, pectic acid.

Some plants like sugar beet, potatoes and pears contain pectins with acetylated galacturonic acid in addition to methyl esters. Acetylation prevents gel-formation but increases the stabilising and emulsifying effects of pectin.

Amidated pectin is a modified form of pectin. Here, some of the galacturonic acid is converted with ammonia to carboxylic acid amide. These pectins are more tolerant of varying calcium concentrations that occur in use.

To prepare a pectin-gel, the ingredients are heated, dissolving the pectin. Upon cooling below gelling temperature, a gel starts to form. If gel formation is too strong, syneresis or a granular texture are the result, whilst weak gelling leads to excessively soft gels. In high-ester pectins at soluble solids content above 60% and a pH-value between 2.8 and 3.6, hydrogen bonds and hydrophobic interactions bind the individual pectin chains together. These bonds form as water is bound by sugar and forces pectin strands to stick together. These form a 3-dimensional molecular net that creates the macromolecular gel. The gelling-mechanism is called a low-water-activity gel or sugar-acid-pectin gel.

In low-ester pectins, ionic bridges are formed between calcium ions and the ionised carboxyl groups of the galacturonic acid. This is idealised in the so-called "egg box-model". Low-ester pectins need calcium to form a gel, but can do so at lower soluble solids and higher pH-values than high-ester pectins.

Amidated pectins behave like low-ester pectins but need less calcium and are more tolerant of excess calcium. Also, gels from amidated pectin are thermo-reversible – they can be heated and after cooling solidify again, whereas conventional pectin-gels will afterwards remain liquid.

High-ester pectins set at higher temperatures than low-ester pectins. However, gelling reactions with calcium increase as the degree of esterification falls. Similarly, lower pH-values or higher soluble solids (normally sugars) increase gelling speed. Suitable pectins can therefore be selected for jams and for jellies, or for higher sugar confectionery jellies.

Sources and production:

Apples, quince, plums, gooseberries, oranges and other citrus fruits contain much pectin, while soft fruits like cherries, grapes and strawberries contain little pectin.
Typical levels of pectin in plants are (fresh weight):
apples, apricot approx. 1%
oranges 0.5 - 3.5%
carrots approx. 1.4%

The main raw-materials for pectin production are dried citrus peel or apple pomace, both by-products of juice production. Pomace from sugar-beet is also used to a small extent.

From these materials, pectin is extracted by adding hot dilute acid at pH-values from 1.5 – 3.5. During several hours of extraction, the protopectin loses some of its branching and chain-length and goes into solution. After filtering, the extract is concentrated in vacuum and the pectin then precipitated by adding ethanol or isopropanol. An old technique of precipitating pectin with aluminium salts is no longer used (apart from alcohols and polyvalent cations; pectin also precipitates with proteins and detergents).

Alcohol-precipitated pectin is then separated, washed and dried. Treating the initial pectin with dilute acid leads to low-esterified pectins. When this process includes ammonium hydroxide, amidated pectins are obtained. After drying and milling pectin is usually standardised with sugar and sometimes calcium-salts or organic acids to have optimum performance in a particular application.

Worldwide, approximately 40,000 metric tons of pectin are produced every year.

Uses:

The main use for pectin is as a gelling agent, thickening agent and stabilizer in food. The classical application is giving the jelly-like consistency to jams or marmalades, which would otherwise be sweet juices. For household use, pectin is an ingredient in jelling sugar (sometimes sold as "sugar with pectin") where it is diluted to the right concentration with sugar and some citric acid to adjust pH. In some countries, pectin is also available as a solution or an extract, or as a blended powder, for home jam making. For conventional jams and marmalades that contain above 60% sugar and soluble fruit solids, high-ester pectins are used. With low-ester pectins and amidated pectins less sugar is needed, so that diet products can be made. Pectin can also be used to stabilize acidic protein drinks, such as drinking yogurt, and as a fat substitute in baked goods. Typical levels of pectin used as a food additive are between 0.5 – 1.0% - this is about the same amount of pectin as in fresh fruit.

In medicine, pectin increases viscosity and volume of stool so that it is used against constipation and diarrhea. Until 2002, it was one of the main ingredients used in Kaopectate, along with kaolinite. Pectin is also used in throat lozenges as a demulcent. In cosmetic products, pectin acts as stabilizer. Pectin is also used in wound healing preparations and specialty medical adhesives, such as colostomy devices.

In ruminant nutrition, depending on the extent of lignification of the cell wall, pectin is up to 90% digestible by bacterial enzymes. Ruminant nutritionists recommend that the digestibility and energy concentration in forages can be improved by increasing pectin concentration in the forage.

In the cigar industry, pectin is considered an excellent substitute for vegetable glue and many cigar smokers and collectors will use pectin for repairing damaged tobacco wrapper leaves on their cigars.

Legal status:

Pectins, including high and low -ester and amidated, are used in food all over the world. At the FAO/WHO joint Expert Committee on Food Additives and in the EU, no numerical acceptable daily intake (ADI) has been set, as pectin is considered safe.

In the US, pectin is GRAS – Generally recognized as safe. In most foods it can be used according to good manufacturing practices in the levels needed for its application, "quantum satis".

In the International Numbering System (INS) pectin has the number 440. In Europe pectins are differentiated into the E numbers E440(i) for non-amidated pectins and E440 (ii) for amidated pectins. There are specifications in all national and international legislation defining its quality and regulating its use.

One bushel of apples weighs about 48 lbs (150 apples). One pound of apples generally consists of 4 small apples or 3 medium or 2 large apples.

1 US beer barrel = 3.33004698 US bushels
3.33*48=160 lbs/barrel = 450-500 apples/barrel
500mg*2.5XF*100:1(pectin:apple)/1000(mg/gm)=125gm of apples = 125gm/28(oz/gm) = 4.5 oz [1 apple]
Apple, medium (150 gm), contains:
Apple, medium (150 gm), contains:
4.2gm insoluble fiber + 1.5gm soluble (pectin) fiber = 5.7gm total fiber
Apple , small (100 gm), with skin:
2.00 gm insoluble fiber + 0.70 gm soluble (pectin) fiber = 2.70 gm total fiber

About fourteen grams of carbohydrates and ten grams of sugar are present in 100 grams of apple. The glucose content is 1.5 g/100 gm of apples. The fructose and sucrose content of apples are 6 gm and 3 gm per 100 grams of the fruit respectively.

General Background on Radionuclide Chemistry

There are about 2,000 known radionuclides, which are species of atoms that emit radiation as they undergo radioactive decay through emission of alpha particles, beta particles, or gamma rays. Naturally occuring radionuclides are ubiquitous trace elements found in rocks and soils and, in general, radionuclides can be categorized in three ways: • by type of radioactive decay (alpha, beta, or gamma emission), • by radioactive decay series, • as naturally occurring or manmade. Some of the naturally occurring and manmade radionuclides are directly regulated by the current drinking-water standards. The natural radionuclides include the primordial elements that were incorporated into the earth's crust during its formation, the radioactive decay products (or progeny) of these primordial elements, and radionuclides that are formed in the atmosphere by cosmic ray interactions. Manmade radionuclides are produced through the use of nuclear fuels, radiopharmaceuticals, and other activities of the nuclear industry and have been released into the atmosphere as the result of atmospheric testing of nuclear weapons and, in rare cases, accidents at nuclear-fuel stations, and discharge of adiopharmaceuticals. Further discussion on manmade radionuclides is beyond the scope of this report. The two types of isotopes with radioactive decay that carry the most health risk due to ingestion of water are alpha-particle emitters and beta/photon-particle emitters (Lappenbusch and Cothern, 1985). Many radionuclides are mixed emitters with either an alpha or beta emission coupled with gamma (photon) emission, or in some cases, all three. Each radionuclide has a primary mode of disintegration. The most common, heavy, naturally occurring radionuclides are largely alpha-particle emitters, although their progeny often emit beta particles. The alpha-particle emitting radionuclides discussed in this report include two isotopes of radium (Ra-224 and Ra-226) and polonium-210. Alpha radiation is composed of a particle, consisting of two protons and two neutrons, spontaneously emitted from the nucleus of a subset of radioactive elements (mostly the heaviest elements) during radioactive decay. Alpha radiation is ionizing radiation, meaning that it strips electrons from adjacent atoms as it passes. Alpha radiation cannot penetrate skin; thus, an alpha-particle emitting radionuclide must be ingested in order to come into contact with internal tissue. Because of the large size, alpha particles are likely to collide with cell tissue, causing tissue damage. An accumulation of tissue damage in the cell nucleus may lead to cell mutation and potential cancer.

The naturally occurring radionuclides derived from uranium-238, thorium-232, and uranium-235 are products of the radioactive decay series known as the uranium, thorium and actinium series, respectively. Each decay series follows a known sequence of radioactive decay, producing various isotopes that also emit either an alpha or a beta particle as they decay (fig. 1). Each series terminates with a stable isotope of lead. The crustal abundance of U-235 is very low in comparison with the other decay series (U-238 to U-235 mass ratio is on the order of 140 to 1).

The food industry uses pectin as a gelling agent. It is mainly used in fruit based foods such as jams and jellies. It does have some pharmaceutical applications too. Chemically, Pectin is a linear polysaccharide. It contains about 300 to 1,000 monosaccharide units. The principle monosaccharide unit of Pectin is D-Galacturonic acid. Pectin also has some neutral sugars present in it. D-galacturonic acid residues are linked together by Alpha-1, 4 glycosidic linkages. These residues can be esterified with methyl groups. If more than 50% of the galaturonic acid residues are esterified, the Pectin is called high methoxyl or HM Pectin. If it is less than 50%, the Pectin is called low methoxy or LM Pectin.

Purple Ribbon NS Apple	
Description	The pectin Purple Ribbon NS Apple is a low methoxyl apple pectin.
Typical application	Fruit spreads and fruit preparation
Composition	Pectin E 440
Legal description	Gelling and thickening agent for foodstuffs
Legal requirements	The product complies with all relevant general standards for pectin as determined by the FAO/WHO (JECFA), the European Union and the Food Chemical Codex (25mg/kg max daily intake for man). GRAS in USA, It is within the customer's sole responsibility to use the product according to current legal standards.

Chemical parameters	
Degree of esterification %]	33 - 38
pH (1% solution, 25°C)	3.3 – 3.8
Particle size	max. 5% > 315 µm
Appearance	fine, free-flowing powder, beige
Smell/taste	almost neutral

Twinlab Apple Pectin Caps (Usp Grade)

Description:
Twinlab apple pectin caps (usp grade) also contain vitamin C. Vitamin C synergistically enhances the effectiveness and health benefits

of apple pectin. Twinlab apple pectin caps (usp grade) are of the highest quality and meet the purest grade of apple pectin obtainable. Usp stands for the united states pharmacopeial convention. The usp sets the official standards of strength, quality, purity, packaging and labeling for nutritional and medical products in the united states. Pectin products that do not meet usp specification are usually impure and diluted or standardized with dextrose, sugars or other fillers. Well tolerated by the most highly allergic individuals.

Nutrition Information Apple Pectin Usp 500 mg Vitamin C 10 mg
Apple Pectin Caps Other Ingredients Vitamin C

Apple Pectin Caps Suggested Use by Twinlab:
As a dietary supplement, take 1-3 capsules with each meal or as directed by a physician or health professional. Keep tightly closed in a cool, dry place.

Nature's Plus - Apple Pectin 500 mg 90 tabs

Description: Nutritional Support for the Digestive Tract and overall well being

Nutrition Information
Apple Pectin (from fresh apples) (equivalent in pectin content to 20.5 grams of whole apples 500 mg) [Why 1:41? MJE]

Apple Pectin Other Ingredients
Di-calcium phosphate, microcrystalline cellulose, stearic acid, magnesium stearate , silica, pharmaceutical glaze.

Apple Pectin Suggested Use by Natures Plus: 1 Tablet daily

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МЕДЕТОПЕКТ®

[http://www.e-apteka.ru/preparats/sanofi_pr/medetopect.asp]

Продукт, содержащий специальный пектин, эффективен для профилактики и детоксикации при отравлении тяжелыми металлами и их радионуклидами.

Рекомендации по применению: В контаминированных областях рекомендуется постоянный прием: По 3-5 таблеток три раза в день (что соответствует 5-8 г/день или 2.75-4.4 г/день волокна). Соблюдать трехдневный интервал через каждые 7 дней в течении целого года. 12 доз по 225 таблеток являются достаточными для одного года.
В профилактических целях рекомендуется постепенный режим:

- Адаптация интестинальной флоры

  7 дней по 3-4 таблетки в день (6.6 г или 3.6 г волокна)

- Повышение дозы

  7 дней от 4 до 10 таблеток 3 раза в день

- Лечение

7 дней по 10 таблеток 3 раза в день (16.5 г или 9 г волокна)
Такой курс повторяется 3 или 4 раза в год. 6-8 доз по 2225 таблеток являются необходимыми для одного года.
Таблетки следует принимать перед едой запивая их 150-200 мл воды. Детям весом от 20 до 35 кг рекомендуется половина дозы.
Медетопект не рекомендуется детям младше 6 лет.
Вес одной таблетки: 550 мг.
Вес содержимого упаковки: 125 г.

Выведение стронция с мочой у пациентов в контаминированных областях, на фоне лечения медетопектом и грубыми волокнами.

{above Russian text translated here:}

The product contains a special pectin, effective for the prevention and detoxification in case of poisoning by heavy metals and radionuclitides.

Directions: The contaminated areas should the reception: 3-5 tablets three times a day (equivalent to 5-8 g / day or 2.75-4.4 g / day fiber). Observe the three-day interval is every 7 days throughout the year. 12 doses of 225 tablets are sufficient for one year.
As a preventive measure recommended gradual mode:
• Adaptation of the intestinal flora
7 days of 3-4 tablets per day (6.6 g or 3.6 g fiber)
• Increasing doses
7 days from 4 to 10 tablets 3 times a day
Treatment •
7 days to 10 tablets 3 times a day (16.5 g or 9 g fiber)
Such a course is repeated 3 or 4 times a year. 6-8 doses of 225 tablets are needed for one year.
[{(7*4)+(7*((4+10)/2)*3)+(7*10*3)}=385, 385*4=1540 tablets/year]
Tablets should take before eating drank 150-200 ml of water. For children weighing from 20 to 35 kg is recommended half the dose.
Medetopekt not recommended for children under 6 years.
Weight of one tablet: 550 mg.
Weight of the package: 125 g

A New Approach to Metastatic Cancer Prevention: Modified Citrus Pectin (MCP), A Unique Pectin that Blocks Cell Surface Lectins
http://www.thorne.com/altmedrev/mcp.html
by Parris M. Kidd, PhD

ABSTRACT

Citrus pectin (CP) is a commercially available, water-soluble fiber with proven health benefits. The branching polysaccharide structure of CP can be altered to produce a lower molecular weight, galactose-rich, modified citrus pectin (MCP) which has unique properties. Specifically, MCP, but not CP, might help retard cancer metastasis by combining with an array of galactose-specific proteins on the cancer cell surface called galectins (for galactose-specific lectins). As with many human cancer cell lines that have been studied, the potentially metastatic B16-F1 (mouse melanoma) and MLL (rat prostate) cells carry galectins, cell surface proteins that bind to galactose on neighboring cancer cells and oligosaccharides on the host cell surface. MCP inhibits metastasis by the cells in the mouse and the rat, respectively. Unlike the much larger CP polysaccharide, galactose-rich MCP may be small enough to access and bind tightly with galectins on the cancer cell surface, saturating the galactose binding sites of the cancer cell lectins, and thereby inhibiting both aggregation of tumor cells and adhesion to normal cells. Thus deprived of adhesion, the cancer cells fail to metastasize. Undeniably, important gaps still exist in the current understanding of MCP's clinical efficacy and its mode(s) of action. But MCP's apparent safety and proven anti-metastatic action, and the lack of proven therapies against metastasis, together may justify its inclusion into comprehensive orthomolecular anticancer regimens. (Alt Med Rev 1996;1:4-10.)

Pektine, natürlich von H&F
Pectins - naturally from Herbstreith & Fox
http://www.pectin.org/funde/englisch/epress06_2.htm

Binding and Excretion of heavy metals and their radionuclides

A special property of pectins is their ability to bind heavy metals by a complexation mechanism. This is possible because pectins are negatively charged polyelectrolytes and can bind positively charged heavy metal ions. The binding affinity is very high for lead, followed by barium, cadmium and strontium and decreases to earth alkali and alkali ions. With that low methoxyl pectins are an antidote for heavy metal poisoning by an increased excretion in the stool and with that a reduced resorption. But also heavy metals once resorpted are excreted in the urine.

This mechanism is based on oligogalacturonides degraded from pectin by microorganisms in the colon and with that resorpable into the body. This oligogalacturonides either catalyze an excretion reaction or bind itself heavy metals resulting in an excretion via urine. The way of action is not clearly understood up to now.

From Herbstreith & Fox and Sanofi-Winthrop the product Medetopekt was developed with the assistance of the Russian Institute of Biophysics and some other medicinal centers. Medetopekt is a tablet consisting of a low methoxyl apple pectin with a special improved binding capacity for heavy metals especially for lead and some other pectin rich apple components like liquid pectin dried, apple fiber and apple powder.

The effectiveness of Medetopekt was first studied with rats. It could be shown that the excretion of lead, cadmium and strontium was improved by Medetopekt. Consequent human studies in Kiew and Minsk varified these results.

Medetopekt was tested against crude wheat fiber. In the first study the lead content in the blood was measured before and after 21 days of Medetopekt therapy. The results with crude wheat fiber were not significant. Medetopekt reduced the lead concentration from 0,48 mg per liter to 0,37 mg per liter by 23 % (see fig. 3).

The excretion of lead via urine was significantly increased after 21 days. The volunteers left during the study their unfriendly environment. With that the lead intake and naturally occuring excretion was reduced (see fig. 4).

After some time the microorganisms probably adapted to the pectin enriched food and produced more pectin degrading encymes and with that more oligogalacturonides were formed resulting in a higher resorption of these substances and a high excretion of lead via urine at the end of the study. A further longer study carried out in these days will show if the excretion will be further increased over a longer period. In the strontium study the radioactive strontium was measured in the urine. The excretion of strontium was not changed significantly by crude wheat fiber but increased with Medetopekt from 0,060 Curie per liter to 0,115 Curie per liter within 21 days (visit 3, see fig. 5).

INFLUENCE OF THE RADIATION ON THE HEALTH OF THE CHILDREN IN BELARUS 12 YEARS AFTER CHERNOBYL

IMPACT OF RADIATION ON THE HEALTH OF CHILDREN IN BELARUS 12 YEARS AFTER CHERNOBYL by Vasily B. Nesterenko corresponding member of the National Academy of Sciences of the Republic of Belarus, Professor, Doctor of Technical Sciences, Director of the..
www.bdg.minsk.by
http://www.bdg.minsk.by/cegi/Chernobyl/1/Nester/NESTER2.html

Medetopekt
http://www.e-apteka.ru/medic/preparats/sanofi_pr/medetopect.asp

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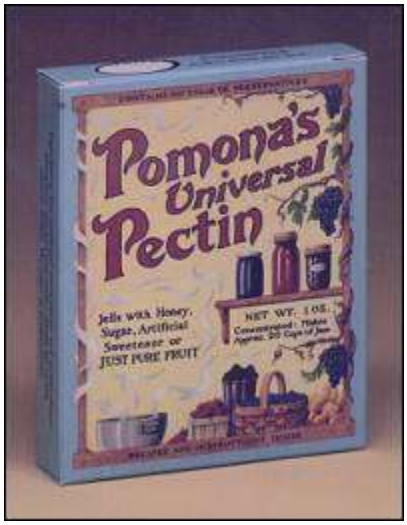


"Pomona's Universal Pectin" is a sugar-free, low-methoxyl citrus pectin that is activated by calcium. Since it does not require sugar to jell, jams and jellies can be made with less, little, or no sugar. Some other possible sweeteners are honey, fructose, sucanat, concentrated fruit sweetener, maple syrup, agave, frozen juice concentrate, stevia, xylitol, Splenda and other artificial sweeteners.

Each 1 oz. box of **"Pomona's Pectin"** contains a packet of pectin, a packet of calcium powder and a sheet of newly revised directions and recipes. A **JAMLINE** telephone number is included in case there are any questions.
* *Concentrated and economical* -- each box makes two to four recipes.
* *Time saving* -- recipes can be doubled and tripled.
* *Shelf Life* -- keeps indefinitely.

Look for **"Pomona's"** at your local Health Food Store, Food Co-op or Farm Stand. If you can't find it locally, then you can mail order it all year from Workstead Industries or Harvest Plus:

1 oz. box $5.35/box 1/2 lb. Bulk $29.25 1 lb. bulk $48.00

$5.99 + $0.99 shipping In Stock. Sold by The Vitamin Shoppe

Vitamin Shoppe - Apple Pectin, 500 mg, 300 tablets

Sale: $5.99 ($0.60 / 10 Items) Package Quantity: 100

Product Features Package Quantity: 100

* Serving Size - 1 tablet

* Does Not Contain: Yeast, Corn, Wheat, Sugar, Salt, Soy, Dairy, Citrus, Fish, Preservatives, Artificial Colors or Flavors Added.

Apple Pectin by Now Foods

List Price: $14.99 Price: $11.09 Ships from and sold by Nutricity.

Product Features Size: 120 caps

* Recommend: As a dietary supplement, take 2 capsules, 1 to 3 times daily with plenty of water or juice, preferably 30 minutes before meals. Be sure to consume additional fluids throughout the day. Start with smaller dosages and gradually increase over several weeks

* Does Not Contain: yeast, wheat, milk, corn, soy, egg, sugar, salt, fillers.

* Disclaimer: These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

* Serving Size: 2 Capsules

Customer Review: I bought this because I read that studies show that apple pectin lowers your cholesterol. You can eat 3 apples a day, or you can take the pectin. I don't like apples enough to eat three of them a day, so I bought this.

Because this is fiber, you don't want to start out with the full dose. Take it slow so you don't have cramping or many, many trips to the bathroom. Your insides have to get used to this. You also want to drink this with a lot of water.
These come in standard sized gelatin capsules. If you have problems swallowing them (for me, sometimes they get stuck midway) you might want to think about getting the powder. Or you can drink something hot to melt the gelatin.

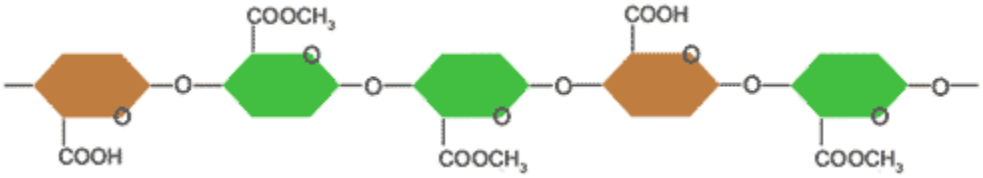
A German-Belarusian project tested apple pectin in a population of 729 children whose body burden of caesium-137 was in excess of the international annual dose of 1 mSv. All children were given non-contaminated foods, additionally half received *Vitapect* and the other half a placebo. The results of the pectin test group indicated a decrease in caesium-137 body burden of 33% against the placebo group with only a 14.2% decrease. The *Vitapect* also influenced the speed the body eliminated caesium-137, resulting in an achieved biological half-life of 69 days for the placebo group and only 27 days for the *Vitapect* group. This simple supplement is made from apple pectin mixed with vitamins, minerals and flavouring agents. **It is regulated and licensed by Belarusian authorities and is given to children in an oral dosage of 5g BID (2x daily) for two weeks. *Vitapect* has the advantages of being affordable and easily available [10].**

The science of Products – IQ Fiber

- Pectin molecules are long, and easily entangle with each other, causing thickening. Pectin can improve the texture of low sugar drinks.
- If enough sugar is added to reduce the availability of water to dissolve pectin molecules fully, the molecules stick together in smooth regions with ester groups to form a gel network. Conventional high sugar jams depend on pectin to set, and also require a minimum sugar content.
- Because the acid groups are relatively weak, changes in the acidity (pH) alter the amount of charge on the pectin chains. Pectins which can link together under acid conditions have enough charge at lower acidity (higher pH) to repel each other. This explains why it needs both sugar and acid to set a jam or jelly.
- The acid groups in pectins can react with calcium ions which have two positive charges, and can link two acid anion groups with negative charges. If enough negative groups occur together, as in low ester pectins, these can link pectin molecules together in a gel network without needing so much sugar. Low ester pectins are used to make low sugar jams, and many different fruit preparations for use in the food industry.
- Pectin molecules with a negative charge can bind to proteins carrying a positive charge and prevent them coagulating when heated. Pectins can stop the milk protein in yoghurt from curdling with heat, so heat treated (UHT) long life yoghurt drinks can be made.

Types of Pectin

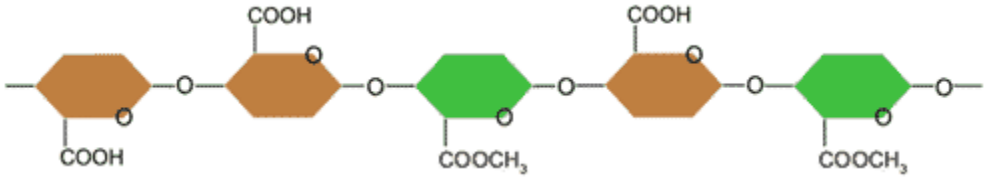
Pectin as extracted normally has more than 50% of the acid units esterified, and is classified as "high methyl ester (HM) pectin".



HM pectin formula

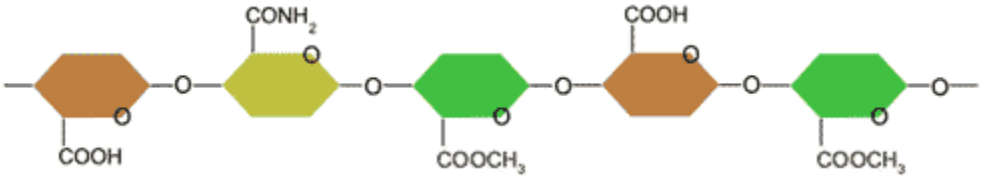
The percentage of ester groups is called degree of esterification. High methyl ester pectins are classified in groups according to their gelling temperature as rapid set to slow set pectins (see application of pectins).

Modification of the extraction process, or continued acid treatment, will yield a "low methyl ester LM) pectin" with less than 50% methyl ester groups.



LM pectin formula

Some pectins are treated during manufacture with ammonia to produce amidated pectins, which have particular advantages in some applications.



Amidated pectin formula

Within each of these main types, there are many detailed variations prepared for different uses.

The structure of pectin molecules is the key to the properties of pectins, and their use in different applications.

Pectins in Preventive Nutrition and Therapy

28. Januar 1998 From "Vitafood Congress" (1-1997)

Pectin

Pectins are natural structural elements of the primary cell wall and the middle lamella of all higher land plants. Its physiological functionalities in plants are connecting and armouring cell structures and influencing the water household.
Pectins mainly consist of the partial methyl esters of polygalacturonic acid and their sodium, potassium, calcium and ammonium salts. Pectin is considered as a soluble dietary fibre. High methoxyl pectin is described in the United States Pharmacopeia and in general in the Austrian "Arzneimittelbuch".
Since a long time the beneficial physiological effects of pectins in human are studied and well-known.
The apple diet of Heisler (1803) and Moro (1929) is one of the most famous application of pectins to treat the inconsciousness of the gut. The phrase "an apple a day keeps the doctor away" can be reducted to the relatively high pectin content of apples.

Isolated pectins are said to have an influence on

- cholesterol, lipoprotein and bile acid metabolisms
- arteriosclerosi
- blood glucose level after a carbohydrate rich meal (diabetes mellitus type II)
- binding of heavy metals and their radionuclides
- weight reduction
- gastric diseases
- hemostasis and wound healing

In oriental medicinal herbs medicines additional influences are documented. According to Yamada (1996) herbal extracts contain substances with both low and high molecular weight. Pharmacological activities have been observed in fraction with high molecular weights from boiled water extracts of the medicinal herbs. Of the high molecular weight substances, various pharmacological activities have been observed in pectic polysaccharides and pectins.
These activities are summarized by Yamada (1996) in table 1.

Table 1

Pharmacological activity of pectins isolated from plants containing medicinal herbs

Immunostimulating activity

- Complement activating activity
- Mitogenic activity
- Fc receptor up-regulation on macrophages
  (enhancing activity of immune complex clearance)
- Stimulation of macrophage phagocytosis

Anti-ulcer activity, Anti-metastasis activity, Anti-nephritis activity and anti-nephrosis activity, Hypoglycemic activity, and Cholesterol decreasing effect
.....
Applications: Vaccine for typhoid fever, Drug delivery (arabinogalactan)

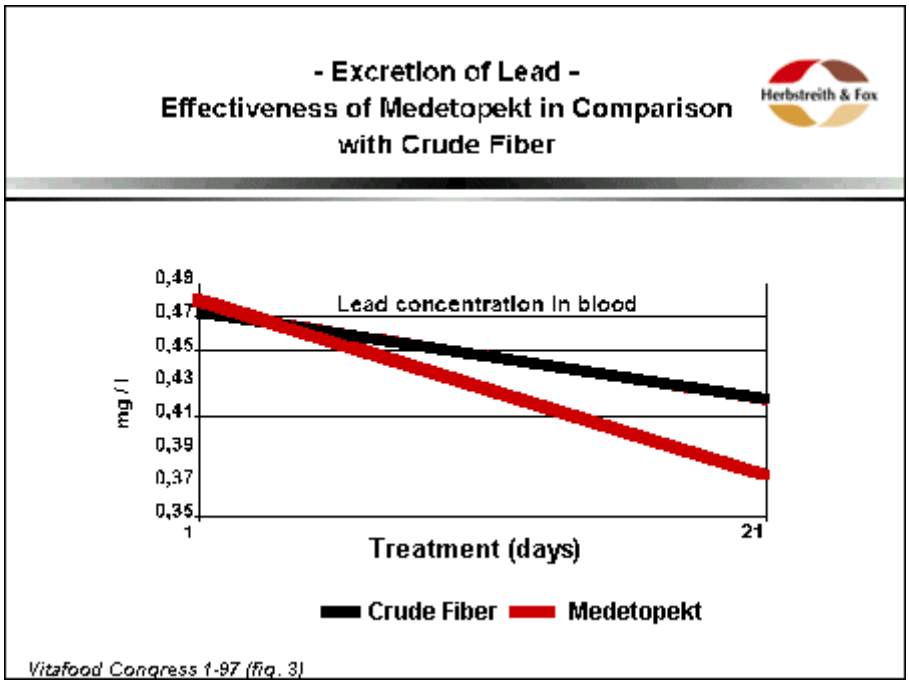
Most of these immunological or anti-metastasis activities are linked to special defined parts of pectic substances like Rhamnose-rich regions, Galactan side chains, 0-acetylated pectins or encymatically or chemically degraded pectic substances. For further information to these special kind of therapeutic effects of pectins we want to refer to Yamada (1996).

Binding and Excretion of heavy metals and their radionuclides

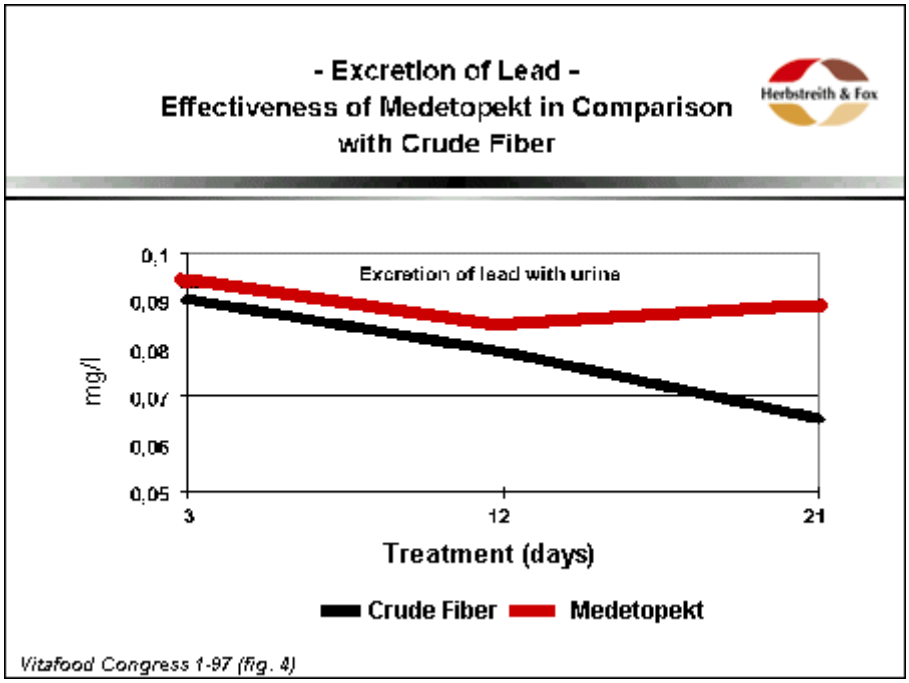
A special property of pectins is their ability to bind heavy metals by a complexation mechanism. This is possible because pectins are negatively charged polyelectrolytes and can bind positively charged heavy metal ions.
The binding affinity is very high for lead, followed by barium, cadmium and strontium and decreases to earth alkali and alkali ions. With that low methoxyl pectins are an antidote for heavy metal poisoning by an increased excretion in the stool and with that a reduced resorption. But also heavy metals once resorpted are excreted in the urine. This mechanism is based on oligogalacturonides degraded from pectin by microorganisms in the colon and with that resorpable into the body. This oligogalacturonides either catalyze an excretion reaction or bind itself heavy metals resulting in an excretion via urine. The way of action is not clearly understood up to now.

From **Herbstreith & Fox** and Sanofi-Winthrop the product **Medetopekt** was developed with the assistance of the Russian Institute of Biophysics and some other medicinal centers. **Medetopekt** is a tablet consisting of a low methoxyl apple pectin with a special improved binding capacity for heavy metals especially for lead and some other pectin rich apple components like liquid pectin dried, apple fiber and apple powder.
The effectiveness of Medetopekt was first studied with rats. It could be shown that the excretion of lead, cadmium and strontium was improved by Medetopekt. Consequent human studies in Kiew and Minsk varified these results.

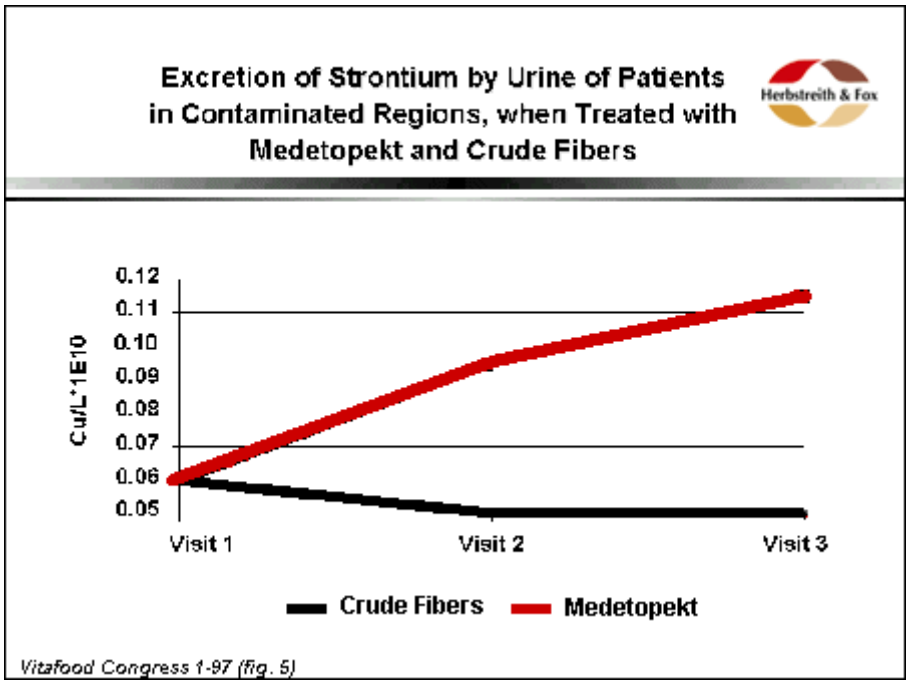
Medetopekt was tested against crude wheat fiber. In the first study the lead content in the blood was measured before and after 21 days of **Medetopekt** therapy. The results with crude wheat fiber were not significant. **Medetopekt** reduced the lead concentration from 0,48 mg per liter to 0,37 mg per liter by 23 % (see fig. 3).



The excretion of lead via urine was significantly increased after 21 days. The volunteers left during the study their unfriendly environment. With that the lead intake and naturally occuring excretion was reduced (see fig. 4).



After some time the microorganisms probably adapted to the pectin enriched food and produced more pectin degrading encymes and with that more oligogalacturonides were formed resulting in a higher resorption of these substances and a high excretion of lead via urine at the end of the study.
A further longer study carried out in these days will show if the excretion will be further increased over a longer period.
In the strontium study the radioactive strontium was measured in the urine. The excretion of strontium was not changed significantly by crude wheat fiber but increased with Medetopekt from 0,060 Curie per liter to 0,115 Curie per liter within 21 days (visit 3, see fig. 5).



Gastric deseases

Finally we can find pharmaceuticals to cure gastric deseases with pectins. In Germany for example exists the drug Diarrhoe San R, a combination of apple pectin and camilla extracts.
Already grandma applied mashed apples to her children to heal their gastric disorders. The effective component is apple pectin and eventually the phenolic components. Pectin is able to bind the harmful substances irritating the gut and/or to influence the microflora supporting the growth of beneficial bacteria and suppressing diarrhoic pathogenes.
The last pictures demonstrate the diverse market of pectin containing food supplements. You can find pure apple pectin powder, mixtures of apple pectin with oat fiber, tablets composed of pectin and grapefruit fibers and so on.
Also products based on liquid pectin, dried, from the Herbapekt product range are wide spread. Mixtures of liquid pectin with apple fiber or vitamines A, C and E, minerals magnesium and calcium and lecithin have been developed.

In the United States you can find 100 % apple pectin tablets. Famous products today are multi-fiber and multi-herb tablets pressed in separate tablets but sold in copackagings.
Germany is a growing market for fruit and fiber drinks. An example is a breakfast drink supplemented with vitamines A, C, E and dietary fibers wheat bran and a low viscosity pectin.

According to nutritional reports and recommendations there is a deficiency of dietary fibers in human nutrition. Today it seems to be more easy to market vitamines and minerals but these substances have not to be supplemented because they can be eaten very easily with regular food.
To close the deficiency of soluble dietary fiber seems to be more difficult according to these recommendations. The components in form of suitable pectins are available and the fundamental research work is done.

This is a big challenge for developing and marketing new and attractive fiber enriched foods.

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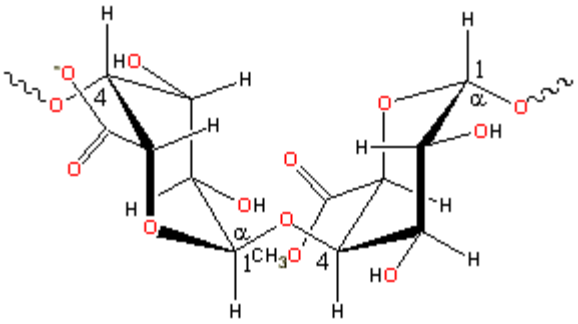
Research and Development
Herbstreith & Fox Corporate Group
Neuenbürg

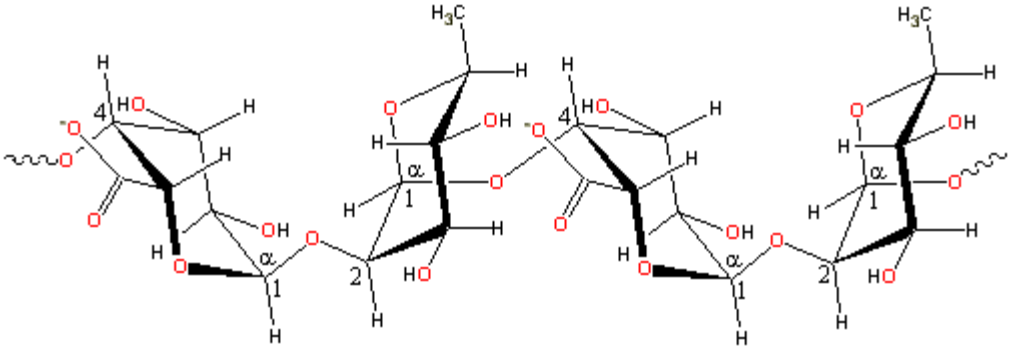
Pectin

Source: Pectin (E440) is a heterogeneous grouping of acidic structural polysaccharides, found in fruit and vegetables and mainly prepared from 'waste' citrus peel and apple pomace.

Structural unit: Pectin has a complex structure. Preparations consist of substructural entities that depend on their source and extraction methodology. Commercial extraction causes extensive degradation of the neutral sugar-containing sidechains.

The majority of the structure consists of homopolymeric partially methylated poly-α-(1⟶4)-D-galacturonic acid residues ('smooth', see right) but there are substantial 'hairy' non-gelling areas (see below) of alternating α -(1⟶2)-L-rhamnosyl-α -(1⟶4)-D-galacturonosyl sections containing branch-points with mostly neutral side chains (1 - 20 residues) of mainly L-arabinose and D-galactose (rhamnogalacturonan I). Pectins may also contain rhamnogalacturonan II sidechains containing other residues such as D-xylose, L-fucose, D-glucuronic acid, D-apiose, 3-deoxy-D-*manno*-2-octulosonic acid (Kdo) and 3-deoxy-D-*lyxo*-2-heptulosonic acid (Dha) attached to poly-α-(1⟶4)-D-galacturonic acid regions [478].





Molecular structure

Generally, pectins do not possess exact structures [328]. D-galacturonic acid residues form most of the molecules, in blocks of 'smooth' and 'hairy' regions. The molecule does not adopt a straight conformation in solution, but is extended and curved ('worm like') with a large amount of flexibility. The `hairy' regions of pectins are even more flexible and may have pendant arabinogalactans. The carboxylate groups tend to expand the structure of pectins as a result of their charge, unless they interact through divalent cationic bridging (their pK_a of about 2.9 [326] ensuring considerable negative charge under most circumstances). Methylation of these carboxylic acid groups forms their methyl esters, which take up a similar space but are much more hydrophobic and consequently have a different effect on the structuring of the surrounding water. The properties of pectins depend on the degree of esterification, which is normally about 70%. Low methoxyl-pectins (< 40% esterified) gel by calcium di-cation bridging between adjacent two-fold helical chains forming so-called 'egg-box' junction zone structures so long as a minimum of 14-20 residues can cooperate [326]. Gel strength increases with increasing Ca^{2+} concentration but reduces with temperature and acidity increase (pH < 3) [463]. It may well be that the two carboxylate groups have to cooperate together in prizing the bound water away from the calcium ions to form the salt links that make up these junction zones. The gelling ability of the di-cations is similar to that found with the alginates (Mg^{2+} << Ca^{2+}, Sr^{2+} < Ba^{2+}) with Na^{+} and K^{+} not gelling. If the methoxyl esterified content is greater than about 50%, calcium ions show some interaction but do not gel. The similarity to the behavior of the alginates is that poly-α-(1⟶4)-D-galacturonic acid is almost the mirror image of poly-α-(1⟶4)-L-guluronic acid, the only difference being that the 3-hydroxyl group is axial in the latter. The controlled removal of methoxyl groups, converting high methoxyl pectins to low-methoxyl pectins, is possible using pectin methylesterases but the reverse process is not easily achieved.

High methoxyl-pectins (> 43% esterified, usually ~67%) gel by the formation of hydrogen-bonding and hydrophobic interactions in the presence of acids (pH ~3.0, to reduce electrostatic repulsions) and sugars (*e.g.* about 62% sucrose by weight, to reduce polymer-water interactions) [664]. Low methoxy-pectins (~35% esterified), in the absence of added cations, gel by the formation of cooperative 'zipped' associations at low temperatures (~10°C) to form transparent gels [684]. This hydrogen-bonded association is likely to be similar to that of alginate (see above). The rheological properties of low methoxy-pectins are highly dependent on the salt cation, salt concentration and pH.

Functionality

Pectins are mainly used as gelling agents, but can also act as thickener, water binder and stabilizer. Low methoxyl pectins (< 50% esterified) form thermoreversible gels in the presence of calcium ions and at low pH (3 - 4.5) whereas high methoxyl pectins rapidly form thermally irreversible gels in the presence of sufficient (*e.g.* 65% by weight) sugars such as sucrose and at low pH (< 3.5); the lower the methoxyl content, the slower the set. The degree of esterification can be (incompletely) reduced using commercial pectin methylesterase, leading to a higher viscosity and firmer gelling in the presence of Ca^{2+} ions. Highly (2-O- and/or 3-O-galacturonic acid backbone) acetylated pectin from sugar beet is reported to gel poorly but have considerable emulsification ability due to its more hydrophobic nature, but this may be due to associated protein impurities [309].

As with other viscous polyanions such as carrageenan, pectin may be protective towards milk casein colloids, enhancing the properties (foam stability, solubility, gelation and emulsification) of whey proteins whilst utilizing them as a source of calcium.

Pectin

In the making of jams and jellies, there is a choice between using the pectin normally in the fruit totally or of adding commercial pectin. Most commercial pectin is made from citrus fruit peels. Apple pomace (the residue after pressing apples for cider) can also be used. Apples can also be used at home to make a pectin rich extract for use with products low in pectin.

How to make your own apple pectin

For use in making jellies from fruits such as peaches, strawberries, cherries, etc., or those fruits which are lacking in pectin. Use 2 lb. apple pulp (or skins and cores), 4 c. water, juice of one lemon, and boil for 40 minutes. Press the juice through a cloth bag, then strain the juice through a flannel bag (or triple layers of cheesecloth) without pressing. Boil this juice rapidly for 15 minutes. This makes about 4 cups of apple pectin. To use: add 1 c. of apple pectin for each cup fruit juice used. If you wish to use the apple pectin at a later date, after the 15 minute boil, pour hot juice into sterilized hot half-pint jars and process for 10 min. in boiling water bath for altitudes over 1000 feet. Source: Kerr, 1993

Pectin purchased in the grocery or extracted from fruit is technically "high methoxyl pectin." A different form called "low methoxyl pectin" also exists. Low methoxyl pectin is unique in that it does not require sugar or as much acid in order to form a gel. However, it does require the addition of calcium or magnesium. This solves the structural problem of omitting sugar, but the preservative nature of sugar still needs to be replaced before successfully making no-sugar jelly. In this situation, sodium benzoate and/or potassium sorbate may be added as preservatives in commercial products. When using low methoxyl pectin, sweetener substitutes or sugar may be used to sweeten the product to the desired level.

Pectin substitutes

Some commercial products replace or supplement the pectin with gums or modified starch products. Efforts to replace pectin at home have used gelatin or a modified cornstarch (ex. ClearGel). Neither gelatin nor modified starches require sugar to form a gel, thus artificial sweeteners can be used. The issue of safety is resolved by keeping the gelatin-based jelly refrigerated and only for limited storage time. Starch-thickened fruit juice can be canned using the time tables available for pie fillings. Neither product is the same as traditional jelly nor jam. Gelatin-based ones tend to spread over bread similar to spreading Jell-O and the starch-based ones yield a sweet gravy-like product. It is also possible to cook fruit pulp down until thick, add artificial sweetener and refrigerate the product for a week or two or freeze the product.

The ingredients listed on packages of commercial pectin or of jelly products are there to serve a function. The following table is to provide a guide to common ingredients.

Reading labels on pectin packages and commercial jam/preserve jars

Pectin	This may be low methoxyl or high methoxyl pectin
Dextrose Sugar High fructose corn syrup Corn Syrup Concentrated fruit juice	Simple sugar used to disperse pectin in package Table sugar (sucrose) from beets or sugar cane Substitute for sucrose. Fructose is a simple sugar. Substitute for sucrose. Dextrose, maltose syrup Juice with most of water removed. High in sugars.
Fumaric acid Citric acid	Both are acid sources to help pectin molecules associate and form the gel structure.
Calcium citrate Calcium chloride	Sources of calcium to help low methoxyl pectins form a gel structure.
Sodium benzoate Potassium sorbate	Control microbial growth Control microbial growth
Maltodextrin Polydextrose Guar gum	Fragmented starch molecule. Adds thickness. Modified starach. Adds bulk. No calories Carbohydrate extract from guar plant seeds. Forms gel.

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90 caps 300 IU $21.95
This natural source of vitamin E is two to five times more bioavailable than synthetic vitamin E (DL-Alpha) in terms of body distribution and tissue retention. Alpha-tocopherol supplements are available in the ester forms: alpha-tocopheryl succinate and alpha-tocopheryl acetate. Tocopherol esters are more resistant to oxidation during storage than unesterified tocopherols. Alpha-tocopherol is the only form of vitamin E that is actively maintained in the human body; therefore, it is the form of vitamin E found in the largest

quantities in blood and tissues. The main function of alpha-tocopherol in humans appears to be that of an antioxidant. [http://www.worldwidehealthcenter.net/category.php?prod=802]

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1: Swiss Med Wkly. 2004 Jan 10;134(1-2):24-7.

Reducing the 137Cs-load in the organism of "Chernobyl" children with apple-pectin.

Belrad Institute of Radiation Safety, Charity House, 11 Staroborisovsky Trakt, 220114 Minsk, Republic of Belarus. nester@hmti.ac.by

As a complement of standard radioprotective measures, apple-pectin preparations are given, especially in the Ukraine, to reduce the 137Cs uptake in the organism of children. The question has been raised: is oral pectin also useful when children receive radiologically clean food, or does this polysaccharide only act in binding 137Cs in the gut, blocking its intestinal absorption? In this case, pectin would be useless if radiologically clean food could be given. The study was a randomised, double blind placebo-controlled trial comparing the efficacy of a dry and milled apple-extract containing 15-16% pectin with a similar placebo-powder, in 64 children originating from the same group of contaminated villages of the Gomel oblast. The average 137Cs load was of about 30 Bq/kg bodyweight (BW). The trial was conducted during the simultaneous one-month stay in the sanatorium Silver Spring. In this clean radiological environment only radiologically "clean" food is given to the children. The average reduction of the 137Cs levels in children receiving oral pectin powder was 62.6%, the reduction with "clean" food and placebo was 13.9%, the difference being statistically significant ($p < 0.01$). The reduction of the 137Cs load is medically relevant, as no child in the placebo group reached values below 20 Bq/kg BW (which is considered by Bandazhevsky as potentially associated with specific pathological tissue damages), with an average value of 25.8 +/- 0.8 Bq/kg. The highest value in the apple-pectin group was 15.4 Bq/kg, the average value being 11.3 +/- 0.6 Bq/kg BW.

PMID: 14745664 [PubMed - indexed for MEDLINE]

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1: Lik Sprava. 1993 Jul;(8):21-4. Links

[Pectin-containing products in the dietary nutrition of subjects exposed to ionizing radiation as a result of the accident at the Chernobyl Atomic Electric Power Station]

[Article in Russian]

Effect of natural and enriched with pectin tanned fruits on radiation-induced metabolic disorders was studied in persons subjected to radiation due to Chernobyl accident. It was shown that products in question beneficially influenced blood antioxidant system as well as brought to the norm contents of triglicerides and albumins in patients with IIa and IV types of hyperlipoproteinaemia.

PMID: 8079467 [PubMed - indexed for MEDLINE]

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From the Magazine | Science

Fallout in the Food Chain

Posted Friday, Sep. 13, 1963

The Eskimo village of Anaktuvuk Pass in Alaska's desolate Brooks Range north of the Arctic Circle has a post office, a school and an airplane landing strip. But for all its modern trimmings, Anaktuvuk is barely out of the Stone Age. Its 15 families (averaging five children and 12 dogs each) are remnants of the nomadic Nunamiuts. Their lives are devoted to hunting the Arctic caribou, which supplies 90% of their food as well as most of their clothing. Merely to stay alive, one Nunamiut family must kill 90 caribou a year.

Fortunately, caribou are still plentiful near Anaktuvuk Pass, and no one is going hungry. But contemporary civilization is closing in with deadly effect. Radioactive fallout from Russian and U.S. nuclear tests has dangerously poisoned the Nunamiuts' barren homeland. Fallout there has been no thicker than in many other parts of the world, but it has concentrated ominously in the bodies of the Eskimos. A report made for the Atomic Energy Commission by General Electric scientists showed that in the summer of 1962, the inhabitants of Anaktuvuk Pass had an average "whole body burden" of 421 nanocuries*of caesium 137, one of the most harmful constituents of fallout. This is nearly 100 times the burden of fallout picked up by people in what Alaskans call "the lower states."

In July, AEC Official H. M. Parker reported an average body-burden increase of 50% in a year. One Eskimo's count increased by 112%; the highest burden measured was 1230 nanocuries. This is more than one-third of the maximum permissible amount (3,000 nanocuries) established by the International Committee on Radiation Protection.

Radioactive Skimmings. University of Alaska Zoologist William O. Pruitt, an authority on caribou, gave the beasts a thorough going over and found that their flesh contained an unusual amount of caesium 137. After that, the story unfolded with dangerous logic. The caribou's winter food is largely lichens, a primitive plant that has no roots but gets its moisture and nutrients entirely from the air. Its spongy tissues soak up the scant Arctic rain like blotting paper and retain a large part of it. The fallout that is carried down by the rain is retained too. Instead of mixing harmlessly with the soil, it goes into the stomachs of caribou and becomes part of their bones and flesh. When Eskimos eat the caribou, they get the radioactive skimmings of many acres of lichen-covered ground.

Once he made his discovery, Dr. Pruitt began a loud vocal opposition to the AEC's Project Chariot, which was a plan to use nuclear explosives to blast a spacious harbor in the Alaskan coast. The side effects, he said, would harm the Eskimos even more. Although he was fired from the university, he continued to make all the noise he could about the danger of feeding more fallout into the Eskimo food chain. The AEC's present management now watches the Eskimos carefully and measures their body burden as it creeps ever higher.

Higher & Higher. It would be helpful, indeed, if the Nunamiuts could change their diet, but in the bleak Brooks Range there is almost nothing but caribou to eat, and any kind of agriculture is impossible. The Eskimos could be fed on handouts of white men's food, which would destroy their self-sufficiency and probably their health, or they could be moved elsewhere. They do not relish either prospect. Says Simon Paneak, head of the village council: "We only know how to live here." Though he remains close kin to Stone Age man, he understands the problems of radiation only too well. "It keeps getting higher and higher, and we just don't know what to do."

So far, the Nunamiut Eskimos have shown no symptoms of the serious illnesses that can come from too much radiation, but no scientist can be confident that such symptoms will not appear. In the future, though, if the U.S. and Russia stick to their recently signed agreement to stop nuclear testing in the atmosphere, the contaminated lichens of northern Alaska will gradually lose their dangerous radioactivity. The body burdens of the caribou will fall little by little. Eventually the people of Anaktuvuk Pass will be no more radioactive than any other Americans.

*Thirty-seven atomic disintegrations per second, or one-billionth of a curie.

From the Sep. 13, 1963 issue of TIME magazine

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Article: 1095 of sgi.talk.ratical
From: (dave "who can do? ratmandu!" ratcliffe)
Subject: ***Nature*** **9/92: Thyroid Cancer 7.5 years after Chernobyl, soaring**
Summary: **fallout from Chernobyl "on schedule" despite Official "No Danger" Myths**
Keywords: **thyroid carcinoma, fetal thyroid concentrating iodine**
Date: 25 Jun 1995 21:15:11 GMT
Organization: Silicon Graphics, Inc.
Lines: 341
(ASCII text)

One of the most pervasive myths about Chernobyl is that only 3% of the reactor core was released into the biosphere when the explosion occurred on April 26, 1986. Vladimir Chernousenko, Scientific Director of the Ukrainian Academy of Sciences' Task Force for the Rectification of the Consequences of the Accident, in his 1991 book *Chernobyl, Insight from the Inside*, dispels this myth (and a partial list of 20 others), citing,
A more official view on `The Nuclear Accident in Block 4 of the Chernobyl Nuclear Power Station and the Safety of the RBMK Reactor' give[s] the following excerpts from an unpublished report by A.A. Yadrikhinskii, Nuclear Safety Inspection Engineer of the USSR State Atomic Energy Survey Commission (Kurchatov town, RSFSR February, 1988):

. . . Radiation emission was no less that 80% of the core (with a total of 192 tons), which amounted to 6.4 x 10^9 Ci.[16] If we divide the figure by the population of the whole earth (4.6 x 10^9 people) then we get 1 Ci per person.[17]

Choosing to ignore the facts about how we are collectively contaminating this Earth with lethal-to-all-life-doses of man-made nuclear fission products will ensure the cessation of billions of years of life exploring itself on this planet. It doesn't have to go down this way. If we were living in the areas that the children described below are, we would not be able to ignore the facts which the International Nuclear Mafia continuously deny when they parrot the line in the global media about how "There's no health danger from nuclear power" and "No one died at Chernobyl" and "This form of energy is clean and safe; anyone who says otherwise doesn't know what they're talking about".

from the *San Francisco Chronicle*, Thursday, September 3, 1992:
And see the June 30, 1999 Reuters story below regarding
Thyroid cancer 10 times higher in Chernobyl kids

Thyroid Cancer on Rise For Chernobyl Children

New York

Children who were exposed to radiation from the Chernobyl nuclear power plant disaster are developing thyroid cancer sooner and in larger numbers than expected, researchers report.

The results are the first reliable data in the population downwind of the Chernobyl accident in 1986, said Dr. Marvin Goldman, a radiation biologist at the University of California at Irvine who was not involved in the new study.

An increase in thyroid cancer had been reported earlier, but some Western health officials had expressed concern about the reliability of the data.

In a letter published yesterday in *Nature*, a British science journal, Dr. Vasily S. Kazakov of the Belarus Ministry of Health in Minsk and his colleagues say that the thyroid cancer rates in the regions most heavily irradiated began to soar in 1990.

In Gomel, the most contaminated region studied, there used to be just one or two cases of thyroid children a year. But Kazakov and his colleagues found that there were 38 cases in 1991. In six regions of Belarus and the city of Minsk, the investigators found 131 cases of thyroid cancer in young children, some of whom were still in the womb when the Chernobyl accident occurred.

Because of questions about the cancer reports, the World Health Organization sent a team of scientists to Minsk to verify the reports. In an accompanying letter in *Nature* yesterday, they confirmed Kazakov's results.

Children are particularly susceptible to thyroid cancer from radioactive iodine because their thyroid glands are small and concentrate the iodine from radioactive fallout because they drink more milk and get larger doses of radioactive iodine and because their thyroids are thought to be more vulnerable to the radiation.

Thyroid cancer is usually very amenable to treatment, said Dr. Blake Cady, a cancer surgeon and thyroid cancer specialist at the New England Deaconess Hospital in Boston. But investigators were struck by the seeming aggressiveness of some of the children's cancers. A 7-year-old child died and 10 other children are seriously ill, they reported.

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SCIENTIFIC CORRESPONDENCE

Thyroid cancer after Chernobyl

SIR--We would like to report a great increase in the frequency of thyroid cancer in children in Belarus, which commenced in 1990 and continues. Table 1 shows the incidence of thyroid cancer in children in the six regions of Belarus and Minsk City from 1986 to the end of the first half of 1992. It can be seen that the overall incidence rose from an average of just four cases per year from 1986 to 1989 inclusive, to 55 in 1991 and is projected to be not less than 60 in 1992. This increase is not uniformly distributed across the country: for example, there is no significant increase in Mogilev, Minsk City or Vitebsk. By far the greatest increase is seen in the Gomel region, from one or two cases per year to 38 in 1991, and a less obvious increase is seen in the Brest and Grodno regions.

TABLE 1 Incidence of thyroid cancer in children in Belarus

Region of Belarus	Years 1986	1987	1988	1989	1990	1991	1992*	Total
Brest	0	0	1	1	6	5	5	18
Vitebsk	0	0	0	0	1	3	0	4
Gomel	1	2	1	2	14	38	13	71
Grodno	1	1	1	2	0	2	6	13
Minsk	0	1	1	1	1	4	4	12
Mogilev	0	0	0	0	2	1	1	4
Minsk City	0	0	1	0	5	2	1	9
Total	2	4	5	6	29	55	30	131

* Six months of 1992

The Gomel region lies immediately to the north of Chernobyl and is known to have received a high level of radioactivity as fallout after the breakdown of reactor number 4 on 26 April 1986. The plume passed first over the Gomel region in the first few hours after the major release of radioactivity, and then over the Brest and Grodno regions. The fallout contained large amounts of iodine-131 and significant amounts of the short-lived isotopes of iodine, although these were too short-lived to be measured.

We have classified the tumours according to the World Health Organisation classification (2nd edn) and find that virtually all are papillary carcinomas (128 of 131). They are, however, relatively aggressive, as can be seen from Table 2. Fifty-five of the 131 cases showed direct extension to the perithyroid tissues and six distant metastases, mostly in the lungs. It can be seen that only about 23 per cent were less than 1 cm in diameter. One of the children has died at seven years of age and ten others are seriously ill.

TABLE 2 Extent of spread (TNM classification) of thyroid cancer in children

TNM symbol		Total number of cases	Lymph node metastases: None(N O)	Ipsilateral(N 1a)	Other(N 1b)
	Tumour size				
<1 cm	T1	30	17	10	3
1-4 cm	T2	33	17	8	8
>4 cm	T3	7	3	4	0
	Extending to surrounding				
tissues	T4	55	14	18	23
	Distant				
metastases	M1	6	1	1	4
Total		131	52	41	38

Classification as in *TNM Atlas* 3rd edn, eds Spiessl, B. *et al.*, UICC (Springer, Berlin, 1990).

The occurrence of this increase in thyroid cancer in children within a few years of exposure to radioactive isotopes of iodine is unexpected, but real. It poses both humanitarian and scientific problems, and is placing great strains upon the health services of our new country. It also provides an opportunity, which we hope will not be repeated, to study the consequences of major exposure of a population to isotopes of iodine from fallout. We are collaborating with several international groups and are preparing detailed reports of various aspects of the problem.

We believe that the only realistic explanation for the increase in the frequency of thyroid cancer is that it is a direct consequence of the accident at Chernobyl.

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SIR--We have recently visited Belarus under the auspices of the WHO regional office for Europe and the Swiss government, and have had the opportunity to see some of the children with thyroid cancer, to study the pathology of the cases and to examine the relevant data.

We examined 11 children who had had operations for thyroid carcinoma and were now hospitalized for post-operative management or evaluation of metastatic disease. We were shown the complete records for these patients, including X-rays and echograms before and after treatment. All were diagnosed during the past 3 years, eight having been living in the Gomel region at the time of the Chernobyl accident and two in the Brest region. The age at diagnosis of the six females and five males was between 4 and 13 years of age; the youngest was born two days after the accident.

We have studied the histological slides from 104 cases of children from Belarus in whom the diagnosis of thyroid carcinoma had been made since January 1989. We agree both with the diagnosis of malignancy and of the type of malignancy in 102 of the cases. We also examined the data on the incidence of thyroid carcinoma in Belarus. There is a marked increase in frequency from 1990 onwards over the average for the years from 1986 to 1990. This increase started only 4 years after the Chernobyl accident, a surprisingly short time by comparison with studies of thyroid carcinoma that have followed exposure to external radiation in infants[1,2]. Of the children with thyroid carcinoma in Belarus since 1990, the eight youngest at exposure were *in utero*, but were more than 3 months of fetal age at the time of Chernobyl. The fetal thyroid is known to start concentrating iodine at 12-14 weeks of gestation.

We do not believe that increased ascertainment of cases could have played more than a minor role in the recorded incidence of thyroid carcinoma. The proportion of resected nodules that are malignant is high and the type of tumour is aggressive. The ratio of thyroid carcinoma in children to that in adults has increased dramatically, although there are now signs that the incidence in patients over the age of 15 is beginning to increase. The rate is greatly in excess of the reported incidence of this disease in children under 15 years of age, which is of the order of I per million per year[3-6]. In the Gomel region (total population about 2.5 million), the region of Belarus that received the highest fallout from Chernobyl, the incidence in 1991 and the first part of 1992 is approximately 80 per million children per year.

It is generally accepted that external radiation to the neck is associated with an increased incidence of thyroid carcinoma in man, and there is an increased sensitivity of the infant thyroid to the carcinogenic effect of radiation[2]. In some animal studies, but not all[7,8], external radiation is found to be a more effective carcinogen for the thyroid than iodine-131. Clear evidence that the diagnostic or therapeutic use of radioiodine in man carries a carcinogenic risk is lacking[9,10], and iodine-131 has provided a safe and effective treatment of Graves' disease in adults, although it is rarely used in young children.

The combination of the high level of exposure to radioactive fallout and the numbers exposed within a short time after its release makes the Chernobyl accident an unprecedented event. In the Marshall Islands, although the doses were probably comparable, the number of people exposed was several orders of magnitude smaller[11]. In the case of the accident at Windscale (now called Sellafield), the number exposed was substantial but the doses were smaller[12], and no adequate study of any long-term thyroid effects has yet been reported. Other studies of fallout from weapons and of nuclear accidents (such as on Three Mile Island) have yielded inconclusive evidence. A close relationship between radiation dose and the incidence of thyroid carcinoma has been documented in atomic bomb survivors in Japan[13], but the radiation received was mostly external and the contribution from fallout is uncertain.

We believe that the experience in Belarus suggests that the consequences to the human thyroid, especially in fetuses and young children, of the carcinogenic effects of radioactive fallout is much greater than previously thought. Studies of the Marshall Islanders, of the atomic bomb survivors and of the effects of external radiation on the thyroid suggest that the incidence of thyroid cancer in Belarus will be raised for many years.

The accident and its impact on Belarus poses a challenge to the international community to help, both in dealing with the extensive present and future public health consequences, and in promoting research for the understanding of the basic processes underlying the phenomenon. Understanding the consequences of Chernobyl will provide an important basis for preventive action in future.

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Thyroid cancer 10 times higher in Chernobyl kids

Wednesday, June 30, 1999

WASHINGTON (Reuters) - The rate of thyroid cancer remains 10 times higher than normal among young Ukrainian children 13 years after the accident at the Chernobyl nuclear power plant, researchers said Wednesday.

They reported 577 cases of thyroid cancer in Ukrainian children between 1986, when the accident occurred, and 1997, compared to 59 cases in the same age group from 1981 to 1985. The reactor at Chernobyl caught fire in the early hours of April 26, 1986, spreading a radioactive cloud over much of Ukraine, Russia, Belarus and other parts of Europe. It killed 31 people and affected thousands more. In Belarus, where 70 percent of the radiation was deposited, the World Health Organization says thyroid cancer rates among children are 100 times pre-accident levels. "Children constitute the most vulnerable group of exposed individuals, because their thyroid sensitivity to radiation is high, and there is a longer life span to manifest its effects," Dr. Virginia LiVolsi of the University of Pennsylvania Medical Center in Philadelphia, said in a statement. "These factors make it necessary to follow thyroid function in exposed subjects for decades." Reporting in the journal cancer, LiVolsi said her team found that 64 percent of all Ukrainian thyroid cancer patients aged 15 or younger lived in the most contaminated regions -- the provinces of Kiev, Chernigov, Zhitomir, Cherkassy and Rovno. More than 40 percent of patients were children 4 or younger at the time of the accident. "The group at maximum risk is those exposed to high radiation levels when they were younger than 5 years," LiVolsi said. "This is the age when the thyroid gland is most sensitive to ionizing radiation." The American Cancer Society predicts that more than 18,000 adults in the United States will be diagnosed with thyroid cancer in 1999. About 1,200 will die. There is a way to help prevent thyroid cancer caused because of exposure to radioactivity. In Poland, where potassium iodide was given to 97 percent of children, there has been no similar increase in thyroid cancer although the country was also exposed to radioactive clouds from Chernobyl. Last week the U.S. Nuclear Regulatory Commission proposed that potassium iodide be stockpiled to protect the public from a major release of radiation during a nuclear power plant accident.

HEALTH EFFECTS OF THE CHERNOBYL ACCIDENT

Ten years ago this April, massive explosions rocked unit 4 at the Chernobyl nuclear power plant in Ukraine, then part of the Soviet Union. It was the worst accident in the history of commercial nuclear energy.

The cause of the accident was twofold: operator error and a flawed reactor design. In an ill-advised and uncoordinated test, operators were running the plant outside its design parameters at very low power. The test got out of control, and the reactor's design flaw caused a sudden, rapid surge in power that led to a chemical explosion. The explosion vaporized some of the nuclear fuel and propelled radioactivity high into the early morning sky. It fell to earth over large areas of Ukraine and its neighboring republics, Belarus and Russia. It was also detected in many countries of Western Europe - and beyond. In the years since, Chernobyl has become a catchword

for disaster. Any Soviet designed reactor is deemed unsafe-and regardless of its design type- is called a Chernobyl-type nuclear reactor. Any disease or death that cannot be satisfactorily explained is blamed on Chernobyl. Reports of thousands, tens of thousands and even hundreds of thousands of Chernobyl-induced deaths are not uncommon. (There is even a report that Chernobyl caused 40,000 deaths in the United States). They are also untrue. In fact, 31 people died as a result of the accident, most of acute radiation sickness. They were either workers at the plant or firemen called in to tame the blazes. The accident is also most certainly responsible for more than 500 cases of childhood thyroid cancer. And the mass evacuation of people from affected areas - not to mention the official secrecy and mishandling of the accident's aftermath- caused tremendous stress, which has resulted in a number of psychological disorders. But other than the thyroid cancer in children, no study to date has shown an increase in leukemia or solid cancers that can be caused by radiation.

The long term health effect of the Chernobyl accident may never be clear. But it's in everyone's interest to continue studying the affected population. Major strides have been made in the past decade n the treatment of children with thyroid cancer, in the quality of cancer registries, health studies and research infrastructures, and in the training of epidemiologists and medical personnel. In addition, Russia and Ukraine - with the support of countries like the United States- have done much to improve safety and reliability of their nuclear power plants. This special report examines what we know - and what we don't - 10 years after the Chernobyl accident.

TRUTHS AND CONSEQUENCES:

It was nearly 1:30 in the morning on Saturday, April 26 1986, and Andrei Glukhov was still awake in his apartment in the town of Pripyat, two miles from the Chernobyl nuclear power plant, when he heard the sound. There were two explosions, followed by a momentary interruption of the electricity supply. The sound was similar to that made by the special relief valves in the plant turbines. When they shut down, there was a boom and sometimes a power interruption says Glukhov, who was an employee of the plant. I assumed that one of the units had gone off line. Five hours later, a friend telephoned. He said that something had happened at the plant, and he asked me to call the control room and get some information, says Glukhov. But when Glukhov telephoned Unit No. 4 no one answered. So he called Unit 2 and talked to one of the reactor operators. I asked him about the status of Unit 4. There was silence. Then he said "Look out your window " . Units 3 and 4 were housed in the same building, which was painted white. But that morning, says Glukhov, the part of the building containing Unit 3 was white, while the part containing unit 4 was black. I saw smoke coming out of unit 4 , and I knew that something serious had happened. "I don't like to remember that time" says Glukhov. But the memory of the accident haunts him still. I can t escape it. The explosion of Chernobyl unit 4 reactor released large amounts of radioactive iodine, cesium and other isotopes. They were carried on the wind and washed out of the skies by rain to contaminate significant areas of Ukraine- where Chernobyl is located- Belarus and Russia. It would be days before the full extent of the accident was known. The local security apparatus immediately drew a veil of secrecy across the plant. Even plant employees , like Glukhov, who had been a reactor operator and was working at Chernobyl 's nuclear safety division at the time, were told nothing. The coverup extended to Pripyat, where plant employees and their families lived. Special troops were sent to the town to carry out initial decontamination. but the official explanation was that they were on a training exercise says Glukhov. Meanwhile, the wind - which had been blown away from Pripyat at the time of the accident- changed direction. The authorities said nothing, and life went on normally that Saturday. Children played outside. There were even several outdoor weddings says Glukhov. That evening, volunteers from the young communist league were sent round to distribute potassium iodine pills to Pripyat residents. But it was a hit-or -miss operation. No one came to our apartment building at all says Glukhov. Then early Sunday morning came the announcement: The town was being evacuated. Residents were told to take only their documentation, plus some pillows, sheets and blankets for a few day s stay in the countryside. The authorities lied. They said that families would be relocated for only three or four days. So people left everything behind says Glukhov. Today Pripyat is a ghost town. Pictures decorate apartment walls, cabinets are stocked with dishes and cutlery, children's toys are scattered about. Pripyat is a legacy of the accident. So too are the more than 550 cases of thyroid cancer diagnosed to date in children below the age of 15- about 330 in Belarus , 200 in Ukraine and 25 in Russia. The incidence of the tumors has risen sharply, especially in Belarus. For the country as a whole , the number of cases between 1990 and 1995 is abut 50 times that in the United Kingdom, says professor Dilwyn Williams, who specializes in thyroid studies at Addenbrokes Hospital in Cambridge, England. And in the Gomel region of Belarus the incidence rate is close to 200 times that found in the United Kingdom.

CONTAMINATED MILK:

Some of the radioactive iodine that spewed out of the damaged reactor ended up in the food chain. It fell onto plants, the plants were eaten by cows, and the milk from those cows was drunk by children. The authorities could have broken the link by simply prohibiting the consumption of milk.

"That's a high crime", says Marvin Goldman, professor emeritus at the University of California at Davis. The cases of childhood thyroid cancer could have been largely prevented if the authorities had supplied powdered milk, for instance. If detected sufficiently early, thyroid cancer can be treated with surgery, followed by iodine 131 therapy and then thyroid hormone replacement. About 15 percent - or roughly one in seven- of all cases of childhood thyroid cancer will result in complications, says Cristoph Reiners, director of the nuclear medicine clinic at the University of Wurzburg in Germany. If the complications aren't treated in time they could result in death at a later date. Reiners has treated 99 children from Belarus at the clinic, using funding from German utilities. He says," We've completed

treatment for 58 percent, and they were cured. The remainder are sill being treated, but I would estimate that 10 percent of them won't respond well to radioactive treatment."

Those children who were among the first to be diagnosed with thyroid cancer in the former soviet union didn't receive optimal treatment, says Reiners. Surgeons didn't have the right instruments, radioiodine treatment wasn't available, at last in Belarus, and imported thyroid hormone was of poor quality. According to an expert at the World Health Organization, at least five children have died of the disease, two in Russia, two in Ukraine and one in Belarus. But treatment is better now, and the long term prognosis for children with the disease is quite good , says Reiners. That the accident was responsible for the dramatic increase in childhood thyroid cancer is generally accepted. I have seen about half of the post-Chernobyl tumors personally , says Williams. I have no doubt that they are in general accurately diagnosed, and that they are related to the Chernobyl accident and almost certainly to the uptake of radioactive iodine. Several studies have suggested a casual relationship. But a small case-control study in Belarus involving 321 children -107 with thyroid cancer and 214 in the unaffected control group- provides the strongest evidence to date that the cancers are the result of the Chernobyl accident, says Gilbert. Beebe, an epidemiologist at the US national cancer institutes radiation epidemiology branch.

MISSING INFORMATION:

What about the accidents other health effects ? That's a much tougher question. Key pieces of information are often missing, such as dosimetric data on the amount and type of radiation people were exposed to. Records of the incidence of disease and causes of death for people in the affected areas - both before and after the accident- often aren't available. The latency period for solid-tumor cancers is at least 10 years. The people affected by the accident fall into two major groups- the cleanup workers called liquidators and the general population. Included in the cleanup worker category are the firemen who tried to contain the blazes and the plant workers who aided their colleagues - a group numbering several hundred. They were exposed to very high levels of radiation, and more than 200 suffered from acute radiation sickness as a result. Within a four-month period, 31 of them died. In addition hundreds of thousands of people from military and civilian walks of life helped clean up in the weeks and months after the accident. They worked at the plant site and within the 30-kilometer (18 mile) restricted zone around Chernobyl. Estimates of the number of these workers range wildly from 300,000 to 800,000 and information on the doses they received is incomplete and often unreliable. More than 400,000 people living in areas affected by the accident were evacuated . Their displacement was a wrenching experience. It severed community ties and forced people to cope with unfamiliar surroundings. This uprooting also feeds people's fear. "They re worried ", says Williams. The stress of knowing that you and your children were exposed to an unknown amount of radiation that you can't see, touch or smell is understandable. And this stress has created a significant he health problem for Ukraine, Belarus and Russia.

RADIOPHOBIA:

There is an epidemic of radiophobia, says Goodman. Scientists may pooh-pooh it. But it s had a hell of an effect on people. The result has been an increase in such stress-induced disorders as high blood pressure and ulcers. But the appearance of cancer- to be expected in any population group- also is being laid at the door of Chernobyl. When a disease occurs, there s a natural tendency to try to find out t he cause of it, says NCI's Beebe. It s common to blame some different experience that you had for your present difficulties. Chernobyl comes in for an awful lot of blame for illness that is probably unrelated to it. "The claims that every childhood malfunction has been caused by Chernobyl are just not true", says Williams. But without accurate data, how can you say they are not true? What's needed is some honesty, says Goldman. Someone needs to say: This is how bad it was. But to do that, he adds , "we need credible dose reconstruction, so we can say: You were in an area with such and such a dose." That entails identifying the type and amount of radioactivity that fell to earth, where it was deposited, who was in the area at the time, for how long, and what they were doing. Even today, some of the pieces of that puzzle are missing. Until we can identify precisely what the liquidators were doing, for example, we won't know if they received significant doses , says Colin Muirhead, head of the epidemiology group at Britain's National Radiological Protection Board (NRPB). John Harrison, who's responsible for the NRPB s medical division, believes that retrieving good data may be difficult because of the stranglehold that the security services had on the release of information at the time of the accident. Hopefully this information will now be made available.

Tracking down people who were living or working in the areas affected by Chernobyl is a problem too. In most cases ,says the NCI's Beebe, we know where they were at the time of the accident but we're not sure where they are now A number have emigrated, some to Israel and some to the United States. For example Glukhov, the former Chernobyl employee, lives with his wife and children in Washington State. Assessing the accident's health effects depends not only on dose reconstruction, but on epidemiological studies, which look at the connection between hazard - in this case radiation- and disease . These studies are difficult to mount in any country. says the NRPB's Harrison. That's because they depend on a system of public health identification of diseases, registration of cancers and registration of deaths . That information isn't as complete or as accurate as western epidemiologists would like. The caliber of historical diagnosis and the accurate identification of the cancer type are critical, says Williams. If a cancer registry is reporting twice as many cases of a particular tumor, we need to know whether it is related to Chernobyl, and that depends in part on any change in the diagnostic criteria and the screening frequency. You're not just taking raw data. You're checking diagnoses and creating a good baseline for epidemiological studies, says Williams. Adds Goodman: if you don't know what the baseline is, how will you know if there are small

increases in the incidence of cancer ? The infrastructure in the former Soviet Union is not designed for such studies . "In the west", says NCI's Beebe, "we estimate the risk of disease in terms of the hazards or the environmental influences". But that whole area of study was quite neglected by soviet medicine. For example, says Beebe, they don't often think in terms of bias. So they may not reach the conclusion they should draw from the experience of two groups because they haven t ensured that there s only one factor of interest , say radiation, involved in the difference between them. Dietary differences or smoking, for instance, could confuse the results. Inconclusive studies benefit no one . If we don't have information that is verified , says Williams, that will allow for people who wish to overplay or underplay the consequences of an accident Funding is another obstacle. Belarus, Ukraine and Russia don t have the money for epidemiological studies says Goodman. They have immediate public health problems to take care of. But if the rest of the world is willing to underwrite such studies, they'll certainly cooperate .

INTENSIVE TRAINING:

One way of underwriting epidemiological studies is to transfer the knowledge needed to carry them out. Organizations in several major industrialized countries have initiated training programs. While generally modest in scale , they seem be working says the NRPB s Harrison. We gave two weeks of intensive training in epidemiology to six traineed last year and they found it of immense value. Two young physicians from Ukraine have attended the summer training course in epidemiology offered by John Hopkins University's school of public health, says the NCI s Beebe. After that they were with a contractor for a week, watching how we collect data - interviewing, getting death certificates, abstracting, setting up files, then they spent five or six weeks in the epidemiology research group at Oak Ridge, Tenn. NCI also has trained Ukrainian endocrinologists, hematologists and pathologists, and shown a Belarussian the computer techniques used to run studies that rely on a data coordinating center. The European union is about to launch a larger training effort, says Williams. The two year program will train about 60 physicians, surgeons, technologists and nurses from Belarus, Ukraine and Russia. Japan too, is providing training - especially in population screening techniques- to support its work in measuring radiation doses of people in the affected countries. The training efforts are admirable, and though they're not always coordinated among the various national and international organizations, the're still effective. When it comes to epidemiological studies themselves however, lack of coordination can doom the outcome. There have already been overlapping studies, says Williams. You don't want different groups to attempt to study the same patients for different purposes. In addition, if many organizations study pieces of the same sample, you may find different changes in samples from the same patient. Despite the desire to help, says Goldman, we haven't been able to develop a central focus, where all cooperated, decided who did what and stuck to it. All we do is pilot studies. Nothing ever gets finished. The challenge may be too much even for the leaders of the countries involved. "We probably need a God," says the NRPB's Harrison. Goldman thinks the answer lies in an independent foundation to which interested countries could contribute. But the affected countries must call the shots, he says. Williams says that nothing will happen until the three big players in terms of funding - the European union, Japan and the United States- reach agreement on how their money is to be spent. A meeting in Minsk, Belarus in march may provide an opportunity for representatives of the three to discuss a joint approach, he says.

IMPERFECT ANSWERS:

Ten years after the Chernobyl accident , experts like Williams say they know of no studies showing a significant increase in the incidence of any type of cancer other than childhood thyroid cancer. But it's far too early to draw any conclusions . There may well be a very large absolute increase in thyroid cancers in adults in the future . Some of those living in areas that were contaminated by the accident will develop cancer in their lifetime. Some of the cleanup workers will too. That is to be expected. Even if dose reconstruction is successful and sound epidemiological studies are carried out, the results may not tell people whether their cancer was the result of Chernobyl or something else. It may well not be possible to detect increases in cancer other than thyroid , says Williams, but we have to be cautious . We're dealing with a whole generation says Goldman. It won't happen in a few months. It will take a generation .And there may never be perfect answers, he says.

Medical centre enhances treatment through research and innovation

Text by Marilyn Smith / Photos by Nigel Dickinson

Any discussion about the links between the accident at the Chernobyl nuclear power plant and human health is guaranteed to create controversy. Just days before the 20th anniversary of the accident, Greenpeace issued a report claiming that 100 000 fatal cancer cases would arise from the accident. With this figure, Greenpeace lobbed heavy criticism at The Chernobyl Forum figures, which estimate a total 4000 deaths. In turn, IAEA experts argue that far too many reports, including the Greenpeace study, try to achieve the impossible –

i.e., obtain accurate results from unsound science. For some scientists, the disparity is, at least in part, a function of when, where and under which regime the disaster occurred.

Dr. Mikhail Balanov was a leading nuclear scientist in the former Soviet Union at the time of the accident, and was directly involved in efforts to decontaminate individuals and the plant site itself."When Chernobyl exploded, there were a few radiation experts in the area," says Mikhail Balonov, a retired TC Technical Officer and a Soviet Union nuclear expert. "We were mostly concentrated at the major research centres in Moscow, Saint Petersburg and Chelyabinsk." Mr. Balonov paints a bleak picture of the days immediately following the disaster. He personally stripped clothing and shaved the head of severely contaminated individuals – who had to travel almost a thousand km to Moscow or Saint Petersburg before receiving appropriate attention. This was an era in which 'liquidators' (individuals who cleaned up after the disaster) did not wear dosimeter devices to measure radiation exposure. In addition, the former Soviet Union was notorious for shoddy record keeping and for concealing the magnitude of the accident for far too long.
Director Eleonora Kapitonova oversees the challenge of ensuring that research, diagnostics and treatment are fully integrated at the Republican Research Centre for Radiation Medicine and Human Ecology in Gomel, Belarus: Such factors create a dual challenge for the Republican Research Centre for Radiation Medicine and Human Ecology in Gomel, Belarus. The Centre provides diagnostic services and treatment for the populations from Belarus who have been affected by the Chernobyl accident. At times the Centre also provides these services for populations from Ukraine and the Russian Federation. The ultimate aim of the Centre is to improve the future outlook for individuals who have been exposed to radiation and to increase scientific knowledge of diseases associated with radiation exposure. Yet it is true that in addressing current health impacts, the Centre's health professionals must also take into account past shortcomings.

The reference to 'human ecology' in the Centre's name reflects a growing awareness that in order to provide effective treatment for diseases resulting from radiation exposure, it is vitally important to better understand how humans interact with nature and their environment. The TC programme is planning to help the Centre acquire the equipment and expertise necessary to build capacity in its research, diagnostic and clinical treatment departments – and to link them together.
Regular monitoring of individual radiation levels is an important aspect of health care in the affected regions.

In the hospital side of the Centre, most of the patients are so-called "liquidators", or inhabitants from the territories that were affected by the Chernobyl accident, who have multiple conditions ranging from cancer, cataracts and cardiac problems to lung disease and malfunction of the haematosis (blood production) system. Children and adolescents in the wards generally come for treatment of thyroid cancer or immune disorders such as leukaemia and alopecia (a condition in which the immune system attacks hair follicles, resulting in hair loss all over the body).

The increased incidence in thyroid cancer, particularly amongst children, is directly linked to the Chernobyl accident and, more specifically, to the early release of radioactive iodine and subsequent consumption of contaminated milk. The thyroid gland requires iodine to produce hormones that regulate various bodily functions. However, it is incapable of distinguishing between the natural, stable element and the radioactive version: it will simply absorb what is available. At the time of the accident, iodine deficiency was widespread in the affected areas (it is still a significant problem). Had Chernobyl occurred in the western world, where something as simple as adding iodine to salt had already significantly reduced deficiencies, the impact might have much more moderate.

Young children and adolescents are particularly susceptible to thyroid cancer and leukaemia.

Dr. Svetlana Matzkevich, Head of the Centre's Division of the State Dosimetry Register, deals with the health consequences of the Chernobyl accident on a daily basis. One of the biggest challenges, she says, is lack of information about exposure doses – particularly when one considers the quality of medical treatment that was available in the Soviet Union at the time.

"It must be recognized that when Chernobyl occurred, exposure control was very poor and exposure records were practically non-existent," says Dr. Matzkevich. "We treat all patients as though their conditions resulted from the disaster. But in some cases, individuals who underwent X rays or radiotherapy around the same time may have acquired greater doses of radiation from those 'controlled' events than from the accident itself."
Dr. Svetlana Matzkevich and TC Programme Management Officer Andrei Chupov work closely to identify needs at the Centre and develop plans through which Agency TC can contribute to new equipment, training or expertise.

The primary involvement of TC in the medical centre has been in training staff to help optimize the use of recently upgraded radiological equipment, including the acquisition of state-of-the-art digital technologies. Ultimately, this is a key component of delivering better health care to populations that have been affected by the Chernobyl accident.

State-of-the-art radiotherapy equipment and new digital technologies are vital to providing effective treatment to individuals with Chernobyl-related conditions. The TC programme helped provide training for staff to ensure optimal use of these tools.In addition, armed with better means to acquire data, Dr. Matzkevich is taking on the issue of record maintenance by overseeing the creation of a state registry for people who have been exposed to radiation. In line with the IAEA's Thematic Safety Areas for radiation protection, the

registry will track doses for three categories of individuals: 1) professionals, covering approximately 10 000 individuals who work in more than 700 Belarusian enterprises that have radiation sources; 2) medical patients who undergo radiation-based diagnosis or treatment protocols; and 3) public exposure that results from accidents or emergencies. The main goal of the registry is to identify critical groups within the population and, thereby, to determine when it is necessary to take action to reduce radiation exposure in a particular demographic group or to develop more effective treatment plans. The registry will also be used by government officials to calculate appropriate settlements and compensation packages. Dr. Matzkevich is also working with other scientists at the Centre to test and validate a new technique, known as 'dose reconstruction', which might help to create a more realistic image of the events which took place in 1986. It has been demonstrated that by sophisticated analyses of some solid materials (e.g., bricks or ceramic tiles) from contaminated sites, it is possible to calculate the radiation dose received at the time of the disaster. Using hard materials (e.g. ceramic or brick) from evacuated areas, scientists can measure current radioactivity levels to calculate contamination at the time of the accident. This process is known as 'radiation reconstruction' and may have application in human health."We believe we can do the same with enamel," says Dr. Matzkevich. "We can take a reading from someone's teeth and determine whether they were contaminated by the Chernobyl accident or by an excessive dose of radiotherapy two years after this event."The technique is not yet 100% accurate, but shows strong potential. Dr. Matzkevich expects to complete the necessary research in two to three years. But she also admits that developing the capacity to pinpoint the time and source of an individual's exposure has political implications. "What is to be done for someone who has been compensated under the 'victims of Chernobyl' plan for 20 years but is, in actual fact, a victim of a poorly regulated medical facility?" Today, it is widely recognized that high level radiation exposure causes general weakening of the immune system, which may be linked to many other diseases. In addition to those mentioned above, Chernobyl is often regarded as the source of increased incidence in diseases of endocrine systems, diabetes, and conditions related to the airway and gastrointestinal tract. Although it is now recognized that low-dose radiation may cause genetic mutation, there is little consensus on the impact in this area of the accident at Chernobyl.
Many of the Centre's adult patients have multiple conditions arising from radiation exposure, which require holistic care. In contrast, there is almost universal agreement about psychological trauma that may be connected to the disaster itself or to chronic stress, depression or anxiety related to current personal health problems and ongoing radiation risks. Even after 20 years, many people view themselves as 'victims' of Chernobyl and have developed a 'dependency' mentality. Many health experts emphasize the need to encourage people to recognize that they are 'survivors' and that they can exercise greater control over their own health and over their futures.

Maxim Orel exemplifies the attitude that health providers believe can make a difference. Along with his family, Maxim was evacuated from a village near Chernobyl at the age of seven, and subsequently grew up near Moscow – beyond the heavy cloud of health anxiety that hangs over the heads of nearby residents. When he first applied for his current position as interpretive guide inside the exclusion zone, friends warned him about the health risks associated with working "on site". Maxim opted to do his own research by talking to people who have worked at the plant for the past 20 years. "I think the real danger is becoming "radio-phobic". If I worry about my health constantly, it creates too much stress in my body. Maybe I will give myself a heart attack," says Maxim. "The key is to be optimistic, to exercise, to eat well and to live as normal a life as possible."The Chernobyl Forum, published in 2005, was sponsored by the IAEA, WHO, UNDP, FAO, UNEP, UNOCHA, UNSCEAR and the World Bank Group, along with the governments of Belarus, the Russian Federation and Ukraine. A summary of the report is available on-line at:
www.iaea.org/Publications/Booklets/Chernobyl/chernobyl.pdf

emergency response personnel. In keeping with that recommendation, KI should be administered to emergency response personnel following the facility's local emergency response procedures. The facility's director of occupational medicine or other appropriate medical official must endorse the local procedures, and supervision by appropriate local medical authority should be exercised as necessary during the implementation of the procedure.

(3) Training and medical information on the use of KI should be provided to all personnel involved in the radiological emergency response plan.

(4) The person administering the KI must ask if the individual is allergic to iodine. Individuals intolerant of KI at protective doses, and neonates, pregnant and lactating women should be given priority with regard to other protective measures (i.e., sheltering, evacuation, and controls of the food supply). If not, KI may be issued. For emergency response personnel, the name, date of issue, and amount of KI issued to each individual must be recorded on an SF 600, Chronological Record of Medical Care. The SF 600 must be maintained in the individual's health care treatment record.

(5) Pregnant women should be given KI for their own protection and for that of the fetus. However, because of the risk of blocking fetal thyroid function with excess stable iodine, repeat dosing with KI of pregnant women should be avoided.

(6) When personnel are actually exposed to radioiodine, notify BUMED so a medical follow-up program can be recommended, based on the estimated dose to the thyroid.

4. Side Effects. Possible side effects include skin rashes, swelling of the salivary glands, and "iodism" (metallic taste, burning mouth and throat, sore teeth and gums, symptoms of a head cold, and sometimes stomach upset and diarrhea). A few people may have allergic reactions with more severe symptoms. These could be fever and joint pains, swelling of parts of the face and body, and at times severe shortness of breath requiring immediate medical attention. Manifestation of these side effects would be expected to be negligible under the dose regimen stated above. FDA maintains that KI is a safe and effective means by which to prevent radioiodine uptake by the thyroid gland, under certain specified conditions of use, and thereby obviate the risk of thyroid cancer in the event of a radiation emergency.

5. Inventory Management

a. Potassium iodide must be maintained under the control of the Medical Department. To enhance early access to KI, KI may be stored near likely issue points provided the locations are identified in the facility's local emergency response procedures. The KI can be obtained from the Defense Supply Center, Philadelphia (National Stock Number 6505-01-116-8198). This KI tablet has been approved by the FDA for use as a thyroid blocking agent and contains 130 mg of potassium iodide per tablet. Each bottle contains approximately 14 tablets, an amount sufficient for a 2-week period when administered at the rate of one tablet per day (cognizant medical authority will provide guidance on recommended dosage and duration of treatment as directed).

From Nuclear med.pdf

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY, WORLD HEALTH ORGANIZATION

TOXICOLOGICAL EVALUATION OF SOME FOOD COLOURS, ENZYMES, FLAVOUR ENHANCERS, THICKENING AGENTS, AND CERTAIN FOOD ADDITIVES

WHO FOOD ADDITIVES SERIES 6

The evaluations contained in this publication were prepared by the Joint FAO/WHO Expert Committee on Food Additives which met in Rome, 4-13 June 1974[1] World Health Organization Geneva 1975 [1] Eighteenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. techn. Rep. Ser., 1974, No. 557. FAO Nutrition Meetings Report Series, 1974, No. 54.

PECTIN (AMIDATED) Explanation

This substance has been evaluated for acceptable daily intake by the Joint FAO/WHO Expert Committee on Food Additives (see Annex 1, Refs Nos 19 and 34) in 1969 and 1973.

Since the previous evaluation additional data have become available and are summarized and discussed in the following monograph. The previously published monographs have been expanded and are reproduced in their entirety below.

BIOLOGICAL DATA

BIOCHEMICAL ASPECTS

These partially methoxylated polygalacturonic acids occur naturally and widely in fruits especially citrus fruits and apples and are part of the cell walls. They are therefore part of the normal diet. For the past 30 years some newer pectins have been in use, in which the de-esterified carboxyl groups have been partially amidated.

At one time pectins have been used as plasma extenders as 1% solution but large intravenous doses have led to pectin deposition in the kidney, liver and lungs with consequential degenerative changes (Merck Index, 1968).

Pectin has been shown to lower blood cholesterol in man (Keys et al., 1961) and in the rat (Wells & Ershoff, 1961). Four groups of three male and three female pigs were given diets for four weeks supplemented with either 5% pectin or 5% cellulose with or without dietary cholesterol. Pectin had no effect on body weight or plasma cholesterol level unless cholesterol was given in the diet. Pectin lowered significantly alimentary hypercholesterolaemia (Fisher et al., 1966; Fisher & Kannitz, 1964). Chicken fed cholesterol in the diet excrete more cholesterol if pectin is also added. Pectin has no effect on endogenous plasma cholesterol or may raise the level (Fisher et al., 1964). On the other hand swine fed pectin developed significantly higher blood cholesterol levels in other experiments (Fausch & Anderson, 1965).

The digestibility of pectin was determined in groups of six rats fed 17.4% or 34.8% pectin in their diet for three weeks. At the lower dietary level there was no adverse effect on the utilization of other nutrients but at the higher level utilization of other nutrients was reduced. Pectin produced diarrhoea and growth was retarded at both dietary levels. Faecal recovery showed only 20% of orally ingested pectin to be digestible (Carey, 1958). Four normal dogs and two dogs with ileostomies were fed 140 g of pectin in a mixed diet over a seven-day eriod. An average of 90% of pectin was broken down. When fed during fasting periods an average of only 50% was broken down. In the case of studies with humans more pectin was broken down than in the dog study. A study involving two human patients with ileostomies showed that the breakdown of pectin occurred in the colon rather than in the upper intestine, and that bacterial enzymes were involved rather than enzymes of the animal organism (Werch & Ivy, 1941). Rats were fed diets containing 0.04 ppm Pb^{210} and either 5% pectin or 5% starch. The control group retained 15.8% of the radioactive lead and excreted 10.9% in the urine and 71.7% in the faeces. The pectin-fed animals retained an average of 24% less lead than controls, significantly less being excreted in the urine and more in the faeces (Murer & Crandall, 1942).

TOXICOLOGICAL STUDIES

Acute toxicity None available.

Short-term studies Rat

Rats were fed 2.5-10% pectin without any deleterious effects - no details are available (Ershoff & McWilliams, 1945).

In another experiment four groups of 10 male and 10 female rats were fed diets containing 0, 5%, 10% or 15% pectin (nonamidated) for 90 days. No adverse effects were noted on general condition, behaviour and survival. Growth was slightly decreased at the 15% level, an observation previously noted in a range-finding test using 20% pectin. At 20% also reduced food consumption and food efficiency had been noted. Total serum protein and albumin were decreased at the 15% level but the haematological indices showed no treatment related differences. Blood chemistry showed no significant findings. The relative caecal weight was increased at the 15% level, a phenomenon also seen with modified starches and other high food intake of complex carbohydrates. Gross and histopathology were essentially normal (Til et al., 1972).

In another experiment four groups of 10 male and 10 female rats were fed on diets containing 0, 5, 10 or 5% pectin (21% amidated) for 90 days. No adverse effects were noted on general condition, behaviour and survival. Growth was slightly decreased at the 15% level and this finding was also noted in a range finding test using 20% pectin in the diet. Some decrease in growth occurred inconsistently also at the 10% dietary level. Food intake and food efficiency were not affected at any level. Haematological parameters showed no significant treatment related changes. Total serum protein and albumin were reduced at the 15% level but the other clinical biochemical parameters and urinalysis were essentially normal. Caecal weights were increased at all levels but in a dose-related manner. These findings are reminiscent of what is seen when high amounts of starch, modified starch or certain other carbohydrates are fed. Gross and histopathology were normal but a slight degree of hyperkeratosis of the forestomach in some males was seen at the 10% and 15% level but is probably not of toxicological significance (Til et al., 1972).

Long-term studies

Rat: Groups of 20 male weanling Wistar rats were fed diets of Purina laboratory meal to which was added L.M. Pectin (approximately 18% amidated) or Pectin, N.F. at 10% of the diet. Control diets contained 10% alphacellulose (Alphacel). The rats were fed for two years. The diets were made isocaloric by supplementing the alphacel with dextrose assuming a caloric equivalent for pectin of 0.6187 cal./mg. Mortality did not vary significantly between groups. Body weights for the pectin fed groups were similar but significantly less than that of the control animals. A comparison of grams of diet/kgm body weight showed a slightly greater food utilization for the pectin fed groups. The controls, however, consumed more food and gained more weight. There was no significant difference in average organ to body weight ratios for adrenal, heart, kidney, liver and spleen. The testes/body of the pectin fed groups did not differ from each other but both were significantly larger than those of the control group. Blood chemistry, SGOT and SPGT done at sacrifice showed no abnormalities in the pectin groups. Gross examination at necropsy showed no unusual findings. Two tumours were noted in the control group and one in the amidated pectin group. All gross lesions and adrenal, heart, kidney, liver, lung, spleen and testes will be examined histologically (Palmer, G. H. & Jones, T. R., 1974).

Wistar rats of the Center for Investigation and Medical Research at Marseille strain were administered 100 mg/kg bw of, and 18.4%, amidated pectin, daily in the synthetic diet of Lacassagne MABI. Feeding was ad lib.
Groups of 20 males and 20 females housed five to a cage were used. Controls consisted of a group of 450 rats fed the basic synthetic diet. Although the design of the experiment is not apparent the author mentions the littering of two generations. The author also stated there was no difference in growth and body weights of fed animals as compared to historical controls. Likewise electrophoretic examination of blood drawn just prior to sacrifice did not differ from controls. A complete histologic examination was carried out on 20 males and 20 females after 24 months on experiment. Tissues of fed animals did not differ from those of the controls. The author states further that no adverse effects were noted on the ability of the animals to reproduce nor was the substance shown to be teratogenic (Mosinger, M., 1974).

Comments: Nonamidated pectins and their salts as specified are normal constituents of the human diet and have also been administered intravenously at high levels to man without acute toxic effects. The available short-term tests show that even at 5% dietary levels no adverse effects are seen. The caecal enlargement without any accompanying histological changes is probably related to the presence of large amounts of a polysaccharide in the diet.

Amidated pectins produced mild growth depression at a lower level (10%) than was seen with nonamidated pectins in a 90-day test as well as in a two-year study in rats. The available short-term study in rats revealed caecal enlargement but not associated with any histological abnormality. The available one-generation reproduction study and the two-year studies in rats lack histopathological and biochemical details. They cannot therefore be used for evaluation.

EVALUATION

Level causing no toxicological effect Rat: 5% (= 50 000 ppm) in the diet equivalent to 2500 mg/kg bw.
Estimate of acceptable daily intake for man 0-25 mg/kg bw.* [* Temporary]

FURTHER WORK OR INFORMATION

Required by June 1978.

The results of histological examinations in the long-term studies. Adequate reproduction and embryotoxicity including teratology studies.

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Pectin (amidated) (WHO Food Additives Series 8)

The evaluations contained in this publication were prepared by the Joint FAO/WHO Expert Committee on Food Additives which met in Geneva, 14-23 April 1975[1]

World Health Organization, Geneva 1975

[1] Nineteenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. techn. Rep. Ser., 1975, No. 576; FAO Nutrition Meetings Report Series, 1975, No. 55.

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PECTIN (AMIDATED)

Explanation: Non-amidated pectin was evaluated for acceptable daily intake for man by the Joint FAO/WHO Expert Committee on Food Additives (see Annex1, Refs No. 20 and No. 33) in 1969 and 1973. Amidated pectin was evaluated in 1973 and 1974 (see Annex 1, Refs No. 33 and No. 35). Since the previous evaluation of amidated pectin, additional data have become available and are summarized and discussed in the following monograph addendum.

BIOLOGICAL DATA TOXICOLOGICAL STUDIES

Long-term studies Rats

Four groups of 10 male and 10 female rats were fed on diets containing 0%, 5%, 10%, or 15% pectin (21% amidated) for 90 days. No adverse effects were noted on general condition, behaviour and survival. Growth was slightly decreased at the 15% level and this finding was also noted in a range finding test using 20% pectin, in the diet. Some decrease in growth occurred inconsistently also at the10% dietary level. Food intake and food efficiency were not affected at any level. Haematological parameters showed no significant treatment related changes. Total serum protein and albumin were reduced at the 15% level but the other clinical biochemical parameters and urinalysis were essentially normal. Caecal weights were increased at all levels but in a dose-related manner. These findings are reminiscent of what is seen when high amounts of starch, modified starch or certain other carbohydrates are fed. Gross and histopathology were normal but a slight degree of hyperkeratosis of the fore-stomach in some males was seen at the 10% and 15% level but is probably not of toxicological significance (Til et al., 1972).

Groups of 20 male weanling Wistar rats were fed diets of purina laboratory meal to which was added L.M. pectin (approximately 18% amidated) or pectin, N.F. at 10% of the diet. Control diets contained 10% alphacellulose (alphacel). The rats were fed for two years. The diets were made isocaloric by supplementing the alphacel with dextrose assuming a caloric equivalent for pectin of 0.6187 cal/g. Mortality did not vary significantly between groups. Body weights for the pectin fed groups were similar but significantly less than that of the control animals. A comparison of grams of diet/kg body weight showed a slightly greater food utilization for the pectin fed groups. The controls, however, consumed more food and gained more weight. There was no significant difference in average organ to body weight ratios for adrenal, heart, kidney, liver and spleen. The testes/body of the pectin fed groups did not differ from each other but both were significantly larger than those of the control group. Blood chemistry, SGOT and SPGT done at sacrifice showed no abnormalities in the pectin groups. Gross examination at necropsy showed no unusual findings. Two tumours were noted in the control group and one in the amidated pectin group. All gross lesions and adrenal, heart, kidney, liver, lung, spleen and testes were examined histologically. No compound related effects were observed (Palmer & Jones, 1974; Abdul-Haj & Palmer, 1974).

Wistar rats of the Center for Investigation and Medical Research at Marseille strain were administered 100 mg/kg body weight of 18.4% amidated pectin, daily in the synthetic diet of Lacassagne MABI. Feeding was ad lib. Group of 20 males and 20 females housed five to a cage were used. Controls consisted of an identical group of rats fed the basic synthetic diet. At this level of pectin in the diet there appeared to be no effects on growth and body weights of fed animals as compared to historic controls. Also, there appeared to be no effects on the serum of fed rats. Since many of the experimental details are lacking it is difficult to reconstruct the complete design of the study. It is clear, however, that tissues from 20 males and 20 females sacrificed at 24 months were studied histologically. Rats dying prior to termination of the study were also said to have been examined microscopically, however, no mention of such animals is made in the detailed pathology. The histopathology revealed no adverse effects on the stomachs or testes of fed males. It should be noted that these were very small rats. Only one male reached 640 g the remainder ranged from 210-420 g with seven of the rats weighing 270 g or less. The weight of the females at sacrifice was similar to the males. A first generation produced by mating 10 animals produced a total of 21 offspring and a second generation produced by mating five animals resulted in only 18 offspring (Mosinger, 1974).

Comments:

There are three studies with amidated pectin available for evaluation. Neither of the two long-term studies was considered adequate. There were no major adverse findings noted.

EVALUATION

Level causing no toxicological effect in the rat 5% in the rat equivalent to 2500 mg/kg body weight.

Estimate of acceptable daily intake for man 0-25 mg/kg body weight.*

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Radiation Treatment Medications

Dr. Guilmette and his team are charged with screening a set of drugs to evaluate their efficacy in treating radioactive materials called "radionuclides" internalized by the body. To do that the team has developed a multidimensional approach; first conducting animal studies on rodents to understand where the radionuclides deposit in the body and how long they remain there, then screening drugs designed to remove the radionuclides from the contaminated animals. He says it's important to understand the distinction between this animal research and testing done for many other drugs, which are generally targeted against human diseases. Due to the nature of the materials being studied, LRRI's experiments fall under the "Animal Rule," a regulation passed in 2002 specifying that the FDA will accept animal data in lieu of human data for specific situations where studies on humans wouldn't be ethical. Therefore, the drugs tested in the Radiation Countermeasures Program can only be tested for efficacy on animals exposed to radiation. Based on the animal study results, researchers will select the most effective drug or drugs and test them on humans, but only to measure safety in the human body. Taken together, the two separate pieces of research will provide the FDA with the information it needs to determine that a drug would be an effective and safe treatment for humans exposed to internal radiation. Before the efficacy of any drugs could be tested, the LRRI scientists needed to understand how radionuclides get into the body and then characterize their biological behavior inside the body. "If you don't understand the fate of the material in the body without treatment, then you can't evaluate how effective a treatment is," explains Dr. Guilmette. People can be exposed to internal radiation as a result of radiological dispersal devices (RDDs) or improvised nuclear devices (IDDs). Through explosions or sprays these weapons disperse radionuclides that humans internalize through ingestion, inhalation, open wounds, and in some cases, through intact skin. Once internalized, the radionuclides can remain in the body from a few days to indefinitely; the length of time depends on the specific radionuclide. Until the radioactive contamination is removed, the body continues to be irradiated. Treatment is difficult because typically the body can't efficiently excrete many of the radioactive materials and they can't be chemically neutralized. Instead, a drug must bind with the radionuclide and essentially drag it from the body. The LRRI team currently is focusing their research on treating internal radiation from three specific radionuclides, plutonium, americium, and curium; all of which are fairly common, have similar radiation and biological properties, and are a concern to the Department of Homeland Security. In the first stage of the research process, the scientists inject trace levels of the different radionuclides into rodents. Then Dr. Guilmette and his team analyze where the radioactive material goes in the body and measure how long it stays there. The team has completed this benchmarking process with plutonium and americium and is working on radioactive cobalt, uranium, and curium compounds.

The second stage of the research involves treating the animals that are internally contaminated with radionuclides with various drugs and then evaluating each drug's efficacy. No single chemical can remove every radionuclide, but there are drugs that show some promise. The LRRI team is testing five such drugs that have been developed by universities or small pharmaceutical companies around the country. One chemical compound called iethylene triamine pentaacetic acid (DTPA) has already been shown to effectively remove plutonium, americium, and curium from the body. However, currently the compound can only be administered as an aerosol or intravenously, processes that are problematic for treating large numbers of people. To make DTPA easier to administer, researchers hope to change DTPA's chemical properties and formulate it into an easily absorbed pill. As part of the second stage of the LRRI research, Dr. Guilmette and his team are testing variants of DTPA to advance that effort. Once each step of the research is complete with the different radionuclides and various drugs, Dr. Guilmette will have a data set showing which drugs are most effective for treatment. The data will be given to NIAID so that decisions can be made about which drugs should be pursued to the next research phase.

At that point the LRRI Radiation Countermeasures Program team could start conducting studies that are more realistic in terms of exposure scenarios and more in depth for drug efficacy. In that next research phase, the LRRI team would add another layer of complexity by employing Good Laboratory Practices (GLP), a set of procedures required by the FDA for certain higher-level drug tests. Initial screening studies currently being done in the Radiation Countermeasures Program don't fall under GLP guidelines, but LRRI scientists who conduct GLP studies regularly, are prepared to do the next phase of pivotal GLP studies. With three radionuclides to analyze, various radiation exposure times to control, and five different treatment drugs to test, LRRI's research for the Radiation Countermeasures Program is complex and multidimensional. But Dr. Guilmette says LRRI is perfectly suited to the challenge. "With our 50-plus years of working safely with these radioactive materials and the fact that we have a long history of successful drug testing using Good Laboratory Practices, we are perfectly poised to do these critical drug development studies."

Treatment of Internal Radioactive Contamination

The goals of internal decontamination are to reduce absorption and to enhance excretion of radioactive contaminants. Treatment is most effective if it is started as soon as possible after contamination. Radioactive contaminants may be internalized via inhalation, ingestion, rthrough wounds and skin. Treatment should be directed by knowledge of the specific radiocontaminant. Ideally, internal decontamination should begin during the first few hours if the treating physician suspects that radiocontaminants may have been internalized. After careful retrospective review of clinical data from human exposures resulting from nuclear detonations or nuclear reactor accidents, Prussian blue, potassium iodide (KI), and calciumdiethylenetriaminepentacetate (Ca-DTPA) and zinc-diethylenetriaminepentacetate (Zn-DTPA), when manufactured under conditions specified in an approved new drug application (NDA), were found safe and effective for the treatment of internal contamination with radioactive cesium; iodine; and plutonium, americium, or curium, respectively. Currently, there are approved Prussian blue, KI, and Ca- and Zn-DTPA products in the United States.

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[http://www.usuhs.mil/afrri/research/rcp.htm]

Background

* Ionizing radiation at certain doses damages the blood-forming system.
* This results in fewer blood cells and platelets in the circulatory system.
* White blood cells form part of the immune system: they attack infectious microorganisms. Platelets form clots and prevent uncontrolled bleeding.
* Therefore, susceptibility to infection and hemorrhage increase after exposure to radiation.
* These can cause death at a certain range of radiation doses (hematopoietic syndrome). Higher radiation doses cause death by damaging the gastrointestinal (GI) system or the central nervous system. There is some overlap: mortality due to the hematopoietic syndrome can be exacerbated by compromise of the GI barrier to bacteria.
* Lower doses of radiation can increase the probability of cancer. (The probability of late effects such as cancer would also increase after higher radiation doses, in people who survived the acute effects.)
* Possible countermeasures to ionizing radiation can be broadly categorized into three groups.
    1. Drugs that prevent the initial radiation injury
        - o Free radical antioxidants
        - o Hypoxia
        - o Enzymatic detoxification
        - o Oncogene targeting agents
    2. Drugs that repair the molecular damage caused by radiation
        - o Hydrogen transfer
        - o Enzymatic repair
    3. Drugs that stimulate proliferation of surviving stem and progenitor cells
        - o Immunomodulators
        - o Growth factors and cytokines
* Military personnel and emergency responders urgently need nontoxic countermeasures to ionizing radiation.
* The only approved countermeasures that can be used in the field are drugs that block the effects of several specific internalized radioisotopes. There are no approved drugs that can be used outside the clinic to ameliorate the effects of external ionizing radiation on the blood-forming or GI systems.
* The availability of medical facilities for radiation casualties after a nuclear detonation near a city will be problematic:

1. Bell WC, Dallas CE. 2007. Intl J Health Geographics 6:5
2. British Medical Association's Board of Science and Education. 1983, The Medical Effects of Nuclear War, John Wiley & Sons, New York.
3. Holdstock D, Waterston L. 2000. Lancet 355:1544–1547
4. Flynn DF, Goans RE. 2006. Surg Clin North Am 86:601–636

* In light of the logistical realities of likely nuclear disaster scenarios, much of our current focus is on drug candidates with extremely low toxicity and ease of administration, suitable for use outside the clinic without physician supervision.

Summary of accomplishments

* Radiation countermeasure candidates tested for efficacy at AFRRI are chosen based on extensive basic research, which increases chances of success.
* All four countermeasures for acute radiation syndrome with Food and Drug Administration (FDA) Investigational New Drug (IND) status are AFRRI products.
* Two (5-AED and BIO-300) were conceived, initiated, and developed at AFRRI.
* The two others (Ex-Rad and CBLB502) were the subjects of company-initiated research programs that AFRRI joined at early stages.
* A fifth candidate, which AFRRI is researching in collaboration with a company, will be the subject of an IND application in the near future.
* The current standard (off-label) treatment for acute radiation syndrome, hematopoietic cytokines such as G-CSF, was conceived, initiated, and developed at AFRRI.

* AFRRI has an ongoing in vivo efficacy screening program and is frequently approached by organizations for research collaboration and/or consultation regarding their promising countermeasure candidates.
* The screening program is supplemented by a robust mechanistic research program that provides supporting data for approval of existing drugs and identifies potential drug targets.
* AFRRI has a history of collaborating with private companies, providing supporting data for FDA applications, and attending meetings with the FDA and other government agencies as appropriate.

Advanced nutraceuticals as radioprotectants

1. Evaluated vitamin E as an effective radioprotectant (Military Medicine 167 Suppl. 1: 57–59, 2002)
2. Characterized radioprotectant properties of soy-derived isoflavones (Journal of Applied Toxicology, 23: 379–385, 2003)
3. 2003 and 2005: Entered into Cooperative Research and Development Agreements (CRADAs) with Humanetics Corporation to jointly develop oral agents that show promise in supporting and protecting the immune system against challenges from exposure to radiation
4. January 2007: The Food and Drug Administration granted Investigational New Drug (IND) status to BIO-300, a Humanetics radiation countermeasure developed at the Armed Forces Radiobiology Research Institute with collaborators at the National Institutes of Health (NIH)
5. Demonstrated induction of cytokines by Vitamin E-related analogs (Experimental and Molecular Pathology, 81: 55–61, 2006)
6. Assessed effects of genistein on hematopoietic progenitor cell recovery in irradiated mice (International Journal of Radiation Biology 83: 141–151, 2007)
7. Documented effects of genistein on radiation-responsive gene expression (Radiation Measurements 42: 1152–1157, 2007)
8. Demonstrated genistein protects against delayed radiation effects in lung (Radiation Research 49: 361–372, 2008)
9. Effects of genistein administration on cytokine induction in whole-body gamma irradiated mice (Int Immunopharmacol. 9: 1401–1410, 2009)
10. Tocopherol succinate: a promising radiation countermeasure (Int Immunopharmacol. 9:1423–1430, 2009)
11. Gamma-tocotrienol, a tocol antioxidant as a potent radioprotector (Int J Radiat Biol. 85:598–606, 2009)
12. Preclinical development of a bridging therapy for radiation casualties (Exp Hematol. 38: 61–70, 2010)
13. Alpha-tocopherol succinate protects mice from gamma-radiation by induction of granulocyte-colony stimulating factor (Int J Radiat Biol 86:12–21, 2010)
14. Demonstrated that gamma-tocotrienol protects hematopoietic tissue by preserving the HSCs and HPCs and by preventing persistent DNA damage (Radiat Res., 173(6): 738–47, 2010)
15. Reviewed novel strategies to ameliorate radiation injury, focusing on a possible role for tetrahydrobiopterin (Curr Drug Targets, June 28, 2010 [Epub ahead of print])
16. Examined targets of potential radioprotective drugs (Curr Drug Targets, June 28, 2010 [Epub ahead of print])
17. Examined the radioprotective mechanisms of gamma-tocotrienol for protecting bone marrow during chemo- and radiotherapy (Curr Drug Targets, June 28, 2010 [Epub ahead of print])

Kinase inhibitors: Documented protection by a new chemical entity, Ex-Rad™ (Radiation Research 171: 173–179, 2009)
Developed chemopreventive strategies for radiation-induced cancer: targeting radiation-induced genetic alterations (Military Medicine 167 Suppl. 1: 54–56, 2002)
Contributed to guidance for medical management of the Acute Radiation Syndrome following terrorist acts (Annals of Internal Medicine 140: 1037–1051, 2004)
Analyzed the effects of isoflurane anesthesia on numbers of circulating white blood cells (Contemporary Topics 43: 9–14, 2004)
Demonstrated beneficial effects of N-palmitoylation of IL-1 radioprotective domain (Immunopharmacology and Immunotoxicology 26: 193–202, 2004) (Peptides 26: 413–418, 2005)
Recent studies of radioprotective thiols:

1. Characterized delivery of amifostine with subcutaneous pellets (International Journal of Radiation Biology 78: 535–543, 2002)
2. Developed electrochemical detection method for measurement of thiols (Journal of AOAC International 85: 551–554, 2002)
3. Investigated effects of thiols on LPS-induced NO production in macrophages (Experimental and Molecular Pathology 74: 68–73, 2003)
4. Developed oral formulation of amifostine nanoparticles (Journal of Pharmacy and Pharmacology 56: 1119–1125, 2004)

Protectans

1. 2004: Entered into Cooperative Research and Development Agreement with Cleveland BioLabs to develop Protectans, drug candidates that protect normal tissues from acute stresses such as radiation
2. 2008: Protectan CBLB502 obtained IND status with the FDA as an acute radiation syndrome countermeasure

Captopril

1. Timing of captopril administration determines radiation protection or radiation sensitization in a murine model of total body irradiation (Exp Hematol. 38: 270–281, 2010)

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1. Evaluated vitamin E as an effective radioprotectant (Military Medicine 167 Suppl. 1: 57–59, 2002)

Mil Med. 2002 Feb;167(2 Suppl):57-9.

Nutritional approaches to radioprotection: vitamin E.

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Abstract

Low-level radiation injury is dependent on the radiation dose and dose rate. The major military use of any potential radioprotectant is to prevent the short-term effects of lethality and the long-term effects of cancer and other pathologies from radiation exposure that may occur in a nuclear battlefield or in a nuclear material contaminated field of operation. Therefore, a radioprotectant should not affect the ability of military personnel to perform tasks. Because exposure to ionizing radiation induces free radical species, effective antioxidants, either alone or in combination with other agents, can be used as potential radioprotectors. To test this hypothesis, we studied vitamin E for its radioprotective efficacy. Using CD2F1 male mice as the model system, we observed that vitamin E at a dose of 400 IU/kg acts as a good radioprotectant against lethal doses of cobalt-60 radiation. Vitamin E was more efficacious when given subcutaneously than when given orally.

PMID: 11873518 [PubMed - indexed for MEDLINE]

Vitamin E succinate (alpha-tocopheryl succinate)

Vitamin E succinate (VES) is a derivative of the fat-soluble vitamin d-alpha-tocopherol or dl-alpha-tocopherol. The general term vitamin E refers to eight naturally occurring and synthetic tocopherols and tocotrienols and their acetate and succinate derivatives. D-Alpha-tocopherol succinate is the succinate ester of natural-source d-alpha-tocopherol. D-Alpha-tocopherol succinate is obtained by the vacuum steam distillation and succinylation of edible vegetable oil. Dl-Alpha-tocopheryl succinate is an all-synthetic form of alpha-tocopherol. It is produced by coupling racemic isophytol with trimethylhydroquinone to form dl-tocopherol.

Although the naturally occurring forms of vitamin E have lipid-soluble antioxidant properties that protect cell membranes against damage by free radicals, the acetate and succinate derivatives that are esterified at the C-6 position of the chromanol ring do not have antioxidant properties unless the esterification is hydrolyzed and free tocopherol is regenerated. The succinate form is water-soluble and the acetate form is fat-soluble. Vitamin E Succinate takes vitamin E's antioxidant action a step further. Succinate feeds directly into the Krebs cycle, our major metabolic pathway for generating energy. This extra dimension from succinate significantly extends the protective properties of vitamin E.

Vitamin E succinate is may inhibit growth and induced apoptic cell death in estrogen-receptor-negative human breast cancer cell lines. Vitamin E succinate is a potent novel antineoplastic agent with high selectivity and cooperativity with tumor necrosis factor-related apoptosis-inducing ligand. Vitamin E succinate may be of clinical use in the treatment of aggressive human breast cancers, particularly those that are resistant to anti-estrogen therapy. Alpha-tocopheryl succinate can suppress the expression of prostate-specific antigen (PSA), a marker for the progression of prostate cancer. VES can also suppress androgen receptor (AR) expression by means of transcriptional and posttranscriptional modulation.

Vitamin E succinate enhances the immune response and induces cellular differentiation and/or growth inhibition. Patent Inhibitor of neuroblastoma. cells, murine melanoma cells, avian lymphoid cells, human HL-60 promyelocytic leukemia cells, and several human breast carcinoma cell lines. VES has been shown to modulate adenylate cyclase and cAMP-dependent protein, inhibit protein kinase C activity, bind to cellular vitamin E binding protein, suppress c-myc and c-H-ras oncogene expression, and regulate TGFb protein production.

Alpha-tocopherol succinate protects mice from gamma-radiation by induction of granulocyte-colony stimulating factor (Int J Radiat Biol 86:12–21, 2010)
Tocopherol succinate: a promising radiation countermeasure (Int Immunopharmacol. 9:1423–1430, 2009)

Demonstrated induction of cytokines by Vitamin E-related analogs (Experimental and Molecular Pathology, 81: 55–61, 2006)
Evaluated vitamin E as an effective radioprotectant (Military Medicine 167 Suppl. 1: 57–59, 2002)

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Hematological Targets of Radiation Damage.

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Abstract

Radiation-induced myelosuppression remains a rate-limiting factor of radiotherapy and chemotherapy. Therefore, hematological targets of radiation damage are of great significance for radiation oncology and normal tissue injury and protection. Protection of hematopoietic stem and progenitor cells is pivotal. In order to develop therapeutic targets, it is necessary to understand the mechanisms of stem cell renewal and differentiation. Recent advances in the molecular pathology of hematopoietic stem cells indicate a fine balance between various extrinsic and intrinsic signaling pathways in preserving the self-renewal and proliferative capacity of stem cells. Extrinsic signaling involves a microenvironment niche factors such as neighboring stromal cells, osteoblasts, and adipocytes secreting cytokines, chemokines, and metalloproteinases; intrinsic regulation involves Wnt/hedgehog/Notch signaling, DNA damage-induced epigenetic alterations, telomere shortening, and early senescence. Various drugs including synthetic cytokine mimetics, cytokine stimulators, and DNA repair modulators are being tested as radioprotectants. Colony-stimulating factors are routinely used in clinics to treat neutropenia induced by chemotherapy and radiotherapy as well as to mobilize and expand progenitors used in autologous transplantation. However, toxicity has limited their use. The vitamin E isoforms gamma tocotrienol, a potent free radical scavenger that has displayed promising anticarcinogenic properties, was recently shown to protect bone marrow (BM) from radiation injury and to stimulate hematopoiesis in a murine model. This chapter focuses on the potential targets of radiation damage in BM and speculates on the mechanisms of protection by gamma-tocotrienol and how these mechanisms can contribute to radioprotection in general and to protection of BM during chemotherapy and radiotherapy in particular.

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Vitamin E

The term vitamin E describes a family of eight antioxidants: four tocopherols (alpha-, beta-, gamma-, and delta-) and four tocotrienols (alpha-, beta-, gamma-, and delta-). Alpha-tocopherol is the only form of vitamin E that is actively maintained in the human body; therefore, it is the form of vitamin E found in the largest quantities in blood and tissues (1). Because alpha-tocopherol is the form of vitamin E that appears to have the greatest nutritional significance, it will be the primary topic of the following discussion. It is also the only form that meets the latest Recommended Dietary Allowance (RDA) for vitamin E.

Function

Alpha-tocopherol

The main function of alpha-tocopherol in humans appears to be that of an antioxidant. Free radicals are formed primarily in the body during normal metabolism and also upon exposure to environmental factors, such as cigarette smoke or pollutants. Fats, which are an integral part of all cell membranes, are vulnerable to destruction through oxidation by free radicals. The fat-soluble vitamin, alpha-tocopherol, is uniquely suited to intercept free radicals and thus prevent a chain reaction of lipid destruction. Aside from maintaining the integrity of cell membranes throughout the body, alpha-tocopherol also protects the fats in low density lipoproteins (LDLs) from oxidation. Lipoproteins are particles composed of lipids and proteins that transport fats through the bloodstream. LDLs specifically transport cholesterol from the liver to the tissues of the body. Oxidized LDLs have been implicated in the development of cardiovascular diseases (See Disease Prevention). When a molecule of alpha-tocopherol neutralizes a free radical, it is altered in such a way that its antioxidant capacity is lost. However, other antioxidants, such as vitamin C, are capable of regenerating the antioxidant capacity of alpha-tocopherol (2, 3).

Several other functions of alpha-tocopherol have been identified that are not likely related to its antioxidant capacity. For instance, alpha-tocopherol is known to inhibit the activity of protein kinase C, an important cell-signaling molecule. Alpha-tocopherol appears to

also affect the expression and activities of molecules and enzymes in immune and inflammatory cells. Additionally, alpha-tocopherol has been shown to inhibit platelet aggregation and to enhance vasodilation (4, 5).

The isomeric form of alpha-tocopherol found in foods is *RRR*-alpha-tocopherol (also referred to as "natural" or *d*-alpha-tocopherol). Synthetic alpha-tocopherol, which is labeled *all-rac-* or *dl*-alpha-tocopherol, has only one-half the biological activity of *RRR*-alpha-tocopherol (see Supplements). Often vitamin E-fortified foods contain synthetic alpha tocopherol, and the amounts are given as a percentage of the daily value of 30 IU. Throughout this article, amounts of alpha-tocopherol are expressed in both international units (IU) and milligrams (mg).

Gamma-tocopherol

The function of gamma-tocopherol in humans is presently unclear. Although the most common form of vitamin E in the American diet is gamma-tocopherol (see Food Sources), blood levels of gamma-tocopherol are generally ten times lower than those of alpha-tocopherol. This phenomenon is apparently due to two mechanisms. 1) Alpha-tocopherol is preferentially retained in the body by the action of the alpha-tocopherol transfer protein (a-TTP) in the liver, which preferentially incorporates alpha-tocopherol into lipoproteins that are circulated in the blood (1) and ultimately delivers alpha-tocopherol to different tissues in the body (6). See the Linus Pauling Institute Newsletter for more information about **a-TTP and vitamin E adequacy**. 2) Forms of vitamin E other than alpha-tocopherol are actively metabolized (6). Because gamma-tocopherol is initially absorbed in the same manner as alpha-tocopherol, small amounts of gamma-tocopherol are detectable in blood and tissue. Breakdown products of tocopherols, known as metabolites, can be detected in urine. More gamma-tocopherol metabolites are excreted in urine than alpha-tocopherol metabolites, suggesting less gamma-tocopherol is needed for use by the body (7). Limited research in the test tube and in animals indicates that gamma-tocopherol or its metabolites may play a role in protecting the body from free radical-induced damage (8, 9), but these effects have not been convincingly demonstrated in humans. Recently, concern has been raised regarding the fact that taking alpha-tocopherol supplements lowers gamma-tocopherol levels in the blood. However, no adverse effects of moderate alpha-tocopherol supplementation have been demonstrated, while many benefits have been documented (see Disease Prevention and Disease Treatment). In one prospective study, increased levels of plasma gamma-tocopherol were associated with a significantly reduced risk of developing prostate cancer. In this study, increased levels of plasma alpha-tocopherol and toenail selenium were protective against prostate cancer development only when gamma-tocopherol levels were also high (10). These limited findings, in addition to the fact that alpha-tocopherol supplementation lowers gamma-tocopherol levels in blood, have led some scientists to call for additional research on the effects of dietary and supplemental gamma-tocopherol on health (11). For more information, see the article, **Which Form of Vitamin E, Alpha- or Gamma-Tocopherol, is Better?**, in the Linus Pauling Institute Research Report. Importantly, relatively high plasma gamma-tocopherol concentrations may indicate a high level of vegetable and vegetable oil intake.

Deficiency

Vitamin E deficiency has been observed in individuals with severe malnutrition, genetic defects affecting the alpha-tocopherol transfer protein, and fat malabsorption syndromes. For example, children with cystic fibrosis or cholestatic liver disease, who have an impaired capacity to absorb dietary fat and therefore fat-soluble vitamins, may develop symptomatic vitamin E deficiency. Severe vitamin E deficiency results mainly in neurological symptoms, including impaired balance and coordination (ataxia), injury to the sensory nerves (peripheral neuropathy), muscle weakness (myopathy), and damage to the retina of the eye (pigmented retinopathy). For this reason, people who develop peripheral neuropathy, ataxia, or retinitis pigmentosa should be screened for vitamin E deficiency (2). The developing nervous system appears to be especially vulnerable to vitamin E deficiency. For instance, children who have with severe vitamin E deficiency from birth and are not treated with vitamin E rapidly develop neurological symptoms. In contrast, individuals who develop malabsorption of vitamin E in adulthood may not develop neurological symptoms for 10-20 years. It should be noted that symptomatic vitamin E deficiency in healthy individuals who consume diets low in vitamin E has never been reported (2, 12).

Although true vitamin E deficiency is rare, marginal intake of vitamin E is relatively common in the U.S. The National Health and Nutrition Examination Survey III (NHANES III) examined the dietary intake and blood levels of alpha-tocopherol in 16,295 adults (over the age of 18). Twenty-seven % of white participants, 41% of African Americans, 28% of Mexican Americans, and 32% of the other participants were found to have blood levels of alpha-tocopherol less than 20 micromoles/liter. This cutoff value was chosen because the literature suggests an increased risk for cardiovascular disease below this level (13). More recently, data from the NHANES 1999-2000 indicate that mean dietary intake of alpha-tocopherol is 6.3 mg/day and 7.8 mg/day for women and men, respectively (14). These intakes are well below the current intake recommendations of 15 mg/day (see RDA). In fact, it has been estimated that more than 90% of Americans do not meet daily dietary recommendations for vitamin E (15).

The Recommended Dietary Allowance (RDA)

The RDA for vitamin E was previously 8 mg/day for women and 10 mg/day for men. The RDA was revised by the Food and Nutrition Board of the Institute of Medicine in 2000 (4). This new recommendation was based largely on the results of studies done in the 1950s in men fed vitamin E deficient diets. In a test-tube analysis, hydrogen peroxide was added to blood samples and the breakdown of red

blood cells, known as hemolysis, was used to indicate vitamin E deficiency. Because hemolysis has also been reported in children with severe vitamin E deficiency, this analysis was considered to be a clinically relevant test of vitamin E status. Importantly, this means that the latest RDA for vitamin E continues to be based on the prevention of deficiency symptoms rather than on health promotion and prevention of chronic disease.

The Recommended Dietary Allowance (RDA) for *RRR*-alpha-tocopherol (*d*-alpha-tocopherol)			
Life Stage	**Age**	**Males; mg/day (IU/day)**	**Females; mg/day (IU/day)**
Infants (AI)	0-6 months	4 mg (6 IU)	4 mg (6 IU)
Infants (AI)	7-12 months	5 mg (7.5 IU)	5 mg (7.5 IU)
Children	1-3 years	6 mg (9 IU)	6 mg (9 IU)
Children	4-8 years	7 mg (10.5 IU)	7 mg (10.5 IU)
Children	9-13 years	11 mg (16.5 IU)	11 mg (16.5 IU)
Adolescents	14-18 years	15 mg (22.5 IU)	15 mg (22.5 IU)
Adults	19 years and older	15 mg (22.5 IU)	15 mg (22.5 IU)
Pregnancy	all ages	-	15 mg (22.5 IU)
Breast-feeding	all ages	-	19 mg (28.5 IU)

Disease Prevention

Cardiovascular disease

Results of at least five large observational studies suggest that increased vitamin E consumption is associated with decreased risk of myocardial infarction (heart attack) or death from heart disease in both men and women. Each study was a prospective study that measured vitamin E consumption in presumably healthy people and followed them for a number of years to determine how many were diagnosed with or died as a result of heart disease. In two of the studies, individuals who consumed more than 7 mg/day of alpha-tocopherol in food were only approximately 35% as likely to die from heart disease as those who consumed less than 3-5 mg/day of alpha-tocopherol (16, 17). Two other large studies found a significant reduction in risk of heart disease only in women and men who consumed at least 100 IU of supplemental *RRR*-alpha-tocopherol (67 mg of *RRR*-alpha-tocopherol) daily (18, 19). More recently, several studies have observed plasma or red blood cell levels of alpha-tocopherol to be inversely associated with the presence or severity of carotid atherosclerosis detected using ultrasonography (20-23). A randomized, placebo-controlled, intervention trial in 39,876 women participating in the Women's Health Study found that supplementation with 600 IU of *RRR*-alpha-tocopherol (400 mg of *RRR*-alpha-tocopherol) every other day for ten years had no effect on the incidence of various cardiovascular events (myocardial infarction and stroke), but the vitamin E intervention decreased cardiovascular-related deaths by 24% (24). Analysis of data from the Women's Health Study also showed that women receiving the vitamin E intervention experienced a 21% reduction in risk of venous thromboembolism (25). The benefits of vitamin E supplementation in chronic disease prevention are discussed in a recent review (26). Intervention studies in patients with heart or renal disease, however, have not shown vitamin E supplements to be effective in preventing heart attacks or death (see Disease Treatment).

Cataracts

Cataracts appear to be formed by protein oxidation in the lens of the eye; such oxidation may be prevented by antioxidants like alpha-tocopherol. Several observational studies have examined the association between vitamin E consumption and the incidence and severity of cataracts. Results of these studies are mixed: some report increased vitamin E intake protects against cataract development, while others report no association (27). A placebo-controlled intervention trial in 4,629 men and women found that a daily antioxidant supplement containing 500 mg of vitamin C, 400 IU of synthetic vitamin E (*dl*-alpha-tocopherol acetate; equivalent to 180 mg of *RRR*-alpha-tocopherol), and 15 mg of beta-carotene did not affect development and progression of age-related cataracts over a 7-year period (28). Similarly, antioxidant supplementation (500 mg of vitamin C, 400 IU [268 mg] of *RRR*-alpha-tocopherol, and 15 mg of beta-carotene) did not affect progression of cataracts in a 5-year intervention trial (29). A 4-year randomized, placebo-controlled trial reported that supplements containing 500 IU/day of natural vitamin E (335 mg of *RRR*-alpha-tocopherol) did not reduce the incidence or progression of cataracts in older adults (30). Another intervention trial found that a daily supplement of 50 mg of synthetic alpha-tocopherol daily (equivalent to 25 mg of *RRR*-alpha-tocopherol) did not alter the incidence of cataract surgery in male smokers (31). Although results from some observational studies suggest that vitamin E may protect against cataract development, results from clinical trials do not support a preventative effect.

Immune Function

Alpha-tocopherol has been shown to enhance specific aspects of the immune response that appear to decline as people age. For example, elderly adults given 200 mg/day of synthetic alpha-tocopherol (equivalent to 100 mg of *RRR*-alpha-tocopherol or 150 IU of *RRR*-tocopherol) for several months displayed increased formation of antibodies in response to hepatitis B vaccine and tetanus vaccine (32). However, it is not known if such alpha-tocopherol associated enhancements in the immune response of older adults actually translate to increased resistance to infections like the flu (influenza virus) (33). A randomized, placebo-controlled trial in elderly nursing home residents reported that daily supplementation with 200 IU of synthetic alpha-tocopherol (equivalent to 90 mg of *RRR*-alpha-tocopherol) for one year significantly lowered the risk of contracting upper respiratory tract infections, especially the common cold, but had no effect on lower respiratory tract (lung) infections (34). More research is needed to determine whether supplemental vitamin E may protect the elderly against the common cold or other infections.

Cancer

Many types of cancer are thought to result from oxidative damage to DNA caused by free radicals. The ability of alpha-tocopherol to neutralize free radicals has made it the subject of a number of cancer prevention studies. However, several large prospective studies have failed to find significant associations between alpha-tocopherol intake and the incidence of lung or breast cancer (4). One study in a cohort of 77,126 men and women reported that use of vitamin E supplements over a 10-year period increased risk of lung cancer in current smokers (35). To date, most clinical trials have found that vitamin E supplementation has no effect on the risk of various cancers, except a possible benefit against development of prostate cancer. A randomized, placebo-controlled trial in 39,876 women participating in the Women's Health Study found that supplementation with 600 IU of *RRR*-alpha-tocopherol (400 mg of *RRR*-alpha-tocopherol) every other day for ten years had no effect on overall cancer incidence or cancer-related deaths (24). This vitamin E intervention also did not affect the incidence of tissue-specific cancers, including breast, lung, and colon cancers. Moreover, a recently published meta-analysis of 12 randomized controlled trials concluded that vitamin E supplementation was not associated with overall cancer incidence, cancer mortality, or total mortality (36). However, vitamin E supplementation may possibly reduce the risk of prostate cancer. A placebo-controlled intervention study that was designed to look at the effect of alpha-tocopherol supplementation on lung cancer development noted a 34% reduction in the incidence of prostate cancer in smokers given daily supplements of 50 mg of synthetic alpha-tocopherol (equivalent to 25 mg of *RRR*-alpha-tocopherol) daily (37). A meta-analysis that combined the results of this study with three other randomized controlled trials associated vitamin E supplement use with a 15% lower risk of prostate cancer (36). However, a large randomized, placebo-controlled intervention study using alpha-tocopherol and selenium supplementation (the SELECT trial), alone or in combination, was recently halted because there was no evidence of benefit in preventing prostate cancer (38, 39). After an average of 5.5 years of follow-up in SELECT trial, participants taking vitamin E (400 IU/day of *all-rac*-alpha-tocopherol) alone had a higher risk of prostate cancer, but the increase was not statistically significant (40).

Disease Treatment

Cardiovascular disease

Observational studies have suggested that supplemental alpha-tocopherol might have value in the treatment of cardiovascular disease. For example, a small observational study of men who had previously undergone a coronary artery bypass surgery found those who took at least 100 IU of supplemental alpha-tocopherol (67 mg of *RRR*-alpha-tocopherol) daily had a reduction in the progression of coronary artery atherosclerosis measured by angiography compared to those who took less than 100 IU/day of alpha-tocopherol (41). A randomized, placebo-controlled intervention trial in Great Britain (the CHAOS study) found that supplementing heart disease patients with either 400 IU or 800 IU of synthetic alpha-tocopherol (equivalent to 180 mg or 360 mg of *RRR*-alpha-tocopherol) for an average of 18 months dramatically reduced the occurrence of nonfatal heart attacks by 77%. However, alpha-tocopherol supplementation did not significantly reduce total deaths from heart disease (42). Chronic renal dialysis patients are at much greater risk of dying from cardiovascular disease than the general population, and there is evidence that they are also under increased oxidative stress. Supplementation of renal dialysis patients with 800 IU of natural alpha-tocopherol (536 mg of *RRR*-alpha-tocopherol) for an average of 1.4 years resulted in a significantly reduced risk of heart attack compared to placebo (43). In contrast, three other intervention trials failed to find significant risk reductions with alpha-tocopherol supplementation. One study, which was designed mainly to examine cancer prevention, found that 50 mg of synthetic alpha-tocopherol (equivalent to 25 mg of *RRR*-alpha-tocopherol) daily resulted in a non-significant decrease in nonfatal heart attacks in participants who had had previous heart attacks (44). However, two other large trials in individuals with evidence of cardiovascular disease (previous heart attack, stroke, or evidence of vascular disease) found that daily supplements of 400 IU of natural alpha-tocopherol (equivalent to 268 mg *RRR*-alpha-tocopherol) or 300 mg of synthetic alpha-tocopherol (equivalent to 150 mg of *RRR*-alpha-tocopherol) did not significantly change the risk of a subsequent heart attack or stroke (45, 46). A trial in patients with either vascular disease or diabetes mellitus found that daily supplementation with 400 IU of natural alpha-tocopherol for an average of seven years had no effect on major cardiovascular events (myocardial infarction or stroke) or deaths; however, this study noted a slightly increased risk of heart failure in subjects taking vitamin E supplements (47). Thus, results of clinical trials using vitamin E for the treatment of heart disease have been inconsistent.

A more thorough discussion of the complex issues involved in analyzing the results of clinical trials of vitamin E in heart disease can be found in the Fall/Winter 1999 issue of the Linus Pauling Institute Newsletter: **Fish Oil, Vitamin E, Genes, Diet, and CHAOS**. For a discussion of some of the limitations of the HOPE study, see the article, **Vitamin E: Hope or Hopeless**, in the Spring/Summer 2000 issue of the Linus Pauling Institute Newsletter.

Diabetes mellitus

Alpha-tocopherol supplementation of individuals with diabetes has been proposed because diabetes appears to increase oxidative stress and because cardiovascular complications (heart attack and stroke) are among the leading causes of death in diabetics. One study found a biochemical marker of oxidative stress (urinary excretion of F_2-isoprostanes) was elevated in type 2 diabetic individuals, and supplementation with 600 mg of synthetic alpha-tocopherol (equivalent to 300 mg of *RRR*-alpha-tocopherol) for 14 days reduced levels of the biomarker (48). Studies of the effect of alpha-tocopherol supplementation on blood glucose control have been contradictory. Some studies have shown that supplemental vitamin E improves insulin action and glucose disposal in type 2 diabetic (49) and non-diabetic (49, 50) individuals, while other studies have reported minimal to no improvements in glucose metabolism of type 2 diabetics (51, 52). Increased oxidative stress has also been documented in type 1 (insulin-dependent) diabetes (48). One study reported that supplementing type 1 diabetics with only 100 IU/day of synthetic alpha-tocopherol (equivalent to 45 mg *RRR*-alpha-tocopherol) for one month significantly improved both glycosylated hemoglobin and triglyceride levels (53). This study also noted nonsignificant improvements in blood glucose levels following alpha-tocopherol supplementation (53). Although there is reason to suspect that alpha-tocopherol supplementation may be beneficial in treatment for type 1 or type 2 diabetes, evidence from well-controlled clinical trials is lacking.

Dementia (impaired cognitive function)

The brain is particularly vulnerable to oxidative stress, which is thought to play a role in the pathology of neurodegenerative diseases like Alzheimer's disease (54). Additionally, some studies have documented low levels of vitamin E in cerebrospinal fluid of patients with Alzheimer's disease (55). A large placebo-controlled intervention trial in individuals with moderate neurological impairment found that supplementation with 2,000 IU of synthetic alpha-tocopherol daily for two years (equivalent to 900 mg/day of *RRR*-alpha-tocopherol) significantly slowed progression of Alzheimer's dementia (56). In contrast, a placebo-controlled trial in patients with mild cognitive impairment reported that the same dosage of vitamin E did not slow progression to Alzheimer's disease over a 3-year period (57). After Alzheimer's disease, vascular dementia (dementia resulting from strokes) is the most common type of dementia in the U.S. A case-control study examining risk factors for vascular dementia in elderly Japanese-American men found that supplemental vitamin E and vitamin C intake was associated with a significantly decreased risk of vascular and other types of dementia but not Alzheimer's dementia (58). Among those without dementia, vitamin E supplement use was associated with better scores on cognitive tests. Although these findings are promising, further studies are required to determine the role of alpha-tocopherol supplementation in the treatment of Alzheimer's disease and other types of dementia.

Cancer

Cancer cells proliferate rapidly and are resistant to death by apoptosis (programmed cell death). Cell culture studies indicate that the vitamin E ester, alpha-tocopheryl succinate, can inhibit proliferation and induce apoptosis in a number of cancer cell lines (59, 60). The ester form, alpha-tocopheryl succinate, not alpha-tocopherol, is required to effectively inhibit proliferation or induce cancer cell death (61). Although the mechanisms for the effects of alpha-tocohpheryl succinate on cancer cells are not yet clear, the fact that the ester form has no antioxidant activity argues against an antioxidant mechanism (62). Limited data from animal models of cancer indicate that alpha-tocopheryl succinate administered by injection may inhibit tumor growth (63-66), but much more research is required to determine whether alpha-tocopheryl succinate will be a useful adjunct to cancer therapy in humans. Certainly, administration by injection would be necessary for any benefit, because alpha-tocopheryl succinate taken orally is cleaved to form alpha-tocopherol in the intestine (67). There is currently no evidence in humans that taking oral alpha-tocopheryl succinate supplements delivers alpha-tocopheryl succinate to tissues.

Sources

Food sources

Major sources of alpha-tocopherol in the American diet include vegetable oils (olive, sunflower, and safflower oils), nuts, whole grains, and green leafy vegetables. All eight forms of vitamin E (alpha-, beta-, gamma-, and delta-tocopherols and tocotrienols) occur naturally in foods but in varying amounts. For more information on the nutrient content of foods, search the USDA food composition database.

Food	Serving	Alpha-tocopherol (mg)	Gamma-tocopherol (mg)
Olive oil	1 tablespoon	1.9	0.1
Soybean oil	1 tablespoon	1.1	8.7

Corn oil	1 tablespoon	1.9	8.2
Canola oil	1 tablespoon	2.4	3.8
Safflower oil	1 tablespoon	4.6	0.1
Sunflower oil	1 tablespoon	5.6	0.7
Almonds	1 ounce	7.4	0.2
Hazelnuts	1 ounce	4.3	0
Peanuts	1 ounce	2.4	2.4
Spinach	½ cup, raw	0.3	0
Carrots	½ cup, raw chopped	0.4	0
Avocado (California)	1 fruit	2.7	0.4

Supplements

Alpha-tocopherol

In the U.S., the average intake of alpha-tocopherol from food is approximately 8 mg daily for men and 6 mg daily for women (14); these levels are well below the RDA of 15 mg/day of *RRR*-alpha-tocopherol (4). Many scientists believe it is difficult for an individual to consume more than 15 mg/day of alpha-tocopherol from food alone without increasing fat intake above recommended levels. All alpha-tocopherol in food is the form of the isomer *RRR*-alpha-tocopherol. The same is not always true for supplements. Vitamin E supplements generally contain 100 IU to 1,000 IU of alpha-tocopherol. Supplements made from entirely natural sources contain only *RRR*-alpha-tocopherol (also labeled *d*-alpha-tocopherol). *RRR*-alpha-tocopherol is the isomer preferred for use by the body, making it the most bioavailable form of alpha-tocopherol. Synthetic alpha-tocopherol, which is often found in fortified foods and nutritional supplements, is usually labeled *all-rac*-alpha-tocopherol or *dl*-alpha-tocopherol, meaning that all eight isomers of alpha-tocopherol are present in the mixture. Because half of the isomers of alpha-tocopherol present in *all-rac*-alpha-tocopherol are not usable by the body, synthetic alpha-tocopherol is less bioavailable and only half as potent. To calculate the number of mg of bioavailable alpha-tocopherol present in a supplement, use the following formulas:

- ***RRR*-alpha-tocopherol (natural or *d*-alpha-tocopherol):**
  IU x 0.67 = mg *RRR*-alpha-tocopherol.
  Example: 100 IU = 67 mg
- ***all-rac*-alpha-tocopherol (synthetic or *dl*-alpha-tocopherol):**
  IU x 0.45 = mg *RRR*-alpha-tocopherol.
  Example: 100 IU = 45 mg

For more information on the **Biological Activity of Vitamin E**, see the article by Dr. Maret Traber in the Linus Pauling Institute Newsletter.

Alpha-tocopheryl succinate and alpha-tocopheryl acetate (alpha-tocopheryl esters)

Alpha-tocopherol supplements are available in the ester forms: alpha-tocopheryl succinate and alpha-tocopheryl acetate. Tocopherol esters are more resistant to oxidation during storage than unesterified tocopherols. When taken orally, the succinate or acetate moiety is removed from alpha-tocopherol in the intestine. The bioavailability of alpha-tocopherol from alpha-tocopheryl succinate and alpha-tocopheryl acetate is equivalent to that of free alpha-tocopherol. Because international units (IU) for alpha-tocopherol esters are adjusted for molecular weight, the conversion factors for determining the amount of bioavailable alpha-tocopherol provided by alpha-tocopheryl succinate and alpha-tocopheryl acetate are not different from those used for alpha-tocopherol (see formulas) (4). The ester alpha-tocopheryl succinate, not alpha-tocopherol, is required to effectively inhibit growth and induce death in cancer cells grown in culture (see Disease Treatment: Cancer). However, there is currently no evidence in humans that taking oral alpha-tocopheryl succinate supplements delivers alpha-tocopheryl succinate to tissues.

Alpha-tocopheryl phosphates (Ester-E®)

There is currently no published evidence that supplements containing alpha-tocopheryl phosphates are more efficiently absorbed or have greater bioavailability in humans than supplements containing alpha-tocopherol.

Gamma-tocopherol

Gamma-tocopherol supplements and mixed tocopherol supplements are also commercially available (68). The amounts of alpha- and gamma-tocopherol in mixed tocopherol supplements vary, so it is important to read the label to determine the amount of each tocopherol present in supplements.

Safety

Toxicity

Few side effects have been noted in adults taking supplements of less than 2,000 mg of alpha-tocopherol daily (*RRR*- or *all-rac*-alpha-tocopherol). However, most studies of toxicity or side effects of alpha-tocopherol supplementation have lasted only a few weeks to a few months, and side effects occurring as a result of long-term alpha-tocopherol supplementation have not been adequately studied. The most worrisome possibility is that of impaired blood clotting, which may increase the likelihood of hemorrhage in some individuals. The Food and Nutrition Board of the Institute of Medicine established a tolerable upper intake level (UL) for alpha-tocopherol supplements based on the prevention of hemorrhage (see table below). The Board felt that 1,000 mg/day of alpha-tocopherol in any form (equivalent to 1,500 IU/day of *RRR*-alpha-tocopherol or 1,100 IU/day of *all-rac*-alpha-tocopherol) would be the highest dose unlikely to result in hemorrhage in almost all adults (4). Although only certain isomers of alpha-tocopherol are retained in the circulation, all forms are absorbed and metabolized by the liver. The rationale that any form of alpha-tocopherol (natural or synthetic) can be absorbed and thus could be potentially harmful is the basis for a UL that refers to all forms of alpha-tocopherol.

Some physicians recommend discontinuing high-dose vitamin E supplementation one month before elective surgery to decrease the risk of hemorrhage. Premature infants appear to be especially vulnerable to adverse effects of alpha-tocopherol supplementation, which should be used only under controlled supervision by a pediatrician (68). Supplementation with 400 IU/day of vitamin E has been found to accelerate the progression of retinitis pigmentosa that is not associated with vitamin E deficiency (69).

Vitamin E Supplementation and All-Cause Mortality

A meta-analysis that combined the results of 19 clinical trials of vitamin E supplementation for various diseases, including heart disease, end-stage renal failure, and Alzheimer's disease, reported that adults who took supplements of 400 IU/day or more were 6% more likely to die from any cause than those who did not take vitamin E supplements (70). However, further breakdown of the risk by vitamin E dose and adjustment for other vitamin and mineral supplements revealed that the increased risk of death was statistically significant only at a dose of 2,000 IU/day, which is higher than the UL for adults. Additionally, three other meta-analyses that combined the results of randomized controlled trials designed to evaluate the efficacy of vitamin E supplementation for the prevention or treatment of cardiovascular disease found no evidence that vitamin E supplementation up to 800 IU/day significantly increased or decreased cardiovascular disease mortality or all-cause mortality (71-73). Additionally, a more recent meta-analysis of 57 randomized controlled trials found that vitamin E supplementation, up to doses of 5,500 IU/day, had no effect on all-cause mortality (74). Furthermore, a meta-analysis of 68 randomized trials found that supplemental vitamin E, singly or in combination with other antioxidant supplements, did not significantly alter risk of all-cause mortality (75). At present, there is no convincing evidence that vitamin E supplementation up to 800 IU/day increases the risk of death from cardiovascular disease or other causes.

Tolerable Upper Intake Level (UL) for Alpha-Tocopherol	
Age Group	**mg/day (IU/day *d*-alpha-tocopherol)**
Infants 0-12 months	Not Possible to Establish*
Children 1-3 years	200 mg (300 IU)
Children 4-8 years	300 mg (450 IU)
Children 9-13 years	600 mg (900 IU)
Adolescents 14-18 years	800 mg (1,200 IU)
Adults 19 and older	1,000 mg (1,500 IU)

*Source of intake should be from foods or formula only.

Drug interactions

Use of vitamin E supplements may increase the risk of bleeding in individuals taking anticoagulant drugs, such as warfarin (Coumadin); antiplatelet drugs, such as clopidogrel (Plavix) and dipyridamole (Persantine); and non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, ibuprofen, and others. Also, individuals on anticoagulant therapy (blood thinners) or individuals who are vitamin K

deficient should not take alpha-tocopherol supplements without close medical supervision because of the increased risk of hemorrhage (4). A number of medications may decrease the absorption of vitamin E, including cholestyramine, colestipol, isoniazid, mineral oil, orlistat, sucralfate, and the fat substitute, olestra. Anticonvulsant drugs, such as phenobarbital, phenytoin, or carbamazepine, may decrease plasma levels of vitamin E (4, 68).

Antioxidants and HMG-CoA reductase inhibitors (statins)

A 3-year randomized controlled trial in 160 patients with documented coronary heart disease (CHD) and low HDL levels found that a combination of simvastatin (Zocor) and niacin increased HDL2 levels, inhibited the progression of coronary artery stenosis (narrowing), and decreased the frequency of cardiovascular events, such as myocardial infarction and stroke (76). Surprisingly, when an antioxidant combination (1,000 mg of vitamin C, 800 IU of alpha-tocopherol, 100 mcg of selenium, and 25 mg of beta-carotene daily) was taken with the simvastatin-niacin combination, the protective effects were diminished. However, in a much larger randomized controlled trial of simvastatin and an antioxidant combination (600 mg of vitamin E, 250 mg of vitamin C, and 20 mg of beta-carotene daily) in more than 20,000 men and women with coronary artery disease or diabetes, the antioxidant combination did not adversely affect the cardioprotective effects of simvastatin therapy over a 5-year period (77). These contradictory findings indicate that further research is needed on potential interactions between antioxidant supplementation and cholesterol-lowering agents like HMG-CoA reductase inhibitors (statins).

Linus Pauling Institute Recommendation

Scientists at the Linus Pauling Institute feel there exists credible evidence that taking a supplement of 200 IU (134 mg) of natural source *d*-alpha-tocopherol (*RRR*-alpha-tocopherol) daily with a meal may help protect adults from chronic diseases, such as heart disease, stroke, neurodegenerative diseases, and some types of cancer. The amount of alpha-tocopherol required for such beneficial effects appears to be much greater than that which could be achieved through diet alone (see Sources). Since supplements containing 200 IU of *d*-alpha-tocopherol are often as expensive as supplements containing 400 IU of *d*-alpha-tocopherol, a less expensive alternative may be to take 400 IU (268 mg) of *d*-alpha-tocopherol every other day. Alpha-tocopherol supplements are unlikely to be absorbed unless taken with food.

Older adults (65 years and older)

The Linus Pauling Institute's recommendation of a supplement providing 200 IU of natural source *d*-alpha-tocopherol daily (or 400 IU of *d*-alpha-tocopherol every other day) with a meal is also appropriate for generally healthy older adults.

References

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The Radiation Emergency Assistance Center/Training Site (REAC/TS) is a valuable resource in the use of drug therapies to treat radiation exposure. REAC/TS maintains a repository of clinical information and qualified staff provide expertise to practitioners worldwide on the use of calcium and zinc diethylenetriaminepentaacetic acid (DTPA) and Radiogardase (Prussian Blue).
Calcium-DTPA and zinc-DTPA are injectable chelating agents used to enhance the excretion of plutonium and other transuranics from the body.
Radiogardase (Prussian Blue) binds to radiocesium and thallium and enhances their excretion from the body.

Before the events of Sept. 11, 2001, REAC/TS managed the Investigational New Drug (IND) status for DTPA and Prussian Blue. In support of our government's efforts to better prepare for potential radiological terrorist attacks, REAC/TS completed extensive paperwork to move both drugs to New Drug Application (NDA) status, thus making them more readily available for a public health emergency.

Staff continue to:
* Manage the DTPA registry, a computerized collection of case histories of DTPA-treated individuals.
* Evaluate new developments in chelation therapy involving either improved protocols for the existing agents or research on improved chelators.

REAC/TS personnel are also familiar with the use of other treatments such as potassium iodide (KI). If radioactive iodine is released into the air during a radiation event and then inhaled, it is quickly absorbed by the thyroid gland and can cause damage. KI acts to block the radioactive iodine from being taken into the thyroid gland, thus protecting this gland from injury.

Radiogardase®
(Prussian blue insoluble capsules)
For Oral Administration

DESCRIPTION

Prussian blue insoluble capsules contain insoluble ferric hexacyanoferrate(II), with an empirical formula of $Fe_4[Fe(CN)_6]_3$ and a molecular weight of 859.3 Daltons. It is provided as 0.5 gram of Prussian blue powder in gelatin capsules with 0 – 38 mg of microcrystalline cellulose. The powder may vary from uniformly fine, dark granules to coarse light and dark-colored granules. The structural formula for Prussian blue insoluble is shown below.
The crystal structure of Prussian blue is a cubic lattice with the FeII and FeIII atoms occupying the corners of the cube and the cyanide groups positioned on the sides.

CLINICAL PHARMACOLOGY

General

Prussian blue insoluble, ferric(III) hexacyanoferrate(II), after oral ingestion is not absorbed through the intact gastrointestinal wall. Its clearance from the body depends on the gastrointestinal tract transit time. Prussian blue insoluble acts by ion-exchange, absorption, and mechanical trapping within the crystal structure and has a very high affinity for radioactive and non-radioactive Cesium and Thallium. Prussian blue insoluble binds Cesium and Thallium isotopes in the gastrointestinal tract after these isotopes are ingested or excreted in the bile by the liver thereby reducing gastrointestinal reabsorption (enterohepatic circulation). In studies of rats, pigs, and dogs that were internally contaminated with Cesium and Thallium, the presence of the insoluble complexes in the gastrointestinal lumen changed the primary elimination route from the kidney to the feces and increased the rate of elimination of these two contaminants.
The rate of Cesium and Thallium elimination was proportional to the duration and dose of Prussian Blue insoluble. (See CLINICAL PHARMACOLOGY, Pharmacokinetics.) A radioactive element has a constant rate of disintegration that is reflected by its physical half-life. The rate of element elimination from the body is reflected by its biologic half-life. The combined rate of radiation disintegration and rate of element elimination is reflected by the effective half-life. Cesium-137 (137Cs) has a physical half-life of 30 years with a beta energy peak at 174.0 keV. Following entry into the blood, it is distributed uniformly through all body tissues. Approximately 10% of Cesium is eliminated rapidly with a biological half-life of 2 days, and 90% is eliminated more slowly, with a biological half-life of 110 days. Less than 1% of the Cesium was retained with a longer biological half-life of about 500 days. Cesium follows the movement of potassium and is excreted into the intestine, reabsorbed from the gut into the blood, then to the bile, where it is excreted again into the gut (enterohepatic circulation).

Without Prussian blue insoluble treatment, ~80% of Cesium is excreted through the kidneys and ~20% in the feces. Because of Cesium's long physical half-life, the rate of radiation elimination is similar to the rate of element elimination from the body. Thallium-201 (201Tl) has a physical half-life of 3 days with electron and photon emissions with a gamma energy peak at 167.4 keV. Following entry into the blood, Thallium is distributed in the kidneys (3%) and all other organs (97%). Non-radioactive Thallium, depending upon the tissue, has a biological half-life of 8 – 10 days. Thallium also follows the movement of potassium and is excreted by the bile in enterohepatic recirculation. Without Prussian blue insoluble treatment, the fecal tourine excretion ratio of Thallium is approximately 2:1. Based on the mechanisms of action, Prussian blue insoluble may bind other elements (e.g., potassium), and cause electrolyte or other nutritional imbalances. (See PRECAUTIONS, Laboratory Tests.)

Dose-Response Relationship

Animal Data: Dose-response studies have not been conducted in human subjects. In a study using rats (n = 40, mean body weight range of 188 – 219 g) injected with 137Cs it was demonstrated that there is a dose response relationship of the amount of radiation elimination with Prussian blue insoluble doses from 1 to 50 mg/day. There is little difference in radiation elimination rate between Prussian blue insoluble doses of 50 to 100 mg/day. In Table 1, the % of Injected Radiation Dose Remaining is defined as the percentage of the total injected dose of 137Cs remaining in the body at 96 hours post administration.

Human Data: The results of fecal analysis from those patients contaminated with 137Cs and treated with Prussian blue insoluble showed higher activities of 137Cs in feces, and the associated whole body radioactivity counts showed a more rapid rate of elimination from the body. The effectiveness of Prussian blue insoluble for one patient is shown in Figure 1. The whole body content of radioactive material of 137Cs in kilo-Bequerels (kBq) is on the y-axis. Time in days is on the x-axis. Line "A" represents the whole body activity of 137Cs during Prussian blue insoluble treatment at 10 gm daily. The dotted line represents extrapolation of the whole body activity if treatment was continued. Line "B" represents the whole body activity of 137Cs, after Prussian blue insoluble was stopped.

Pharmacokinetics

Absorption/Elimination

In an animal study (pigs, n = 38), after a single dose of 40 mg of labeled Prussian blue insoluble, 99% of the administered Prussian blue dose was excreted unchanged in feces. Absorption from multiple doses has not been studied.

Food Effects

Food effect studies were not identified in the literature. In animal studies, Prussian blue insoluble was not significantly absorbed. Food may increase the effectiveness of Prussian blue insoluble by stimulating bile secretion. Food is known to increase bile production and enterohepatic circulation. The increase in enterohepatic circulation may increase the amount of Cesium and Thallium in the gastrointestinal lumen, and may increase the amounts available for binding with Prussian blue insoluble.

Renal Impaired and/or Compromised Liver Function Patients

Adequate and well-controlled pharmacokinetic and pharmacodynamic studies in renal impaired and/or compromised liver function patients were not identified in the literature. Prussian blue insoluble is not systemically bioavailable and does not rely on renal elimination or hepatic metabolism; therefore, the use of Prussian blue insoluble is not contraindicated in these groups of patients. However, Prussian blue insoluble may be less effective in patients with impaired liver function due to decreased excretion of Cesium and Thallium in the bile.

Clinical Trials

[Effective half-life: the time required for the amount of a radionuclide deposited in a living organism to be diminished by 50% as a result of the combined action of radioactive decay and biologic elimination.]

Epidemiological studies and literature review data were reported in 106 subjects who received Prussian blue insoluble after excessive exposure to 137Cs or non-radioactive Thallium.

Cesium-137 Contamination

Overall, in literature reports, 65 patients and 7 normal human volunteers received Prussian blue insoluble after internal contamination with 137Cs.

In a 1987 incident in Goiânia, Brazil, 46 persons with heavy internal contamination with 137Cs were treated with Prussian blue insoluble. Data on the whole body effective half-life of 137Cs, during and after Prussian blue insoluble treatment, was completed on 33/46 of these patients. The untreated mean whole body effective halflife of 137Cs is 80 days in adults, 62 days in adolescents, and 42 days in children. Prussian blue insoluble reduced the mean whole-body effective half-life of 137Cs by 69% in adults, by 46% in adolescents and by 43% in children. The following table shows the decrease in whole body effective half-life of 137Cs in patients during Prussian blue insoluble treatment as compared to being off treatment.

Data from additional literature articles including a study of 7 human volunteers contaminated with trace doses of 137Cs and reports on 19 patients contaminated with 137Cs in other incidents show a similar reduction in whole

body effective half-life after Prussian blue insoluble treatment.

Thallium Contamination

Thirty-four patients treated with Prussian blue insoluble for non-radioactive Thallium poisoning are reported in the literature. Prussian blue insoluble treatment reduced the mean serum biologic halflife of Thallium from 8 days to 3 days.

INDICATIONS AND USAGE

Prussian blue insoluble is indicated for treatment of patients with known or suspected internal contamination with radioactive Cesium and/or radioactive or non-radioactive Thallium to increase their rates of elimination.

CONTRAINDICATIONS

None

WARNINGS

Prussian blue insoluble is administered to decrease radiation exposure. It does not treat the complications of radiation exposure. Patients contaminated with high doses of 137Cs may develop radiation toxicity including bone marrow suppression with severe neutropenia and thrombocytopenia. Supportive treatment for radiation toxicity symptoms should be given concomitantly with Prussian blue insoluble treatment.

In radiological emergencies, the type of elemental exposure may not be known. Prussian blue insoluble may not bind to all radioactive elements and some radioactive elements may not undergo enterohepatic circulation, which is needed for Prussian blue insoluble binding and elimination. Patients contaminated with unknown or multiple radioactive elements may require treatment with other agents in addition to Prussian blue insoluble.

PRECAUTIONS

General: Gastrointestinal

Prussian blue insoluble can cause constipation. Decreased gastrointestinal motility will slow the transit time of 137Cs bound to Prussian blue insoluble in the gastrointestinal tract, and may increase the radiation absorbed dose to the gastrointestinal mucosa. Constipation occurring during Prussian blue insoluble treatment may be treated with a fiber based laxative and/or a high fiber diet. Prussian blue insoluble should be used with caution in patients with disorders associated with decreased gastrointestinal motility.

Information for Patients

Cesium-137 is excreted in the urine and feces. Appropriate safety measures should be taken to minimize radiation exposure to others. When possible, a toilet should be used instead of a urinal, and it should be flushed several times after each use. Spilled urine or feces should be cleaned up completely, and patients should wash their hands thoroughly. If blood or urine gets onto clothing, such clothing should be washed separately.

Parents and child-care givers should take extra precaution in handling the urine and feces of pediatric patients. Care is intended to prevent re-exposure to the adult and pediatric patient.

In patients with constipation, a fiber based laxative and/or high fiber diet is recommended during treatment with Prussian blue insoluble. Patients taking Prussian blue insoluble should be informed that their stools might be blue-colored.

In patients who cannot swallow capsules, when the capsules are opened and the contents are mixed with food and eaten, the mouth and teeth might be colored blue.

Laboratory Tests

Prussian blue insoluble may bind electrolytes found in the gastrointestinal tract. Asymptomatic hypokalemia, with serum potassium values of 2.5 – 2.9 (normal 3.5 – 5.0), was reported in 3/42 (7%) of patients on treatment with Prussian blue insoluble. Serum electrolytes should be closely monitored during Prussian blue insoluble treatment. Caution should be exercised when treating patients with pre-existing cardiac arrhythmias or electrolyte imbalances. Prussian blue insoluble may bind some orally administered therapeutic drugs. As appropriate, blood levels or clinical response to oral medications should be monitored.

Drug-Drug Interactions

Adequate and well-controlled drug-drug interaction studies in humans were not identified in the literature. In preliminary studies, animals were contaminated with several different radioisotopes and treated with several different radioeliminators. Based on these animal data, co-administration of Prussian blue with other radioeliminators does not affect the efficacy of Prussian blue for 137Cs.

Binding to some therapeutic drugs and essential nutrients is possible. The literature contains anecdotal reports of asymptomatic hypokalemia and decreased bioavailability of oral tetracycline. The serum levels and/or clinical response to critical orally administered products should be monitored.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies with Prussian blue insoluble to evaluate carcinogenesis, mutagenesis and impairment of fertility have

not been performed.
All males who received a whole body radiation absorbed dose greater than 1 Gy of 137Cs, 2 – 8 years later had either oligospermia or azospermia.

Pregnancy Category C
Comprehensive animal reproductive studies have not been conducted with Prussian blue insoluble. Since Prussian blue insoluble is not absorbed from the gastrointestinal tract, effects on the fetus are not expected. In one patient that became pregnant 3 years and 8 months after being treated with Prussian blue insoluble for internal contamination with 137Cs (8 mCi), complications or birth defects were not identified in the literature report. Cesium-137 is known to cross the human placenta. One patient, in Goiânia, was contaminated with 0.005 mCi 137Cs during her 4th month of pregnancy. She was not treated with Prussian blue insoluble. At birth the concentration of 137Cs was the same in the mother and the infant. Thallium crosses the human placenta. Reported fetal effects in the reviewed literature include fetal death, failure to thrive, alopecia, or in some instances outwardly normal development. The risk of toxicity from untreated radioactive cesium or Thallium exposure is expected to be greater than the reproductive toxicity risk of Prussian blue insoluble.

Nursing Mothers
Studies to determine if Prussian blue insoluble is excreted in human milk have not been conducted. Since Prussian blue insoluble is not absorbed from the gastrointestinal tract, its excretion in milk is highly unlikely. However, cesium and Thallium are transmitted from mother to infant in breast milk. Women internally contaminated with Cesium or Thallium should not breast feed.

Pediatric Use
The safety and efficacy of Prussian blue insoluble and its dosing for the pediatric population was extrapolated from adult data and supported by pediatric patients who were internally contaminated with 137Cs and treated with Prussian blue insoluble in the Goiânia accident.
Overall, 27 pediatric patients received Prussian blue insoluble in the range of 3 – 10 grams per day in divided doses. Prussian blue insoluble treatment reduced the whole body effective half-life of 137Cs by 46% in adolescents and by 43% in children aged 4 to 12 years of age. In 12 patients for whom the rate of radiation elimination data are available, the rate was similar to that in adults treated with 3 grams TID and in pediatric patients treated with 1 gram TID. (See CLINICAL PHARMACOLOGY, Clinical Trials, Table 2.) By body weight, the dose ranged from 0.32 gram/kg in the 12-year old patient (10 gram Prussian blue daily dose, 31 kg weight) to 0.21 gram/kg in the 4 year old patient (3 gram Prussian blue daily dose, 14 kg weight).
Pediatric patients aged 2 up to 4 years are expected to have biliary and gastrointestinal function that is comparable to a 4-year old. There are variations in the developmental maturity of the biliary system and gastrointestinal tract of neonates and infants (0 – 2 years). The dose-related adverse effects of Prussian blue insoluble on an immature gastrointestinal tract are not known. Dosing in infants and neonates has not been established.

ADVERSE REACTIONS
Deaths or serious or severe adverse events attributed to Prussian blue insoluble have not been reported.
Constipation was reported in 10/42 (24%) patients in the Goiânia accident treated with Prussian blue insoluble. Severity of constipation was mild in 7 patients and moderate in 3 patients. Constipation was successfully treated with a high fiber diet.
Undefined gastric distress was reported in 3 patients treated with 20 gram/day of Prussian blue insoluble. In these patients the dose was reduced to 10 gram/day for continued treatment.

OVERDOSAGE
The clinical effects of overdosing with Prussian blue insoluble are not known. Based on reported adverse events and mechanism of action, possible overdose symptoms may include obstipation, obstruction, or severe decrease in electrolytes.

DOSAGE AND ADMINISTRATION
Adults and Adolescents:
The recommended dose of Prussian blue insoluble is 3 grams orally three times a day.
Pediatrics (2 – 12 years):
The recommended dose of Prussian blue insoluble is 1 gram orally three times a day.
In patients who cannot tolerate swallowing large numbers of capsules, the capsules may be opened and mixed with bland food or liquids. This may result in blue discoloration of the mouth and teeth. Prussian blue insoluble capsules may be taken with food to stimulate excretion of Cesium or Thallium.
Treatment with Prussian blue insoluble for radioactive Cesium (137Cs) contamination: Treatment with Prussian blue insoluble should be initiated as soon as possible after contamination is suspected. Contamination should be verified as soon as possible. However, even when treatment cannot be started right away, patients should be given Prussian blue insoluble as soon as it becomes available. Treatment with Prussian blue insoluble

is still effective even after time has elapsed since exposure.
Treatment should continue for a minimum of 30 days and then the patient should be reassessed for the amount of residual whole body radioactivity. The duration of treatment after exposure is dictated by the level of contamination and the judgment of the attending physician. Before, during and after therapy, pertinent measurements for radioactivity should be made to help determine when to terminate treatment.
During treatment, the following information should be collected:
• the radioactivity counts in urine and fecal samples should be measured and recorded weekly to monitor 137Cs elimination rate, and
• the occurrence of any adverse events from Prussian blue insoluble (i.e., constipation, which can be treated by increasing the amount of fiber in the diet).
When the internal radioactivity is substantially decreased, the Prussian blue insoluble dose may be decreased to 1 or 2 grams TID to improve gastrointestinal tolerance.
Treatment with Prussian blue insoluble for Thallium contamination: Treatment with Prussian blue insoluble should be initiated as soon as possible after contamination is suspected. Contamination should be verified as soon as possible. However, even when treatment cannot be started right away, treatment with Prussian blue insoluble is effective and should not be withheld.
Further considerations for radioactive Cesium contamination
1. Health professionals should follow appropriate radiation protective attire and procedures at all times. Protect health professionals handling patients from unnecessary radiation exposure and monitor health professionals and the area of operation for radiation levels, using radiation detection, indication, and computation devices (RADIAC) or thermal luminescent devices (TLD). Control spread of radiation contamination through the establishment of a patient triage site, patient decontamination area, and a contaminated or "dirty" material dumpsite. Proper labeling, handling, and disposal of contaminated material needs to be established and followed.
2. Manage the patient to minimize further injury and to stabilize before external decontamination.
3. Establish if the patient suffers from a single or combined injury (e.g., radiation, burns, trauma, chemical, biological, etc.) and whether the contaminant may be internalized.
The route of entry of the radiation contaminant needs to be identified and recorded. The route of entry will determine other treatment methods needed (e.g., wound debridement or stomach lavage if ingested). Patients need to be triaged based on their injuries and the level and type of contamination.
4. A quantitative baseline of the internalized contamination of 137Cs should be obtained by appropriate whole-body counting and/or by bioassay (e.g., Biodosimetry), or feces/urine sample whenever possible to obtain the following type of information to establish an elimination curve:
• Estimated internalized radiation contamination of 137Cs,
• Rate of measured elimination of radiation in the feces.
Further considerations for Thallium contamination (radioactive and non-radioactive)
General therapy guidelines for Thallium contamination should follow the radioactive decontamination procedures listed above for 137Cs, except that there is no need for radiation safety precautions when treating patients contaminated with non-radioactive Thallium. For both radioactive and nonradioactive Thallium contamination, a quantitative baseline of the internalized Thallium contamination should be ascertained by appropriate whole body counting and/or by bioassay whenever possible.
Patients should also have weekly CBC, serum chemistry and electrolytes while under treatment. The response to other orally administered medications should be closely monitored. (See Drug-Drug Interactions.)
In cases of severe Thallium intoxication, additional types of elimination treatment may be necessary, such as:
• Induced emesis, followed by gastric intubation and lavage.
• Forced diuresis until urinary Thallium excretion is less than 1 mg/24h.
• Charcoal hemoperfusion may be useful during the first 48 hours after Thallium ingestion (biodistribution phase).
• Hemodialysis has also been reported to be effective in Thallium intoxication.
Considerations for multiple contaminant exposure (radioactive and non-radioactive) In patients who have contamination with multiple or unknown radioactive isotopes, additional decontamination and treatment procedures may be needed.
HOW SUPPLIED
Radiogardase® (Prussian blue insoluble capsules) is supplied as 0.5 gram blue powder in gelatin capsules for oral administration. It is packaged in brown glass bottles containing 30 capsules each. The product is manufactured by Haupt Pharma Berlin GmbH for distribution by HEYL Chemisch-pharmazeutische Fabrik GmbH & Co. KG, Berlin.
NDC 58060-002-01
Storage
Store in the dark at 25°C (77°F), excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].
PATIENT TREATMENT DATA
To develop long-term response data, detailed information on patient treatment should be provided to the manufacturer whenever this drug is administered. These data should include a record of the radioactive body

burden and bioassay results at defined time intervals, a description of measurement methods to facilitate analysis of data, and adverse events (see attached patient data form). In cases where exposure is limited in terms of number of patients, it may be possible to collect more detailed patient information. Please see the following website, www.heyltex.com for additional suggested data collection.
Questions regarding patient treatment data collection and the use of Prussian blue insoluble for the treatment of patients exposed to radioactive Cesium and/or radioactive or non-radioactive Thallium may be submitted to:

[http://www.eurekalert.org/pub_releases/2009-07/bumc-noa071009.php]

New oral agents may prevent injury after radiation exposure
(Boston) – Researchers from Boston University School of Medicine (BUSM) and collaborators have discovered and analyzed several new compounds, collectively called the "EUK-400 series," which could someday be used to prevent radiation-induced injuries to kidneys, lungs, skin, intestinal tract and brains of radiological terrorism victims. The findings, which appear in the June issue of the Journal of Biological Inorganic Chemistry, describe new agents which can be given orally in pill form, which would more expedient in an emergency situation.

These agents are novel synthetic "antioxidants" that protect tissues against the kind of damage caused by agents such as "free radicals." Free radicals, and similar toxic byproducts formed in the body, are implicated in many different types of tissue injury, including those caused by radiation exposure. Often, this kind of injury occurs months to years after radiation exposure. The BUSM researchers and their colleagues are developing agents that prevent injury even when given after the radiation exposure.

This paper describes a newer class of compounds, the "EUK-400 series," that are designed to be given as a pill. According to the researchers, experiments described in their paper prove that these agents are orally active. They also show that the new agents have several desirable "antioxidant" activities, and protect cells in a "cell death" model.

These same BUSM researchers and collaborators had previously discovered novel synthetic antioxidants that effectively mitigate radiation injuries, but had to be given by injection. "We have developed some of these agents and have studied them for over 15 years beginning with our work at the local biotechnology company Eukarion," said senior author Susan Doctrow, PhD, a research associate professor of medicine at BUSM's Pulmonary Center. "These injectible antioxidants are very effective, but there has also been a desire to have agents that can be given orally. A pill would be more feasible than an injection to treat large numbers of people in an emergency scenario," she adds.

Future studies will focus on the EUK-400 compounds' effects in various experimental models for radiation injury. Data showing their benefits in models for radiation injury in blood vessel cells have been presented at two major scientific conferences and will be the topic of future publication. More broadly, beyond the potential for treating victims of radiological terrorism, these compounds could also be useful drugs against a variety of diseases where an effective antioxidant has potential benefits, for example, various neurological, pulmonary, cardiovascular, and autoimmune disorders. Previously, Doctrow's lab and others have published studies showing that the injectible versions of these compounds are beneficial in models for several such diseases.
Public release date: 10-Jul-2009
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Boston University Medical Center
Funding for this study was provided by the U.S. Centers for Medical Countermeasures Against Radiation (CMCR) program, administered by National Institute of Allergy and Infectious Diseases. The study was initiated with CMCR "Pilot Grant" funding awarded to Dr. Rosalind Rosenthal, first author of the paper and currently a research associate at BUSM. Doctrow's laboratory at BUSM is a member of a five-institution CMCR program, based at the Medical College of Wisconsin in Milwaukee.

THE CHERNOBYL CATASTROPHE AND HEALTH CARE

By Michel Fernex
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This manuscript represents a chapter in a book to be published in France on Belarus. The original is in French and it is also available in Russian.

The origin and consequences of the Agreement concluded between the World Health Organisation (WHO) and the IAEA are discussed. This Agreement may explain why the WHO remained absent during the first five after the Chernobyl accident on health studies and in particular studies on the genome.

The WHO-IAEA Agreement has led to risks for scientists intending to study and publish on the real consequences of such accidents or even the show damages due to chronic, low-dose radiation in the organism due to incorporation of radionuclides with food.

This paper is a message addressed to NGOs, e.g.: IPPNW, GSIEN, ISDE and those who signed the petitions in behalf of professor Bandazhevsky[1]s case.

You can find this text and Bandazhevsky[1]s file in Internet at: www.chernobyl.da.ru

THE CHERNOBYL CATASTROPHE AND HEALTH

Michel Fernex

Introduction

After the explosion and the fire in the atomic reactor N. 4 in Chernobyl, radioactive fallout were registered in large parts of the Northern Hemisphere of the planet. The northern part of Ukraine, the South-East of Russia and the territory of Belarus have been contaminated to the greatest extent. The level of the radioactive fallout on the territory of Belarus, a non-nuclear state, was two times as high as that of Ukraine and Russia together.

It would have been essential to thoroughly investigate the consequences of the Chernobyl accident. The Belarusian population, which suffers most, should have been extensively studied from the medical and genetic point of view. Unfortunately, the pronuclear lobby, including the International Agency of Atomic Energy (IAEA) made use of all their influence to reduce the significance or to deny the data coming from the most affected countries. Their goal may have been to avoid paying compensations to the states and to the victims: in Belarus two million people, of 500.000 children, still live in heavily contaminated areas. Moreover, the evacuated population and 800,000 workers in charge of the decontamination of the area close to the exploded reactor, the so-called liquidators, are now scattered in different republics of the former USSR.

It is necessary to understand by which methods the pronuclear lobby and the IAEA achieve their goals and to assess the price of this attitude for Belarus: economic, medical, demographic and social problems of the republic appear to be the consequence of this policy. Twenty five per cent of the national budget is spent for the alleviation of the consequences of Chernobyl. In order to ensure a real protection for the victims, it would be necessary to provide much more help to the population, and in a different way, compared to the actual strategy. Rich countries possessing nuclear technology would have been in a position to take over these expenses. Contrary to other industries, the nuclear industry does not need to contract insurance capable to compensate the consequences of a catastrophe such as Chernobyl. This would cost such an amount, that nuclear electricity would become too expensive. Therefore, it would be fair to assign to the states the payment of the debt of civil responsibility.

It is difficult to understand why the Belarusian authorities seem to follow the demands of the pronuclear lobby. It is much easier to explain why the World Health Organization (WHO) became so inefficient in this field: it is still blocked by an "Agreement" signed in 1959 with the International Agency for Atomic Energy, (IAEA).

The agreement between the WHO and the IAEA and the Chernobyl disaster.

After the explosion of the reactor, the authorities concealed the information, released it finally much too late and did not consider it necessary to tell the truth [1, 2, 3, 4]. This reaction of the authorities was responsible for ***"ignorance and uncertainty"*** concerning the radioactive contamination, which followed the explosion of the reactor. Up to the year 2000, the flow of misinformation has not stopped. Thereby it is useful to remember a technical report published by the WHO in 1958 [5]. The report contains a chapter devoted to a "policy in case of an accident" and ends with a wish:

"Nevertheless, from the point of view of mental health, the most favorable solution for future uses of peaceful atomic energy would be the appearance of a new generation, which would learn to adapt to ignorance and uncertainty..."

This apology of ignorance reflects an absence of respect for populations which contradicts the spirit and the letter of the Constitution of the WHO (8). This paragraph was read by Mr. Claude Haegi, representing the government of Geneva at the Conference organized by the WHO on the consequences of the Chernobyl accident, in November 1995 in Geneva. Mr. Haegi also quoted a statement of the Director-General of the IAEA, who, according to the newspaper "Le Monde" of August 28, 1986, four months after the accident, declared that "in view of importance of nuclear energy, the world could bear with one accident of the Chernobyl dimension per year". And Mr. Haegi concluded his speech declaring: ***"One Chernobyl is enough. It is necessary to aspire to absolute security"***.

This statement of M. Haegi, as well as so many others presented at the WHO Conference, was to be published in the Proceedings by March 1996. However, these texts have still not been published [6]. Apparently, the papers presented in Geneva could have influenced negatively the IAEA Conference, in Vienna, in April 1996. The only explanation for the non publications appears to be the Agreement between the WHO and the IAEA, signed in 1959. This Agreement states that the research programs of the WHO should previously be agreed, so that their results would not harm the IAEA main objective, which is:
"To accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world".

This excerpt from the Statute of the IAEA is printed on the first pages of every publication of this Agency, including the Proceedings of the April 1996 conference of the IAEA already published in September 1996 devoted to the Chernobyl accident [7].

The Agreement guarantees that the research will not negatively affect the development of nuclear energy.

Article I, § 3 of the Agreement, specifies in particular that:
"Whenever either organization proposes to initiate a program or activity on a subject in which the other organization has or may have a substantial interest, the first party shall consult the other with a view to adjusting the matte by mutual agreement."

According to Article III of the mentioned Agreement:
§ 1: The International Atomic Energy Agency and the World Health Organization recognize that they may find it necessary to apply certain limitations for the safeguarding of confidential information furnished to them.
§ 2: Subject to such arrangements as may be necessary for the safeguarding of confidential material, the Secretariat of the IAEA and the Secretariat of the WHO shall keep each other fully informed concerning all projected activities and all programs of work which may be of interest to both parties.

The requirement of Article III, demanding confidentiality, which means silence, is contrary to the Constitution of the WHO. In fact, the purpose of the WHO is specified in chapter I of the Constitution of this Organization:
"The attainment by all peoples of the highest possible level of health".

Chapter II, Article 2 specifies how the WHO intends to attain its objective, and defines, in particular, the following functions:
(a) To act as the directing and co-ordination authority on international health work;
(d) To furnish appropriate technical assistance and, in emergencies, necessary aid, upon the request or acceptance of Governments;
(q) To provide information, counsel and assistance in the field of health;
(r) To assist in developing an informed public opinion among all peoples on matters of health ;

It is evident, that the provisions of the Agreement prevent open information that is contrary to the Constitution of the WHO. Nevertheless, the Agreement was signed during the 12th World Health Assembly, May 28, 1959. The above quoted clauses can be found in ***Basic Documents of the WHO*** *[8]*.

A very early publication of the WHO warning against the development of the nuclear industry, has been prepared by a group of outstanding experts in the field of genetics, who met in Geneva in 1956. The winner of the Nobel Prize M. J. M. Muller signed this joint statement. [9]:
"The genome is the most valuable treasure of humankind. It determines the life of our descendants and the harmonious development of the future generations. As experts, we confirm, that the health of future generations is threatened by an increasing development of nuclear industry and the growth of the quantity of radioactive sources... we also consider the fact of appearance of new mutations observed at people to be fatal for them and for their descendants".

The publication of the proceedings of this conference was not acceptable to the pronuclear lobby. The IAEA decided soon after its creation to put an end to the freedom of expression in this field by concluding an Agreement with different UN organizations, and especially the WHO. This lasts until today.

The attempts of the WHO to disseminate information about Chernobyl in November 1995.

Dr. Hiroshi Nakajima, Director-general of the WHO, organized an international conference ***"Consequences of Chernobyl and other radiation accidents and their influence on human health",*** in Geneva, in November 20-23, 1995. Mr. Y. Fujita, governor of the Hiroshima prefecture, was the chairman of the conference. This conference considered the destruction of Hiroshima and Nagasaki as

well as the explosion of the Chernobyl reactor as radioactive accidents, deserving to be compared. Considerable differences were ascertained between these two types of accidents (the above-mentioned three explosions had to be categorized in this context as "accidents" and not "catastrophes"). As the Proceedings of this Geneva Conference have not been published, it is impossible to refer to the presentations. It is useful to remind its objectives as stated in the program [10]:

**** To present the principal results of the first phase of the international program on health effects of Chernobyl accident (IPHECA).***
**** To compare the obtained results to the results of similar research, related to the health effects of Chernobyl accident.***
**** To improve (and to update) awareness of the type, the total extent and the harm for health of the Chernobyl accident, as known presently and to be foreseen in the future.***
**** To make new results of research concerning consequences of other radioactive accidents, available, in order to give more complete information on their health effects.***
**** To study the effectiveness of the protective measures undertaken in the area of public health during and after the accidents, and to offer recommendations for the future.***
**** To ensure the development and/or to clarify the state of knowledge concerning the consequences of influence of radiation on human health.***
**** To provide information on existing or future research within the framework of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR).***
**** To earmark the interesting tendencies and changes, which should become an object of steadfast attention of the researchers.***

This program convinced 700 doctors and experts, many from the most contaminated countries to participate in the work of the congress. The IAEA also mobilized the supporters of the atomic industry. Thus, contrary opinions were expressed, which allowed for hot debates. The representatives of the pronuclear lobby tried to prevent the dialogue and Prof. S. Yarmonenko from the Moscow Oncologic Center, demanded that the organizers would remove from the programs of future congresses those speakers, who intended to speak on the effects of low level radiation on living organisms. This apparently became a rule for all the following international conferences, especially in Vienna, 1996.

The reports, debates and presentations of the posters in Geneva were not published. The large document, which presents on 519 pages the statistical data gathered during the first phase of the WHO pilot project IPHECA [11]: "Influence of Chernobyl accident on health", confirms the very slow response of the WHO on the Chernobyl accident. Although the majority of people considered Chernobyl as an extreme incident, demanding urgent measures, the IAEA alone supervised the studies and provided the information on this catastrophe. The IAEA coordinated with the national medical authorities the protective measures for the population, considering as its priority to reduce the expenses.

The WHO was never the "co-ordinating authority" as required by its Constitution. At meetings, where the destiny of the victims was discussed, the WHO was even represented by Prof. Pellerin, a promoter of the development of nuclear industry [1]. Five years after the accident, the WHO, finally started studying the problems in the field, selecting 5 priority subjects, among them dental caries, whereas birth defects and hereditary alterations, which the Committee of experts gathered by the WHO [9], considered as a priority, were carefully overlooked.

As the Proceedings of the WHO-Geneva Conference remain unpublished, it seems to be useful to recall some presentations.

M. Martin Griffiths from the UN Humanitarian Department in Geneva, stated that people still do not know the truth, and that many are still living in contaminated zones. He requested the WHO to continue its research work and to provide assistance, as he feared that everything would be stopped without adequate financial support. According to M. Martin Griffiths 9 million people are sufferers from Chernobyl, and the victims of the accident are constantly growing in number.

Dr. Y. Korolenko, Minister of Health of the Ukraine, noted that the nuclear fallout contaminated the largest part of his country. Thirty million people drink contaminated water from the Dniepr. Everyone was affected by I-131 and the specialists now perform measures to reconstruct the radiation dose of Cs-137, received by the population. The minister mentioned lesion of the endocrine system and declared that diabetes mellitus had increased by 25 percent (This was not related to diet). Knowing about the social consequences of the insulin-dependent form of diabetes, it is easy to understand the deep concern of the Minister, who recalled the financial situation of his country in that situation, and asked all the states for help.

Prof. E.A. Netchaev from the Ministry of Health and Medical Industry (Moscow) indicated that 2,5 million people were irradiated in the Russian Federation following Chernobyl, and that 175.000 people continue to live in contaminated regions. He showed the increased incidence of a very aggressive form of cancer of the thyroid gland in small children, and the increase of birth defects from 220 up to 400 in 100,OOO newborns in the contaminated regions. The frequency of similar diseases ranges within 200/100,000 in clean regions of Russia.

Prof. Okeanov from Belarus presented the results of his epidemiological research, in particular, data based on the national register of cancer, recognized by the WHO, which has been established in Belarus in 1972. Whereas leukemia increased in Hiroshima within the first years after the bombing with a peak between the sixth and the eighth years in Chelyabinsk the maximum occurred after 15-19 years. Okeanov noticed an increase of leukemia among liquidators only after 9 years, but the peak has not yet been reached. He stated that those liquidators, who worked more than 30 days in contaminated areas, have three times as many leukemia as their colleagues who worked there less than 30 days. The period of exposure to radiation seems thus to play an important role. Other forms of cancers are also increasing: cancers of the bladder doubled among the liquidators. The number of cancers of the kidneys, the lungs, and other organs also increased in the Gomel region, an area heavily contaminated by the nuclear fallout with.

The report of this group of Belarusian scientists showed also an increase of cardiovascular diseases among the liquidators, from 1,600 up to 4,000 per 100,000, and up to 3,000 per 100,000 persons living in zones of heavy radioactive contamination. They noticed marked alterations of the immune system, increase of chromosomal aberrations, loss of sight, in particular due to cataract among young subjects. The speakers showed a doubling of mental retardation observed in children as well as mental changes in adults. He insisted on the necessity to study the increase of gastro-intestinal disorders, which he also observed. Among documents received by the WHO, there were unpublished presentations, e.g.: a document of professor Okeanov in Russian of 1994 [12].

All the data submitted in Geneva in November 1995, were not available in March 1996 as officially promised [6]. This delay may well be in relation with the decision of the IAEA, to definitely close the debate about Chernobyl at its own Conference, in Vienna, April 1996 [7]. The publication by the WHO of the Proceedings of its 1995 Conference could have prevented the IAEA from achieving its objective: to put an end to discussions about the health effects of the Chernobyl "accident".

The IAEA Conference, April 8-13, 1996, in Vienna;

The title of this Conference was "***Ten Years after Chernobyl"***. The participants had been selected according to the approval by the ministry of industry and the ministry of international affairs; the ministry of health was not consulted. During the plenary sessions, the speakers expressed contempt and haughtiness towards victims of the disaster. Actions to be taken after the future major accidents, which were considered as unavoidable, were also discussed at the congress. The aim of the discussion on this topic was very clearly formulated: to reduce expenses for the relevant industries, to limit or even avoid evacuation of people from highly contaminated zones, to keep the media under severe control. They believed that "alarmist", "stressful" reports were basically causing practically all the Chernobyl connected health problems.

The speakers for the main reports and especially the chairpersons of the sessions had been instructed to avoid discussions on ³ difficult ² problems related to health, particularly those deriving from the chronic incorporation of Chernobyl radionuclides from the environment in the organism. Those speakers also called for the silence of mass media in case of a catastrophe, since, they believed that ³alarmist² reports were basically causing practically all the Chernobyl-connected health problems.

The authors of the main presentations confined themselves to the three types of illnesses (acute irradiation syndrome, mental deficiency in children irradiated in utero, and thyroid cancer, in children exclusively), which had been admitted to be the essential pathological findings due to the increased ionizing radiation caused by Chernobyl. All the other illnesses put into the large catalogue of psychosomatic diseases associated with unjustified fears, or to some kind of social protest, having nothing to do with radioactivity.

The acute radiation syndrome was one of the rare real "accident's outcome". This syndrome led to discussions to determine if the number of deaths was 31 or 32. These deaths were practically the only ones taken into consideration by the IAEA, as a consequence of the Chernobyl catastrophe.

However, when IPPNW members had rallied in Kazakhstan in order to help the population to stop the Soviet atomic tests, General-in-Chief Ilienko showed memorial shields on the walls of the Officers¹ House in Semipalatinsk. The featured the names of local residents killed during the two world wars and the Afghanistan War. There was a further list of people who died for the nation. The General asked us: "Do you know who are on this list? They are our Chernobyl liquidators!"

The Soviet Union sent 800,000 soldiers, civil experts and foremen, their average age being 33 years, to the site of the disaster to try to decontaminate it, isolate and stabilize the reactor¹s ruins. We met the widows of liquidators in Moscow. Several years ago, there were already more than a thousand of them, and they kept gathering new files and photos of other deceased liquidators "Moscovites husbands", who died from new diseases, which they heroically acquired during their service, neither generally acknowledged posthumously nor always glorified by the nation.

As for the liquidators, E. Marchuk, the Ukrainian Prime Minister pointed out at the IAEA Conference [7], that in his country, 3.1 million people were exposed to radiation at the time of the explosion. Many remain in the contaminated area. Among the 360,OOO Ukrainian liquidators, 35,OOO were already invalid.

Although at the conference IAEA conceded the existence of neuropsychic diseases in children whose mothers had been exposed to radiation during their pregnancy. The speakers denied the existence of similar diseases in adults due to the radiation around Chernobyl,

although this is a well-known phenomenon. The organizers tried to present victims suffering from neuropsychic diseases (in particular, among the 800,OOO liquidators) as malingerers, raising claims for more financial support, or possessed by unjustified fear of radioactivity. IAEA experts first invented the new terminology of "radiophobia". Later, when negative reaction to this concept arose, the term of "environmental stress" was created to qualify neurovegetative and subjective disturbances as well as a complex of other illnesses, caused by Chernobyl.

The Permanent People's Tribunal (3) judged the behavior of international organizations, especially the IAEA, national commissions for atomic energy as well as governments, which finance them on behalf of the interest of the nuclear industry as follows: **"The absence of concern for these real outcomes of radiation exposure, was in itself one of the ways in which the victims were revictimized after the disaster"**.

The IAEA has done its best to allow those responsible for what had happened, as well as the countries possessing nuclear know-how and the Western atomic lobby, to save as much as possible on the expense of the victims of the Chernobyl catastrophe.

Cancer diseases caused by Chernobyl.

After many years of obstruction, in particular during the IAEA conference in 1991, the experts of the IAEA had to admit the existence of thyroid pathologies, partially brought about by Iodine 131, discharged into the atmosphere by the blow-up in Chernobyl. According to Bandazhevsky that illness are caused by several radionuclides (e.g. Cs-137, Sr-90 in tissues of different organs. Their toxicity may be synergistic [13]. During discussions on the thyroid cancers, the official speaker of IAEA mentioned that this was "a good cancer". We do not think, that mothers of children, ill with cancer and often having metastases in their lymph nodes and even in their lungs, or that the surgeons who operate those children share this view.

The IAEA tried to show that it would be easy to distribute tablets of stable, non-radioactive iodine among the population in order to prevent thyroid cancer. Doctors were aware of such preventive measures before the catastrophe. However, with the exception of Poland, neither the politicians nor the technical equipment allowed to undertake in time such preventive actions.

During this debate, one of the speakers specified that iodine tablets have to be ingested before the radioactive cloud appears, thus ensuring their maximal efficiency. This seems to be quite problematic, as they call at the same time on the mass media to remain silent in case of a future accident [3] as to avoid fears [2]. The immediate distribution of iodine pills should be envisaged not only in the radius of 5-30 km, but of 500 km and over.

The IAEA officials considered also long-term effects [7] and made the following conclusion:
"Ten years after the Chernobyl accident, in the three affected countries, there are no serious after-effects caused by the radioactivity as a consequence of this accident, except the dramatic increase in numbers of thyroid cancer diseases in children, exposed to the radioactivity in the most contaminated regions. The death rates do not show any substantial raise due to cancers, which could be related to the accident at the Chernobyl nuclear power plant. In particular, there is no serious increase in the number of blood diseases even among liquidators, i.e. the diseases which were of greatest concern after a radioactivity explosion."

The wording of this conclusion will be discussed later. However it was contradicted by the co-chair person, Prof. Okeanov, who elaborated on the cancer diseases. His task may well have been on the contrary to remain silent.

The discussion following the "official" report on cancer diseases and the conclusions set up, was strictly restricted to radiometry. The first speaker tried to discuss the problems of cancers, but was forced to leave the floor. When I answered the question as to the topic of my report, I claimed my great interest in radiometry, thus gaining a chance to ask a question to Prof. Okeanov: "At the WHO Conference [6] in Geneva in 1995 and later at the congress run by an NGO in Minsk in March 1996, you have shown data of significant increase of cancer? Would you care to comment?". Okeanov had showed that the global tendency of number of cases of cancers was increasing, liquidators being at the peak of the curve. The incidence of cancers and leukemia was depending on the duration of their exposure to radioactivity (14).

The increase in numbers of thyroid cancers has been registered in Minsk since 1989. Leukemia in small children, whose mothers had been exposed to radioactivity during their pregnancy, was observed that early, too [15], and followed the mechanism described in the late fifties by Alice Stewart & al (16).

Since 1993-1995, epidemiologists have been observing an increase in the numbers of cancers, mainly among young people, connected with a strong dose of radioactivity after Chernobyl. The liquidators were on the average 33 years old.

The chart of AE Okeanov, which I presented at the IAEA conference, was published in the Proceedings [7].

The number of cases of cancers per 100,000 inhabitants who have been irradiated to some extent compared to 30,000 liquidators

exposed more and less than thirty days.

Cancer Belarus
population Belarusian liquidators (More than 30,000 cases)
Total number of
irradiated > 30 days of
Irradiating < 30 days of
Irradiating
large intestine (colon) 12 18,5 20,1 13,4
Urinary bladder 13 31,1 32,1 27,1
Leukemia
Total : 10,4

35,4 23,3

72,9 25,8

77,0 16,4

56,9

During the discussion in Vienna Prof. Okeanov confirmed his data and added that the cancer of the thyroid gland in liquidators also increases. He stated that in Gomel, 180 km from Chernobyl, ***"an apparent increase in the number of cancer of the colon, the rectum, the lungs, the breast and the urinary system is observed".***

Okeanov underlined the importance of continuing the epidemiological research. Alas, his Institute, whose quality was recognized by the WHO (France, Germany, Switzerland do not have similar national cancer registers), has been dismembered some time later. This appears to be a deliberate step aimed at the suppression of epidemiological data in connection with Chernobyl.

In Hiroshima, the latency period for cancers of the thyroid gland and leukemia in small children was 4 to 5 years. Petridou & al [15] observed an epidemic of leukemia in small children after the passage of the radioactive cloud in Greece, 1,000 km from Chernobyl. It is therefore very disappointing that the WHO involvement started its studies too late to assess leukemia in infants irradiated in utero.

For the majority of other cancers however, the latency period lasts about 9-30 years and more. This explains the haste with which the pronuclear lobby wanted to stop research in this field. The dismantling of the cancer register, an institution that could demonstrate with accuracy to the world how many tens of thousands of cancers would be caused by Chernobyl serves well the IAEA and the pronuclear lobby.

Let's return to the conclusion of the Proceedings of the IAEA Conference, which contains the following statement: ***"No major increase in the incidence or mortality for all cancers has been observed that could be attributed to the accident".*** Not knowing the context, it is possible to assume that the phrase is not a barefaced lie. However, it is preceded by the statement, which clarify the essence: ***"..Apart from thyroid cancers, ... there are no evidence of a major public health impact to date of radiation exposure as a result of the Chernobyl accident in the three most affected countries".***

Utilizing a misleading technique, the IAEA selects the false parameter: the mortality rate caused by cancers just 10 years after the catastrophe. At this stage only the morbidity rate would be a permissible parameter in this context [17]. Cancer in younger persons is a dramatic event for families, friends and of course for the patient himself. The treatment of such cancers requires long-term hospitalizations, surgical interventions, chemotherapy, and absence from professional activity, which are extremely expensive both for the society and for the families. Meanwhile, the modern methods of treatment allow to cure some forms of cancer and, in many cases, to put off the lethal outcome. Therefore in 1996, the selected parameter should have been the morbidity and not the mortality

Will the parents, whose children undergo medical treatment for leukemia, even when the child has completely recovered, consider that there were ***"no serious health effects"?***

Such outright lies, contained in this conclusion were designed to permit the nuclear lobby to keep on building "reliable" nuclear power plants. Did not the promoters of nuclear reactors tell us over and over again that this industry in completely reliable? Today the nuclear lobby intends to sell nuclear power plants with a new advertising slogan: "they are even more reliable than before". This commercial argument is not related to any scientific reality. We do not want to prove this hypothesis after all those lies we heard so far.

Diseases caused by radionuclides incorporated in the organisms

Chernobyl diseases affect up to 90 % of children in the contaminated zones. These diseases must be categorized, according to the opinion of the IAEA, as not related to radioactive contamination. **"If real, these increases (in the frequency of a number of non-specific detrimental health effects) may be attributable to stress and to anxiety resulting from the accident."**. The stress contributes to symptoms in 80 % of adult population, consulting with practitioners in Western Europe. The IAEA may have hoped to find at least a similar percentage of stress in the inhabitants of the contaminated regions, as well as among the liquidators and the settled out population.

Nevertheless, despite a severe selection of the speakers, and a strict control on the discussions at the Vienna conference in 1996, the chairmen of sessions and experts invited by IAEA could not achieve unanimity in this area.

During the first weeks after the accident, the territories of Europe, Scandinavia, the Alps, the Jura, the Balkans and Turkey were contaminated by enormous amounts of iodine 131. Byelorusian doctors revealed quite early the health effects of this contamination. After 1986 other radionuclides with relatively long-lived half-lives (approximately 30 years for Cs-137 and Sr90; 240 centuries for plutonium), had already begun to alter the functions of organs (heart, kidneys), nervous and immune systems, and the totality of the genes in cells, especially of those that were closer to incorporated radiation.

The map of the nuclear fallout (I-131 and Cs- 137), appeared soon after the explosion of the nuclear reactor due to the outstanding work performed by the team of Vasily Nesterenko [18], whose scientifically proved, but alarming reports were the cause of his dismissal.

Facing the dramatic problems of his country, this physicist could fortunately continue his research due to support provided by western charitable funds, and his work to protect the population forced to live in contaminated regions [19]. His information on the contamination was not made public by the authorities. The world was late to find out about it, too late [20].

In the Gomel State Medical Institute under the leadership of its outstanding young rector, Professor Youry Bandazhevsky, the researchers studied the influence of radionuclides incorporated by the human organism, and the pathological changes leading to serious diseases of various organs [21]. Those are the diseases of the majority of the adults and 90 % of children forced to live in zones with a heavy radio-contamination.

Professor Bandazhevsky, a pathologist, showed in experimental models, that the laboratory animals, feeding on contaminated food similar to the one that the inhabitants of the contaminated regions are obliged to eat, present morphological and functional changes similar to the processes observed in the people. His experiments show, in particular, the damage caused by Cs 137, and prove, that for this isotope, whose period of biological half-decay (i.e. the time necessary for a human being to halve concentration of a mentioned radionuclide in organism) is shorter than a year, it is possible to use medical drugs to reduce its toxic and radioactive burden for the organism.

The studies of the Department of Pathology of the Gomel Medical Institute offer also to the researchers a better understanding of the diseases provoked by a chronic intoxication of organs or systems after incorporation of Cs 137. In addition to the whole program of research at his Institute Bandazhevsky supervised 30 candidate dissertations and has published 200 articles and reports, some of them already translated into English [13, 21, 22].

The damage caused by Cs-137 starts already in the prenatal phase. The placenta serves as a filter between maternal blood and the blood of the foetus, and protects against foreign molecules such as drugs, but also against this radionuclide during the whole period of pregnancy. Placenta therefore accumulates considerable quantities of Cs 137, more than tissues of the maternal organism [21]. This accumulation of toxic molecules and radioactivity in the placenta, close to the cells responsible for the secretion of hormones necessary for the normal evolution of the pregnancy, appears to be responsible for the abnormal levels of several hormones. Morphological anomalies are more common when high Cs 137 concentrations are found in the placenta. The fetus suffers from anoxia, the risk of abortion increases. Furthermore, incidence of birth defects in children whose mothers live in contaminated zones is twice as high as compared to those, whose mothers live in clean regions.

If the mother lives in zones of radio-contaminated zones, breast-feeding will lead to rapid accumulation of radionuclides in the organism of the child. During childhood, children will continuously incorporate radionuclides, in particular Cs - 137 contained in milk, vegetables, fruit etc. This chronic intoxication of different organs leads to frequent diseases, such as abnormal blood pressure, cardiac arrhythmia, but also to allergic diseases, chronic infections, due to immune deficiency.

Bandazhevsky has developed methods to protect those children. This would require from the authorities, on the one hand, to recognize the problem and, on the other, the willingness to help these populations by educational measures, adequate food intake and intermittent treatments. There exist possibilities to remove partially the Cs 137. Professor Bandazhevzky tested several substances: pigments, adsorbents, algae, among others. The best results were achieved with an extract of apple pectin, able to fix Cs 137 and to prevent its absorption. It may also remove it partially from the organism, the mobilization and elimination being mainly with feces.

All these measures reduce the load of toxic radionuclides in the organism; this approach is essential from the medical point of view. The high concentration of Cs 137 in certain organs or tissues lead to irreversible damages, when this radioactive load lasts for years or exceeds certain limits.

From 1996 to 2000, Professor Vasily Nesterenko and his Belarusian Institute of Radiation Safety ³Belrad² carried out measures on the internal contamination using spectrometers. More than 50.000 children at schools and kindergarten of contaminated regions of Belarus took part in this project. The Institute of radiation safety found excessive levels of Cs - 137 in the organisms of children in contaminated areas. Many accumulated 200-400 Bq/kg Cs - 137 in their organism. Children living in Narovliansky. Yelsky, Tchetchersky, Vetkovsky, Kormiansky, and Stolinsky regions had up to 1500-2000 Bq/kg, some children have reached contamination doses of 4000-7000 Bq/kg.

The correlation made by Professor Y. Bandazhevsky, show that if a child¹s organism has a content of Cs - 137 of more than 50 Bq/kg, pathological disorders of the vital organs or systems will occur. That is why the Institute "Belrad" has carried out since 1995 the protection of such children, using a preparation with pectin, vitamins and essential elements, ³Yablopect².

The intermittent use of pectin is recommended for children with an internal Cs 137 contamination of more than 20 Bq/kg in their organism. The reduction of radionuclides in a child¹s organism is 30-40 % after taking 2-3 tablets per day of this preparation for one month, 3 to 4 times in a year with at least 2 months intervals between treatments. The reduction of the internal dose of Cs - 137 in children's organisms, reduces 2-3 times the annual contamination dose.

These tablets diluted in water are well accepted by children (the drink tastes like an apple) and are well tolerated. If this treatment is initiated early enough, the symptoms may be attenuated. The goal would be to prevent the diseases or in advanced cases, to stop their malignant evolution such as cardiac failure, hypertension etc.

This research should raise interest among physician, concerned by the health care of the victims of the Chernobyl accident. Non-governmental organizations (NGOs) of Ireland, Sweden, Belgium have generously contributed to these programs.

It is surprising, that this assistance to the victims became an object of spiteful pamphlets and inappropriate irony in some places. When Professor Nesterenko had the possibility to present the results of his research in Western Europe, in order to find new ideas and support, some participants made rather aggressive remarks. There may be a competition between people working the whole year to help local population and scientific tourists from different western countries who collect data during their visits in the contaminated regions.

Electrocardiographic changes were noticed in a large number of first year students of the Gomel Medical Institute, coming from contaminated regions. Unfortunately, those changes tended to worsen during the following 4 years of their studies. The heart muscles (myocardium) concentrate more Cs-137 than other tissues. The circulatory system is affected by the "Cesium cardiomyopathy", described by Bandazhevsky. The preventing of this disease in people living in contaminated areas would be their relocation, or a correct diet, which as a rule is too expensive for the population, and intermittent pectin cures.

The endocrine system is also very sensitive to Cs-137. The thyroid and the placenta have already been mentioned; there are several diseases of the thyroid many are associated with the increase of the antibody titers against the thyroid cells, which leads to hypothyroid function. Such functional disturbances are 100 times more frequent than cancers. They may have a very negative impact on mental and physical development of children.

The immune system is highly sensitive both to internal and external radiation. This protective system relies on the white blood cells, e.g. lymphocytes. Alterations of this cell system may lead to immune deficiencies as in AIDS. Titov et al. have shown, that the production of antibodies is abnormal in contaminated children [23]. The health disturbances of this complex system include allergic diseases, like asthma. Allergy for cow milk and fruits is observed in 50% of the school children and students in Gomel.

Autoimmune diseases occur when the cells, designed to fight intruding organisms such as bacteria, viruses or cancer cells, attack the normal cells of an organ. When Beta cells of the pancreas face a self-attack by lymphocytes, this may cause severe diabetes mellitus.

Many aspects of this pathology were presented during the NGO congress in Minsk (24). As a consequence of Chernobyl the incidence of diabetes mellitus had increased by 28%, more or less the same as in the Ukraine; Research conducted by Tatiana Voitovich, endocrinologist in Minsk, shows that after Chernobyl, a new form of diabetes has appeared: an insulin-dependant, unstable form of diabetes in very young children. The child is unconscious when he enters into the hospitals. His blood sugar is very difficult to stabilize with insulin injections. This form of diabetes affects the patient¹s condition during all his life. It was very rare before Chernobyl. The number of cases of insulin-dependant diabetes has doubled in the Gomel region.

Ignoring the Problems

At the IAEA conference, the problem of insulin-dependant diabetes has not been quoted among the diseases caused by Chernobyl, although it was described after the bombing in Hiroshima. The technique for evading this issue during this pronuclear conference is worth telling. During the discussion, I asked whether there existed any link between diabetes and ionizing radiation. The chairman of the session spoke before the speaker could answer, and said: "You have here experts from all over the world, the best specialists in this field. The fact that none of them has raised his hand to answer your question proves that the *ionizing radiation cannot cause this type of disease".*

In connection with this answer of the chairperson, Prof. Viel (17) exposed methods, used by those who do not want to show a link between ionizing radiation and pathological findings. He quoted similar answers or statements to the one I heard: "The experts were unanimous in the view that... there is no association between radiation and any health". Prof. Viel added that such experts may [3]conduct inadequate epidemiological researches by integrating epistemological errors. A classical method was to select mortality instead of morbidity, e.g.: to stop the investigations too early when studying cancers, as it was the case after Chernobyl.

The results of such studies show no statistically significant differences. The hypothesis has therefore not been proved. Promoters conclude that it is false, which allows them to pretend that everything is in order and the atomic industry safe.

The dismantlement Gomel Institute

Lesions of the immune system in organisms contribute to the development of cancers in younger subjects. We must keep in mind that cancers are only the visible part of the iceberg, represented by the totality of the diseases caused by Chernobyl. That is why the scientific world was extremely interested by the research of Professor Bandazhevsky [22), which allow to discover or imagine the true dimension of the iceberg. The systematic studies of this research group allowed characterizing new diseases due to cellular damages caused by the accumulation of radionuclides.

Bandazhevsky studied also other radionuclides, e.g. Sr-90, which accumulates in the bones, close to the blood-producing cells, erythrocytes, including mother cells of the immune system. Sr-90 is much more stable in the human organism than Cs 137. Internal contamination of the organism may also be due to particles of plutonium fixed in the lungs, lymphatic or other tissues. Bandazhevsky considers the synergy between the toxicity of the different radionuclides as a complementary problem.

The arrest of Yuri Bandazhevsky, Rector of the Gomel Medical on July 13, 1999, shocked those who knew him and his publications. This dynamic teacher and highly motivated researcher devoted himself totally to his work, which he considered to be his debt to his country, and in particular, to the victims of Chernobyl. Bandazhevsky created the Gomel Medical Institute and designed its scientific and research work on the causes of the diseases of the population living in the contaminated areas.

Amnesty International reacted at once, considering Bandazhevsky as a potential prisoner of conscience [26]. This opinion was reinforced when the Prosecutor, Oleg Bozhelko, said 9 months after his arrest that he held no proof for his accusation.

Now the Institute has been placed under the direction of a rector "of a follower", who rejected the previous direction of research. This is one of the most brilliant victories of the pronuclear lobby over.

The international solidarity was able to release the prisoner. However Professor Bandazhevsky lost his job, his research instrument, his data, the teaching activity and his income. He is in need of help. His health has been seriously undermined; he has lost 20 kg due to extremely severe conditions in jail. Our solidarity should now allow him to find the way and means to continue his research and to publish his findings. It is also necessary to find money to pay the services of a lawyer

Mutagenic and teratogenic effects

From the ethical point of view, the genetic and hereditary damages are the most disturbing consequence of the radioactive pollution The impact on the genome, i.e. the change in chromosomes or genes, which cause an increase of genetic diseases and birth defects in the coming generations is threatening the workers of the nuclear industry. At all stages of the uranium cycle, from the uranium mining to the management of wastes, including the maintenance of "normally functioning" nuclear facilities, radionuclides are released, in the as gazes or particles, liquids or solids. Radiation lead to an increase of a number of genetic. These were the warnings expressed by the experts invited by the WHO in 1956, when the nuclear industry began to develop [9].

After Chernobyl, changes of the genome were found not only in rodents close to Chernobyl or in Sweden. Children living in contaminated regions, in a radius of 250 - 300 km from Chernobyl show an increase in mutations; [27]. Dominant mutations may be apparent at birth, or become manifest during life. However most of them are not compatible with survival and can cause abortions. Recessive mutations induce genetic diseases and congenital deformities in the next generations. Thus, it will be necessary to wait up to the third to fifth generations of affected by the Chernobyl fallout to observe the full extent of the damage caused by the Chernobyl catastrophe in the families.

Genetic anomalies in fishes, swallows and rodents

A. Slukvin, a former USSR fishing expert, compared two industrial fish farms for carps. The first was situated 200 km from Chernobyl in a zone with a relatively low level of contamination (about 1 Curie per square km), the second, 400 km away from Chernobyl, in a zone of very low contamination. Since 1988 up to 70% of the fertilized eggs did not produce larvae, and after 6 months, the young fishes in the area where the muddy bottom was contaminated with Cs 137 major deformities were observed in 10 to 20% of the carps, depending on the radio-contamination of the pond [28]. The normal development of carps was still possible 400 km from the exploded nuclear power plant. Prof. Rose Goncharova directed Dr. Slukvin¹s thesis.

The generations of rodents and birds around Chernobyl follow much quicker than in man. This allows already studying the increase in deformities, caused by recessive genes in animals living in contaminated areas.

A group of Swedish researchers compared a population of swallows, nesting in Chernobyl, with swallows from uncontaminated regions in the Southern Ukraine and a region of Italy. They studied the DNA structure of the minisatellites of adult and young swallows, as did Dubrova in human [27], in chromosomes in the adult swallows and their offspring. The Swedish researchers discovered a statistically significantly higher mutation rate in Chernobyl swallows compared to those living in clean area [29]. Furthermore, they observed an increase of recessive genetic abnormalities in the Chernobyl swallows. Mutants had white spots on their feathers; they had also a much lower chance to survive. Year after year, observations showed a progressive increase in those disorders in the contaminated areas compared to the Southern Ukraine or to the control zone in Italy. The differences were statistically significant.

A number of studies were devoted to rodents living in more or less contaminated areas [30, 31, 32]. The habitat, where these wild rodents (bank voles) live, has a decreasing radioactivity rate, since Caesium-137 is seeping in the soil with rainwater. One could have expected a positive reaction of these animals to these improving radiological conditions. Yet, genetic abnormalities increased from one generation to another [30, 31]. Goncharova and Ryabokon consider this as a kind of reverse adaptation to radioactivity, an increased fragility of the genome.

Baker and his colleagues [32] studied the DNA in one of the genes, transferred to baby bank voles exclusively from their mothers. They observe various mutations from generation to generation, i.e. an alteration of the base of the studied chromosomes, which overpasses 100 times the mutation rate observed until today in any animal species.

For geneticists point of view, human beings and rodents may well be compared. Commenting the publication of Dubrova & al. and that of Baxter & al, Prof. Hillis, from the Texas University, concluded his editorial in *Nature* (April 25, 1996) as follows:
"We know now know that the mutational effects of nuclear accidents can be much greater than suspected and that evolutionary rates in at least parts of n eucariotic genome can be raised well beyond levels previously considered possible *(33).*

The article by Y. Dubrova & al. was published in the same issue Nature [27]. This team working with Prof. A. Jeffreys, Nobel laureate examined children and their parents, living in the contaminated areas 250 -300 km north from Chernobyl. Compared with children in uncontaminated regions. These children of Belarus showed suffered a doubling of mutations in minisatellite loci. The mutation rate decreased with the degree of radioactivity in their parents¹ residence place. A control group was selected in the United Kingdom due to the overall contamination of the Belarusian territory.

Experts think that a low, but chronic dose of radioactivity, is very dangerous thing for the human genome

In May 1997, the WHO annual report, published on the occasion of the World Health Assembly (WHA) attested that the number of cases of cancers will double within the next ten years. However, this report says that this is due to the growing life expectancy [34]. Such an analysis does not distinguish between the cancers in very old people and those in children and in young adults, which increases most in the Chernobyl regions.

The same publication of the WHO (34) shows an important increase in the number of cases of diabetes. In rich countries, Type II concern people with excessive food intake. Without further explanation, this report indicates that the number of insulin-dependant type I diabetes will also increase in young people. Here we should recall the report of Mr. Korolenko, Ukrainian Minister of Health at the WHO conference in 1995, which was not published [6]. He underlined the 25% increase in the number of cases of diabetes after the accident at the Chernobyl nuclear power plant in a population where excessive food intake is rare.

Birth defects in children

At the IAEA conference in Vienna, 1996 [7], the speaker reporting on teratology as a consequence of the Chernobyl accident, made use of the same argument as the lawyers of the chemical industry that produced in the sixties a tranquilizer, Thalidomide, which appeared to be extremely teratogenic, i.e. provoking a number of birth defects in children whose mothers had absorbed it; This drug caused also birth defects in monkeys, birds and insects [35]. The speaker asserted *"The absence of any register proves that the development of birth defects is not caused by the Chernobyl accident"*.

Of course, the absence of a register is not a proof of the absence of a causal relationship between the increase of birth defects and Chernobyl. But the falsity of this statement is more shocking when Belarus is concerned. Since 1982, i.e. 4 years before Chernobyl, Belarus had a national register of birth defects, developed by the Belarusian Institute of Birth Defects and Inherited Diseases, under the leadership of Professor Gennady Laziuk [36]. This Institute records and checks the cases of birth defects, observed in the country. It is compulsory to report ten birth defects, to be detected in children up to 7 days after birth, or in fetuses in case of spontaneous or therapeutic abortions. Following anomalies must reported in any case: anomalies of the development of the central nervous system as major brain damage, dysraphia of the face or spina bifida, polydactylism, absence of limbs or serious defects in their development, rectal stenosis, mongolism and multiple birth defects.

The incidence of birth defects have increased in Belarus in a direct proportion to the contamination by Cs - 137 in the regions, where the mother was living during her pregnancy [36]. Rates of birth defects of probable dominant genetic origin, e.g. polydactylism and multiple deformities, compatible with survival, have considerably increased [37]. Deformities probably caused by the teratogenic property of radionuclides are also increasing.

There is practically no region spared from radioactive contamination in Belarus, as 90 % of the contamination is caused by the ingestion of contaminated food. No region of the country can be considered as a control area. That is why the findings registered from 1982 to 1985, constitute the best control data available.

During the WHO conference of November 1995, Dr. Smolnikova from Gomel, in charge of the health of 46 thousand children living in an area contaminated by 40 Curies of Cs-137/km2, had already mentioned a high perinatal death-rate and an alarming increase of birth defects in the region [6].

Despite all these reports, the experts from IAEA denied in 1996 any increase of birth defects, related to the Chernobyl catastrophe.

After the epidemic of birth defects caused in Europe by the drug thalidomide (Contergan), and in spite of the fact that thalidomide is not mutagenic, the pharmaceutical industry was forced to exclude, all over the world, substances with mutagenic and teratogenic properties. The fact that similar measures do not apply to the nuclear industry may well be connected with the Agreement signed between the IAEA and other UN organizations, including the WHO. The radionuclides released in the environment by this industry, have mutagenic, teratogenic or cancerogenic properties.

The destruction of scientific structures in Belarus

As long as the World Health Assembly, the governing body of the WHO, does not amend the Agreement, concluded in 1959 with the IAEA, which holds it hostage to the nuclear lobby with regard to the radiation induced health effects, there is no hope for independent research groups to receive any substantial support.

The most efficient structures that study in Belarus the health consequences of the Chernobyl accident are being progressively dismantled.

Professor Nesterenko was one of the physicists, who came immediately to the place of the accident. As an expert and, sometimes, he acted as a fireman, flying with a helicopter within the radioactive cloud, pouring containers of liquid nitrogen in the burning reactor. It is incredible that he survived. The three other passengers of that helicopter have died owing to the irradiation. Together with his colleagues, Nesterenko established the map of the radioactive contamination of all the territory and formulated proposals for the protection of the people.

He continued his work, until his data and his recommendations were considered as unsatisfactory, he was considered as an ³alarmist² and lost his Institute, his functions and his sources of income. Due to the help of Alex Adamovich, Andrej Sakharov, the chess champion Karpov, the Foundation for Peace, the Northern Ireland Foundation Ady Roche, and others, Nesterenko founded a state-independent research Institute ³Belrad², which works to assist victims of Chernobyl, teaching them the best possible methods of self-defense, when they are forced to live in contaminated territories, and tries to rehabilitate children.

The Minister of Health, Dr. Dobrishevskaya, who supported the most efficient research groups in this field, according to a joint report published in 1996 [24], was also not maintained in her function.

Professor Okeanov witnessed the same disorganization of the research structure he was in charge. It was a most valuable instrument, aimed at revealing the true dimensions of the epidemic of cancer diseases caused by the Chernobyl accident. The coincidence with his reports at the conference of the WHO (1995), the NGO conference in Minsk (1996), and his non-observance of the required silence at the conference of the IAEA in Vienna (1996), shows clearly who wanted get rid or to achieve the destruction of this working instrument.

The removal of Professor Bandazhevsky is the last strike in this destructive series. This pioneer of research of health consequences of the Chernobyl accident has revealed the mechanisms of the action of chronic low dose radiation by incorporated radionuclides in organisms: after iodide-131, Cs-137 and Sr-90. With his group of young researchers from the Gomel Medical Institute and numerous volunteers, Bandazhevsky has described typical diseases occurring in a large proportion of the population and almost all the children living in the highly contaminated regions.

These systematic and repeated strikes, which negatively influence the well being of the country and its population, are, sometimes supported by western scientists perhaps jealous these discoveries. However, those who gain the greatest satisfaction and benefit of such actions, are the richest countries with the most advanced nuclear industry, and the nuclear lobby

It is necessary that the WHO recover its independence, in order to be able to act again in this field according to its Constitution. Epidemiological research should start without delay. Who will study the genetic damages in children in the five coming generations? Who will devote himself to the rehabilitation of the victims, to their treatment and to the most effective protection of children and pregnant women? Rich nuclear states should come to the aid of victims of Chernobyl in Belarus and in other suffering countries.

It is also necessary to remove the present mandate of the IAEA to promote commercial nuclear industry. This Agency has much more important problems to solve: to keep under surveillance plutonium, uranium and all the fissionable materials, from dismantled nuclear warheads, military and commercial nuclear facilities. The IAEA must also control the problems of the safe storage of the radioactive waste, which humanity managed to produce in only two generations, since the beginning of nuclear age. This surveillance must unfortunately continue for centuries and millenaries.

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Michel Fernex, MD, Professor emeritus, Medical Faculty of Basel, former member of Steering Committees of Scientific working groups on malaria and filariasis, WHO Geneva. Address : F-68480 Biederthal, France.

Miguelz KI label/ebook statement:

Potassium iodide does NOT protect against radiation. It over-saturates the body with a 1000x (@130mg KI/day) the normal RDA of potassium iodine (130 mcg/day), which is why it can be toxic with long term use (thus the 14 day suggested use). Thyroid iodine receptive locations will have fewer radioactive iodine atoms because of the high number of non-radioactive ions (KI) in the bloodstream.

The high number of non-radioactive ions in the blood stream (from the KI) means the thyroid iodine receptive locations will have reduced radioactive atom saturation.

All of the KI in the world is still packaged as it was back in the 1950's-60's. Once you saw a Russian nuke go off nearby, 130mg of KI per day for 14 days per person was distributed/taken. It was and is a one stop-shop for all exposure levels. End of story.

Two of the FalloutX products have USP grade Potassium Iodide (KI)… but only the maximum dose (15 caps/day) yields the FDA suggested 130mg amount. This makes my products UNIQUE.

Today, taking the KI @ 130mg/day is only complimentary to the Fukushima location. Take 130mg of KI here in CA and it would be an excessive amount for the small fallout concentrations here (100's of times greater than necessary). I designed FalloutX in congruence with the pectin dose requirements. Currently, if I was in Japan I would be getting the max dose of KI and Pectin (15 caps/day) but being here I am only taking 1-2 capsules, depending on the observed fallout counts.

The pectin binds to radioactive cesium 137, strontium 90, Barium, Lead, etc. and is excreted. The KI shields the thyroid as the body slowly excretes the radioactive Iodine 131.

As far as I know, FalloutX is the only dose specific KI product – ALL OTHERS ARE STILL IN THE 20th CENTURY… [and because of this I step very carefully as the Big Boys won't like this exposure]

General Background on Radionuclide Chemistry

There are about 2,000 known radionuclides, which are species of atoms that emit radiation as they undergo radioactive decay through emission of alpha particles, beta particles, or gamma rays. Naturally occuring radionuclides are ubiquitous trace elements found in rocks and soils and, in general, radionuclides can be categorized in three ways: • by type of radioactive decay (alpha, beta, or gamma mission), • by radioactive decay series, • as naturally occurring or manmade. Some of the naturally occurring and manmade radionuclides are directly regulated by the current drinking-water standards. The natural radionuclides include the primordial elements that were incorporated into the earth's crust during its formation, the radioactive decay products (or progeny) of these primordial elements, and radionuclides that are formed in the atmosphere by cosmic ray interactions. Manmade radionuclides are produced through the use of nuclear fuels, radiopharmaceuticals, and other activities of the nuclear industry and have been released into the atmosphere as the result of atmospheric testing of nuclear weapons and, in rare cases, accidents at nuclear-fuel stations, and discharge of radiopharmaceuticals. Further discussion on manmade radionuclides is beyond the scope of this report. The two types of isotopes with radioactive decay that carry the most health risk due to ingestion of water are alpha-particle emitters and beta/photon-particle emitters (Lappenbusch and Cothern, 1985). Many radionuclides are mixed emitters with either an alpha or beta emission coupled with gamma (photon) emission, or in some cases, all three. Each radionuclide has a primary mode of disintegration. The most common, heavy, naturally occurring radionuclides are largely alpha-particle emitters, although their progeny often emit beta particles. The alpha-particle emitting radionuclides discussed in this report include two isotopes of radium (Ra-224 and Ra-226) and polonium-210. Alpha radiation is composed of a particle, consisting of two protons and two neutrons, spontaneously emitted from the nucleus of a subset of radioactive elements (mostly the heaviest elements) during radioactive decay. Alpha radiation is ionizing radiation, meaning that it strips electrons from adjacent atoms as it passes. Alpha radiation cannot penetrate skin; thus, an alpha-particle emitting radionuclide must be ingested in order to come into contact with internal tissue. Because of the large size, alpha particles are likely to collide with cell tissue, causing tissue damage. An accumulation of tissue damage in the cell nucleus may lead to cell mutation and potential cancer.

The naturally occurring radionuclides derived from uranium-238, thorium-232, and uranium-235 are products of the radioactive decay series known as the uranium, thorium and actinium series, respectively. Each decay series follows a known sequence of radioactive decay, producing various isotopes that also emit either an alpha or a beta particle as they decay (fig. 1). Each series terminates with a stable isotope of lead. The crustal abundance of U-235 is very low in comparison with the other decay series (U-238 to U-235 mass ratio is on the order of 140 to 1).

… In a double-blind, placebo-controlled trial, oral apple pectin powder, given for 23 days to children receiving radioactively clean food, lowered the 137Cs burden by some 60%, while the "clean" diet alone lowered the burden by only 14%. Since 1996, different apple pectin preparations have been used in the Chernobyl regions of the Ukraine and Belarus to protect children in the most contaminated areas. So far, some 70,000 children in Belarus have received up to four 1-month pectin courses per year.

…
All highly radio-contaminated children were fed on privately produced food probably containing high levels of 137Cs. It is well known that privately grown vegetables and milk produced at home represent a major risk of radioactive contamination. The use of ashes as fertilizers from highly contaminated wood collected in the forests leads to an increase in the 137Cs burden in the alimentary chain, ashes contributing also to an external irradiation in the kitchen, close to the fireplace. Mushrooms and wild berries consumed at home are another important source of radioactive contamination, but this factor is difficult to quantify based solely on questioning of the children and their families. [1]

Frequently Asked Questions on Potassium Iodide (KI)

In December 2001, the Food and Drug Administration (FDA) issued a final Guidance on Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies (PDF - 40KB)[1]. The objective of the document is to provide guidance to other Federal agencies, including the Environmental Protection Agency (EPA) and the Nuclear Regulatory Commission (NRC), and to state and local governments regarding the safe and effective use of potassium iodide (KI) as an adjunct to other public health protective measures in the event that radioactive iodine is released into the environment. The adoption and implementation of the recommendations are at the discretion of the state and local governments responsible for developing regional emergency-response plans related to radiation emergencies. The recommendations in the guidance address KI dosage and the projected radiation exposure at which the drug should be used. This guidance updates FDA's 1982 recommendations.

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1. What does potassium iodide (KI) do?

The effectiveness of KI as a specific blocker of thyroid radioiodine uptake is well established. When administered in the recommended dose, KI is effective in reducing the risk of thyroid cancer in individuals or populations at risk for inhalation or ingestion of radioiodines. KI floods the thyroid with non-radioactive iodine and prevents the uptake of the radioactive molecules, which are subsequently excreted in the urine.

2. Can potassium iodide (KI) be used to protect against radiation from bombs other than radioactive iodine?

Potassium iodide (KI) works only to prevent the thyroid from uptaking radioactive iodine. It is not a general radioprotective agent.

3. Who really needs to take potassium iodide (KI) after a nuclear radiation release?

The FDA guidance prioritizes groups based on age, which primarily determines risk for radioiodine-induced thyroid cancer. Those at highest risk are infants and children, as well as pregnant and nursing females, and the recommendation is to treat them at the lowest threshold (with respect to predicted radioactive dose to the thyroid). Anyone over age 18 and up to age 40 should be treated at a slightly higher threshold. Finally, anyone over 40 should be treated with KI only if the predicted exposure is high enough to destroy the thyroid and induce lifelong hypothyroidism (thyroid deficiency).

4. What potassium iodide (KI) products are currently available?

As of January 2005, Iosat, ThyroSafe, and ThyroShield are FDA approved KI products. You can find out more about these products at Drugs@FDA[2]. Please be aware that only the KI products approved by FDA may be legally marketed in the United States.

5. How are these products available?

In addition to distributing to state, local and federal agencies, Anbex, Inc., has made Iosat Tablets (130 mg) available to the general public via the Internet. For further information on KI products, you can contact these companies as noted below:

- Anbex, Inc. for Iosat Tablets (130 mg) at 212-580-2810 (M-F 9am-5pm), at 1-866-463-6754 (other times), or http://www.anbex.com[3] [4]
- Recipe for ThyroSafe Tablets (65 mg) at 1-866-849-7672 or http://www.thyrosafe.com/recip.html[5] [6]
- Fleming & Company, Pharmaceuticals for ThyroShield Solution at 636-343-8200 or http://www.flemingcompany.com[7] [8] or http://www.thyroshield.com[9] [10]

6. What dosages of potassium iodide (KI) should be taken for specific exposure levels?

FDA recommends the following dosing of KI for thyroid blocking:

Threshold Thyroid Radioactive Exposures and Recommended Doses of KI for Different Risk Groups

	Predicted Thyroid gland exposure (cGy)	KI dose (mg)	Number or fraction of 130 mg tablets	Number or fraction of 65 mg tablets	Milliliters (mL) of oral solution, 65 mg/mL***
Adults over 40 years	≥ 500	130	1	2	2 mL
Adults over 18 through 40 years	≥ 10	130	1	2	2 mL
Pregnant or Lactating Women	≥ 5	130	1	2	2 mL
Adolescents,	≥ 5	65	½	1	1 mL

12 through 18 years*					
Children over 3 years through 12 years	≥ 5	65	½	1	1 mL
Children 1 month through 3 years	≥ 5	32	Use KI oral solution**	½	0.5 mL
Infants birth through 1 month	≥ 5	16	Use KI oral solution**	Use KI oral solution**	0.25 mL

* Adolescents approaching adult size (≥ 150 lbs) should receive the full adult dose (130 mg)

** Potassium iodide oral solution is supplied in 1 oz (30 mL) bottles with a dropper marked for 1, 0.5, and 0.25 mL dosing. each mL contains 65 mg potassium iodide.

*** See the Home Preparation Procedure for Emergency Administration of Potassium Iodide Tablets to Infants and Small Children[11].

7. How long should potassium iodide (KI) be taken?

Since KI protects for approximately 24 hours, it should be dosed daily until the risk no longer exists. Priority with regard to evacuation and sheltering should be given to pregnant females and neonates because of the potential for KI to suppress thyroid function in the fetus and neonate. Unless other protective measures are not available, we do not recommend repeat dosing in pregnant females and neonates.

8. Who should not take potassium iodide (KI) or have restricted use?

Persons with known iodine sensitivity should avoid KI, as should individuals with dermatitis herpetiformis and hypocomplementemic vasculitis, extremely rare conditions associated with an increased risk of iodine hypersensitivity. Individuals with multinodular goiter, Graves' disease, and autoimmune thyroiditis should be treated with caution -- especially if dosing extends beyond a few days.

9. What are the possible risks and side effects of taking potassium iodide (KI)?

Thyroidal side effects of KI at recommended doses rarely occur in iodine-sufficient populations such as the U.S. As a rule, the risk of thyroidal side effects is related to dose and to the presence of underlying thyroid disease (e.g., goiter, thyroiditis, Graves'). FDA recommends adherence to the Guidance on Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies (PDF - 40KB)[12] for intervention threshold and dose, though we recognize that the exigencies of any particular emergency situation may mandate deviations from those recommendations. With that in mind, it should be understood that as a general rule, the risks of KI are far outweighed by the benefits with regard to prevention of thyroid cancer in susceptible individuals.

10. Should I check with my doctor first?

Potassium iodide (KI) is available over-the-counter (OTC). However, if you have any health concerns or questions, you should check with your doctor.

11. As a doctor, should I be recommending potassium iodide (KI) for my patients who request it?

As with any drug, physicians should understand the risks and benefits of KI before recommending it or prescribing it to patients. We recommend that physicians read our guidance for more information. It is available on the FDA Drug Guidances[13] web page, under procedural guidance #18. The FDA guidance discusses the rationale and methods of safe and effective use of KI in radiation emergencies. It specifically addresses threshold predicted thyroid radioiodine exposure for intervention and dosing by age group. The recommendations for intervention are based on categories of risk for thyroid cancer, with the young prioritized because of increased sensitivity to the carcinogenic effects of radioiodine.

12. Should I go out and buy potassium iodide (KI) to keep on hand?

KI works best if used within 3-4 hours of exposure. Although FDA has not made specific recommendations for individual purchase or use of KI, the Nuclear Regulatory Commission has contracted to purchase KI for states with nuclear reactors and states that have population within the 10-mile emergency planning zone, e.g., Delaware or West Virginia.

13. How do I know that potassium iodide (KI) will be available in case of an emergency?

FDA will continue to work with interested pharmaceutical manufacturers to assure that high quality, safe, and effective KI products are available for purchase by consumers, by state and local authorities, and by federal government agencies electing to do so.

http://emergency.cdc.gov/radiation/emergencyfaq.asp#potassium

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http://emergency.cdc.gov/radiation/ki.asp

Potassium Iodide (KI)

Key Facts

- **You should only take potassium idodide (KI) on the advice of emergency management officials, public health officials, or your doctor.**
- **There are health risks associated with taking KI.**

What is Potassium Iodide (KI)?

Potassium iodide (also called KI) is a salt of stable (not radioactive) iodine. Stable iodine is an important chemical needed by the body to make thyroid hormones. Most of the stable iodine in our bodies comes from the food we eat. KI is stable iodine in a medicine form. This fact sheet from the Centers for Disease Control and Prevention (CDC) gives you some basic information about KI. It explains what you should think about before you or a family member takes KI.

What does KI do?

Following a radiological or nuclear event, radioactive iodine may be released into the air and then be breathed into the lungs. Radioactive iodine may also contaminate the local food supply and get into the body through food or through drink. When radioactive materials get into the body through breathing, eating, or drinking, we say that "internal contamination" has occurred. In the case of internal contamination with radioactive iodine, the thyroid gland quickly absorbs this chemical. Radioactive iodine absorbed by the thyroid can then injure the gland. Because non-radioactive KI acts to block radioactive iodine from being taken into the thyroid gland, it can help protect this gland from injury.

What KI cannot do

Knowing what KI cannot do is also important. KI cannot prevent radioactive iodine from entering the body. KI can protect only the thyroid from radioactive iodine, not other parts of the body. KI cannot reverse the health effects caused by radioactive iodine once damage to the thyroid has occurred. KI cannotprotect the body from radioactive elements other than radioactive iodine—if radioactive iodine is not present, taking KI is not protective.

How does KI work?

The thyroid gland cannot tell the difference between stable and radioactive iodine and will absorb both. KI works by blocking radioactive iodine from entering the thyroid. When a person takes KI, the stable iodine in the medicine gets absorbed by the thyroid. Because KI contains so much stable iodine, the thyroid gland becomes "full" and cannot absorb any more iodine—either stable or radioactive—for the next 24 hours.

Iodized table salt also contains iodine; iodized table salt contains enough iodine to keep most people healthy under normal conditions. However, table salt does not contain enough iodine to block radioactive iodine from getting into your thyroid gland. You should not use table salt as a substitute for KI.

How well does KI work?

Knowing that KI may not give a person 100% protection against radioactive iodine is important. How well KI blocks radioactive iodine depends on

- how much time passes between contamination with radioactive iodine and the taking of KI (the sooner a person takes KI, the better),
- how fast KI is absorbed into the blood, and
- the total amount of radioactive iodine to which a person is exposed.

Who should take KI?

The thyroid glands of a fetus and of an infant are most at risk of injury from radioactive iodine. Young children and people with low stores of iodine in their thyroid are also at risk of thyroid injury.

Infants (including breast-fed infants): Infants need to be given the recommended dosage of KI for babies (see How much KI should I take?). The amount of KI that gets into breast milk is not enough to protect breast-fed infants from exposure to radioactive iodine. The proper dose of KI given to a nursing infant will help protect it from radioactive iodine that it breathes in or drinks in breast milk.

Children: The United States Food and Drug Administration (FDA) recommends that all children internally contaminated with (or likely to be internally contaminated with) radioactive iodine take KI, unless they have known allergies to iodine. Children from newborn to 18 years of age are the most sensitive to the potentially harmful effects of radioactive iodine.

Young Adults: The FDA recommends that young adults (between the ages of 18 and 40 years) internally contaminated with (or likely to be internally contaminated with) radioactive iodine take the recommended dose of KI. Young adults are less sensitive to the effects of radioactive iodine than are children.

Pregnant Women: Because all forms of iodine cross the placenta, pregnant women should take KI to protect the growing fetus. However, pregnant women should take only one dose of KI following internal contamination with (or likely internal contamination with) radioactive iodine.

Breastfeeding Women: Women who are breastfeeding should take only one dose of KI if they have been internally contaminated with (or are likely to be internally contaminated with) radioactive iodine. Because radioactive iodine quickly gets into breast milk, CDC recommends that women internally contaminated with (or are likely to be internally contaminated with) radioactive iodine stop breastfeeding and feed their child baby formula or other food if it is available. If breast milk is the only food available for an infant, nursing should continue.

Adults: Adults older than 40 years should not take KI unless public health or emergency management officials say that contamination with a very large dose of radioactive iodine is expected. Adults older than 40 years have the lowest chance of developing thyroid cancer or thyroid injury after contamination with radioactive iodine. They also have a greater chance of having allergic reactions to KI.

When should I take KI?

After a radiologic or nuclear event, local public health or emergency management officials will tell the public if KI or other protective actions are needed. For example, public health officials may advise you to remain in your home, school, or place of work (this is known as "shelter-in-place") or to evacuate. You may also be told not to eat some foods and not to drink some beverages until a safe supply can be brought in from outside the affected area. Following the instructions given to you by these authorities can lower the amount of radioactive iodine that enters your body and lower the risk of serious injury to your thyroid gland.

How much KI should I take?

The FDA has approved two different forms of KI—tablets and liquid—that people can take by mouth after a nuclear radiation emergency. Tablets come in two strengths, 130 milligram (mg) and 65 mg. The tablets are scored so they may be cut into smaller pieces for lower doses. Each milliliter (mL) of the oral liquid solution contains 65 mg of KI.
According to the FDA, the following doses are appropriate to take after internal contamination with (or likely internal contamination with) radioactive iodine:

- Adults should take 130 mg (one 130 mg tablet OR two 65 mg tablets OR two mL of solution).
- Women who are breastfeeding should take the adult dose of 130 mg.
- Children between 3 and 18 years of age should take 65 mg (one 65 mg tablet OR 1 mL of solution). Children who are adult size (greater than or equal to 150 pounds) should take the full adult dose, regardless of their age.
- Infants and children between 1 month and 3 years of age should take 32 mg (½ of a 65 mg tablet OR ½ mL of solution). This dose is for both nursing and non-nursing infants and children.
- Newborns from birth to 1 month of age should be given 16 mg (¼ of a 65 mg tablet or ¼ mL of solution). This dose is for both nursing and non-nursing newborn infants.

How often should I take KI?

A single dose of KI protects the thyroid gland for 24 hours. A one-time dose at the levels recommended in this fact sheet is usually all that is needed to protect the thyroid gland. In some cases, radioactive iodine might be in the environment for more than 24 hours. If that happens, local emergency management or public health officials may tell you to take one dose of KI every 24 hours for a few days. You should do this only on the advice of emergency management officials, public health officials, or your doctor. Avoid repeat dosing with KI for pregnant and breastfeeding women and newborn infants. Those individuals may need to be evacuated until levels of radioactive iodine in the environment fall.

Taking a higher dose of KI, or taking KI more often than recommended, does not offer more protection and can cause severe illness or death.

Medical conditions that may make it harmful to take KI

Taking KI may be harmful for some people because of the high levels of iodine in this medicine. You should not take KI if
• you know you are allergic to iodine (If you are unsure about this, consult your doctor. A seafood or shellfish allergy does not necessarily mean that you are allergic to iodine.) or
• you have certain skin disorders (such as dermatitis herpetiformis or urticaria vasculitis).

People with thyroid disease (for example, multinodular goiter, Graves' disease, or autoimmune thyroiditis) may be treated with KI. This should happen under careful supervision of a doctor, especially if dosing lasts for more than a few days.

In all cases, talk to your doctor if you are not sure whether to take KI.

What are the possible risks and side effects of KI?

When public health or emergency management officials tell the public to take KI following a radiologic or nuclear event, the benefits of taking this drug outweigh the risks. This is true for all age groups. Some general side effects caused by KI may include intestinal upset, allergic reactions (possibly severe), rashes, and inflammation of the salivary glands.

When taken as recommended, KI causes only rare adverse health effects that specifically involve the thyroid gland. In general, you are more likely to have an adverse health effect involving the thyroid gland if you

- take a higher than recommended dose of KI,
- take the drug for several days, or
- have pre-existing thyroid disease.

Newborn infants (less than 1 month old) who receive more than one dose of KI are at particular risk for developing a condition known as hypothyroidism (thyroid hormone levels that are too low). If not treated, hypothyroidism can cause brain damage. Infants who receive KI should have their thyroid hormone levels checked and monitored by a doctor. Avoid repeat dosing of KI to newborns.

Where can I get KI?

KI is available without a prescription. You should talk to your pharmacist to get KI and for directions about how to take it correctly. Your pharmacist can sell you KI brands that have been approved by the FDA.

Other Sources of Information

- The FDA recommendations on KI can be reviewed on the Internet at Frequently Asked Questions on Potassium Iodide (KI) .
- The Centers for Disease Control and Prevention's Emergency Response Site is available at CDC Radiation Emergencies.