TEAM AUTHORS:
Center for Rural Affairs, Martin Kleinschmit, Hartington, Nebraska
Northeast Nebraska RC&D, Plainview, Nebraska
Holistic Management® Certified Educator, Terry Gompert, Center, Nebraska

PURPOSE:
This fact sheet is prepared to educate both the consumer and producer on facts about raw milk. Raw milk sales are legal in over half the states (rules vary state by state). Most of the raw milk purchased in the U.S. is done so legally at the dairy farm. Check with the Department of Agriculture in the state you live for specific rules. As with other foods, milk may cause allergies in some people. Consulting a nutritionist, medical personnel, and other food experts would be well advised here. Producers and marketers of raw milk need to know the liabilities.

The demand for unpasteurized milk is increasing in this country. Although many consumers perceive a nutritional and health benefit from its use, the facts presented in this paper are intended to address the safety issues for purchasing, transporting, and storing unprocessed milk.

DEFINITIONS:
Milk (milk) n. a white or yellowish liquid consisting of small fat globules suspended in a watery solution, secreted by the mammary glands for the nutrition of the newborn. It contains all the nutrient substances (proteins and enzymes, fats, sugars, minerals and vitamins) necessary for growth, but is deficient in iron; such a secretion drawn from a cow, goat, etc. for use as human food. Webster’s Dictionary

Whole Raw Milk. Also called “real milk” or “living milk.” Whole milk has a rich taste that comes from the fat content of the milk. Whole milk will contain 3 to 5% fat depending on the individual cow, the cow breed, and the type of feed or pasture the cow is eating.

Conventional and/or Confined Dairy. Animals are confined and fed a highly processed ration of grain and forage. Seldom are the animals allowed to graze. The facilities are designed for efficiencies and the owner.

Grass Based Dairy. Animals primarily graze their pastures for their nutrition being supplemented primarily with forages. The facilities are designed to optimize the consumption of green growing pasture and forage.

OPEN COMMUNICATIONS ESSENTIAL FOR PURCHASING OR SELLING RAW MILK
Trust is the key to a safe and successful raw milk market. Relationships build trust. Farmers need to be transparent and open with their customers. Good customer relations will reduce the liability.

Both customers and farmers need to be comfortable bringing up a problem. Farmers are more likely to be concerned about milk quantity or availability.

The consumer is more likely to be concerned about taste or flavor.

Customers need to be aware that taste is often a result of feed changes as well as speed of cooling and does not necessarily indicate contamination. However, the communication lines must be open enough so the customer feels free to contact the farmer immediately if there is a reason to suspect that an illness was caused by consuming milk. These who choose to use raw milk should know the farmer and be comfortable with higher husbandry practices.
This Fact Sheet is divided into various modules. These modules include: Science, Farmer, Consumer, and Resources.

Raw Milk Use and Safety Fact Sheet

Science Module

A French scientist, Louis Pasteur, invented pasteurization to preserve wine nearly a century and a half ago. Pasteurization involves heating a product to 145 - 150 degrees Fahrenheit (F) for 30 minutes or to 164 - 168 degrees F for 15 seconds.

Pasteurization is said to kill all life in the milk, including disease-producing bacteria that may be present. The process was first used to treat milk in the US in the early 1920s. During that period, food-borne illnesses associated with milk consumption were common due to poor sanitation in the dairies, diseased farm employees, inadequate refrigeration, and poor animal health conditions because brewery byproducts were used as a major part of the milk cow’s diet and because the cows were housed in filthy conditions in inner city confinement dairies.

Pasteurization is said to be responsible for reducing milk-borne outbreaks in that period. Milk as a source of food borne illness has declined from nearly 25% to only 1% of outbreaks in today’s environment. Outlawing of inner city dairies and the advent of refrigeration also contributed to reducing milk-borne outbreaks.

Most conventionally produced milk from confined cows should still be properly pasteurized to reduce potential disease outbreaks. For example, in recent University of California Davis tests, 31% of raw milk samples taken from farm tanks of conventional milk intended for pasteurization, contained detectible human pathogens. Since most milk processors buy milk from many different dairies and co-mingle it with other milk to obtain appropriate volume, their entire output is likely to be contaminated.

Pasteurization can be carried out by the processor or the consumer. In either case, pasteurization must be totally completed. Incomplete or improper pasteurization can actually increase the risk to human health by failing to kill the “bad bacteria.”

The four main disease-causing pathogens of concern today are listeria, salmonella, staphaureus, and E. coli 0157:H7. FDA also reports a list of other types of bacteria that might be found in raw milk, including campylobacter, escherichia, yersina and brucella. FDA also lists diseases raw milk products can cause, such as tuberculosis, diphtheria, polio, strep throat, scarlet fever and typhoid fever.

The pasteurization standard today calls for heating milk to 161 degrees F for 15 seconds, in order to destroy the harmful bacteria. However, most processors heat to 175 degrees F and are moving toward ultra pasteurization, with temperatures of 282 degrees F, which allows a shelf life of 60 to 120 days. To keep posted on the most current, legal pasteurization standards check with your state’s Department of Agriculture office.

Pasteurization not only kills bad bacteria and pathogens, but also kills beneficial bacteria and destroys enzymes. Phosphatase is destroyed by pasteurization. Phosphatase is essential for the absorption of calcium. Another enzyme, lipase, aids in the digestion of fats. Pathogen inhibitors destroyed by pasteurization include lactobacillus bacteria, bacteriocins (nisin and others which kill listeria), lactoperoxidase, lactoferrin, xanthine oxidase, lysozyme, and other pathogen inhibiting, natural elements.

Protein – lysine and tyrosine are altered by heat as are the fat – soluble vitamins. The loss of vitamin A, D, E and F can run as high as 66%. Vitamin C loss usually exceeds 50%. Losses on water soluble vitamins are affected by heat too and can run from 38% to 80%.
Take Home Points:
(1) If choosing to home pasteurize, make sure the process is understood and completed.
(2) Pasteurization kills both the good and bad bacteria in the raw milk and destroys beneficial enzymes and protective components
(3) Most milk from confinement cows should be pasteurized if used for human consumption

HOMOGENIZATION
Homogenization has been around for decades. Homogenization is a process that breaks up fat globules in cream into very small particles which then do not separate from the rest of the milk. Homogenized milk is more eye appealing and somewhat easier to use, thus easier to market in the grocery stores. There is no known health or nutritional advantage to homogenization. Some research suggests that homogenization creates free radical compounds that can cause allergic reactions and even heart disease. Others suggest that it is really the heating of the milk protein in the water fraction of the milk that provides allergic reactions, not homogenization.

In homogenized milk, the cream separates and rises to the top (goat milk is an exception to this rule). Once non-homogenized, whole raw milk has set for some time, the cream can be skimmed or poured off for use as a separate product. Some prefer to leave the cream in the milk and use it as whole milk. In that case, shake the container until the cream is fully mixed in the milk before use.

Take home points:
(1) Homogenization gives no known health or nutritional value to milk, but does keep the cream from separating
(2) Whole raw cow’s milk needs to be shaken each time before use to mix the cream back into the milk. Thus, keeping it in suspension

THE COW’S DIET
What the cow eats affects the milk quality. Milk quality includes many things - fats, minerals, vitamins, enzymes, flavor and more. If the cow’s diet is primarily forage from green, growing pastures, her milk will contain more conjugated linoleic acid (CLA), increased vitamins and minerals, and slightly higher levels of omega 3 fatty acids. This milk is generally more yellow in color, primarily because of the increased carotene. Grazing improves the quality of the milk and also the health of the animal. Lactating cows that graze on lush pastures with no or little supplemental grains tend to live longer and have increased fertility. Milk from cows grazing during May and June tend to be the highest quality.

If grain is fed to the lactating cow, the milk will be slightly lower in omega-3 fatty acid, slightly higher in omega-6 fatty acid, and lower in CLA content.

When dairy cows are fed grains and kept in confinement, the vitamins A & D disappear, the CLAs disappear, the omega 3 fatty acids lower and the omega 6 fatty acids increase. For heart health, the omega 3 and omega 6 ratios should be as narrow as possible. For some cancer prevention the CLA needs to be higher.

Milk produced from high quality land will have higher mineral content. Certified organic lands tend to be higher in mineral content. However, organic feed sources, in and of themselves, do not change the fat, mineral or vitamin content of the milk simply because they are organic. By feeding organic feed sources, the consumer can be assured that minimal pesticides, growth hormones or genetically modified products were used. Although research is inconclusive on whether these factors are passed on to the milk itself, using organic feeds lowers the risk of pesticides and antibiotic potential being passed into the milk.
The Union of Concerned Scientists, in their publication, Greener Pastures: How Grass-fed Beef and Milk Contribute to Healthy Eating, makes the following statement: “We believe these results support the appropriateness of choosing fully pasture-raised milk and beef over conventionally produced milk and beef. When the environmental benefits of pasture feeding are considered along with the health benefits - particularly those associated with reduced antibiotic use - the case for choosing pasture-raised milk and beef is even stronger.”

**Take home points:**
1. What the cow eats affects the milk quality
2. Cows that consume feed, forage, and pasture from highly mineralized soil produce the best possible quality milk
3. Milk produced from organic feed sources gives producers assurance that minimal pesticides, growth hormones or genetically modified products were used to produce the milk

**ORIGIN OF MILK PATHOGENS**

The origin of milk pathogens (actually human pathogens found in milk) is primarily a result of poor sanitation, animal stress, and animal sickness. Cows need to be clean and healthy. Allowing them to sleep or stand in livestock waste exposes them to more infections and environmental stress. Animals that are confined and/or treated with large amounts of antibiotics, growth hormones and fed a high-grain diet tend to have a weak immune system and consequently are more prone to disease. Animals allowed to graze fresh grass in the comfort of fresh air with ample room to move and exercise have less stress and have a stronger immune system able to ward off disease. When animals are raised entirely outdoors on green grass and/or hay, their milk will be greatly reduced in pathogens.

On-farm testing and independent laboratory testing does not guarantee food safety, but it is an excellent way to monitor milk quality. Buying raw milk from a Grade A herd assures that the milk is being tested for pathogens on a regular basis. If a farmer is selling directly to the public, he or she should be willing to post all lab tests, with explanation of what they mean for his or her customers’ review. When purchasing milk directly from the farmer, make sure the quality tests exceed the minimal requirements for Grade A. The somatic cell count of up to 300,000 cells/ml is the minimum standard for a Grade A facility. Raw milk standards should be even better.

Note: Somatic cell count (SCC) is one indicator of the quality of milk. Somatic cells are body cells, including leukocytes (white blood cells). The number of somatic cells increases in response to pus-producing bacteria like Staphylococcus aureua, a cause of mastitis.

**Take home points:**
1. Pathogens in milk are in-part the result of poor sanitation, animal stress, and animal sickness
2. On-farm milk testing can be done in a timely and economical manner. Consider on farm testing, independent laboratory testing and Grade A testing
3. Raw milk standards should be superior to traditional milk supply
4. The consumer should be comfortable with the farmer and husbandry practices

**COOLING MILK**

Milk is approximately 99 - 102 degrees Fahrenheit (F) when it is removed from the cow. Because bacteria numbers double every 20 minutes at this temperature, milk needs to be cooled to 40 degrees F as soon as possible, preferably within an hour of milking. If milk is not cooled properly, it will sour and separate.

Cooling the milk quickly insures a longer self life. Milk tastes better (will have less off flavors) if it is cooled quickly and maintained at a cool temperature. Rapid cooling inhibits the lactic-acid bacteria which causes milk to sour and will also inhibit the growth of bacteria. The bulk tank at the farm is the beginning of the “cold chain”. For optimal preservation of the milk quality, the milk should be cooled as quickly as possible and kept cool during transportation, storage and use.
For large quantities of milk, bulk milk tanks are designed to cool the milk properly within one hour. For small quantities of milk, an ice water bath with a stirring mechanism works well. Milk can be put in a freezer to lower the temperature more quickly, but milk must be stirred during the chilling process. Storage of milk, once chilled, should be below 40 degrees F.

If it is legal to deliver raw milk to the customer, it is very important that the milk be kept below 40 degrees F at all times in the system. Containers that maintain proper temperature are needed all the way to the delivery point. Remember, never break the cold chain.

Note: Sally Fallon, president of the Weston A. Price Foundation, said, “The anti-microbial components of raw milk are more effective at room temperature than chilled. The reason to chill milk is to keep the fresh taste, it is not for safety reasons.” She also said, “Cooling inhibits both good and bad bacteria.”

Take home points:
(1) Chilling milk quickly to 40 degrees F lengthens shelf life and maintains milk quality
(2) It is important that the cold chain is not broken

Raw Milk Use and Safety Fact Sheet
Farmer Module

Principles for the Farmer:
* Use common sense
* Keep clean / exceed legal standards
* Test for quality and safety / document
* Treat your customer as yourself
* Cool milk quickly and keep cool
* Practice safe product transportation, storage, processing and use
* Treat cows humanely, with consideration for their overall well being
* Feed cows mostly grass and hay with only minimal amounts of grain to improve CLA’s, vitamins, minerals, and omega 3 fatty acids.
* Continue to educate yourself
* Follow the rules / help change the rules if changes are needed

HIGH STANDARDS/RELATIONSHIP/COMMON SENSE
If raw milk is to be sold for human consumption, the farmer needs to be above reproach and use common sense. He or she needs to have high standards, testing should be done regularly, and consumer relations must be good.

Soil health and life should continually be enhanced and improved because cows that consume feed and pasture from live, highly mineralized soils produce the best possible quality milk. The green grass in the cow’s diet maintains healthy digestive micro-flora and greatly reduces the likelihood of E. coli 0157:H7, the highly pathogenic type of E. coli. Not all E. coli bacteria will make you sick. Thus, green grass should provide as much of the diet as possible. Add hay and only small amounts of grain or other energy sources when there is no green pasture to graze. The primary portion of this feed should be mold free, high quality forage. Appropriate minerals may be given to balance the diet.

Take home points:
(1) Cows that consume grass and hay from live, highly mineralized soil produce the best possible quality milk
(2) Relationships and communication are important
(3) Be above reproach and use common sense
MILKING PROCEDURES
Ultimate cleanliness should be the standard for those producing, using and marketing raw milk. Cows should not be allowed to stand or sleep in manure. The milking barn should be spotless prior to milking. The barn should be built and maintained with floors and fixtures for easy cleaning.

Always wash your hands before starting to milk. Dirty hands are a great source of contamination. A hand-washing sink with hot running water, soap and disposable towels is required. Any adjacent toilet area must be kept closed off to reduce the possibility of contamination and absorption of odors. Any person suffering from any sickness should not be allowed to milk cows.

Thoroughly clean the cow, removing dirt and/or manure. Wipe teats with iodine solution (or equivalent) before milking with a one-time-use tissue per cow. Then dry. Remember that you haven’t cleaned it until you’ve dried it.

Observing any signs of mastitis is a routine part of preparing to milk. Milk from cows with mastitis should not be used for human consumption.

For the farmers selling raw milk to the public, the level of cleanliness must be beyond reproach. Regular cleaning routines at the farm and milk parlor must be followed. General observations are important. Is there a place for everything, a sense of order? Is all equipment stored on shelves (i.e., no floor storage)? Is there running water?

Take Home Points:
(1) Ultimate cleanliness should be standard
(2) General observations are important

MILKING EQUIPMENT
Using an automatic milking unit is preferred over hand milking because it is easier to insure safety. If hand milking, practice utmost sanitation. Your hands, cows, and equipment need to be clean and dry.

The milking stall must be separate from the rest of the barn. Cows are only there when being milked. Keep stalls clear of other animals, chickens, cats etc. Water is an excellent bacteria carrier. Stalls should be cleaned after milking so they will be dry for the next milking time. Floors should be concrete or painted metal so you can see the manure, (i.e., no dirt floor, so it can be kept clean).

Consider the milking equipment. The first choice is an enclosed system with a filter, (i.e., single bucket milker for one to five cows, larger operations use larger equipment.) Milking utensils should be stainless steel or glass, if possible. Meeting Grade A certification standards is a good way to organize, even if not applying for certification. There must be thorough cleaning and drying of all equipment immediately after every use.

For large quantities of milk, bulk milk tanks are designed to cool the milk properly within one hour. For small quantities of milk, an ice water bath with a stirring mechanism works well. Milk can be put in a freezer to lower temperature more quickly, but milk must be stirred during the chilling process. Storage of milk, once chilled, should be below 40 degrees F.

If it is legal to deliver raw milk to the customer, it is very important to keep the milk below 40 degrees F at all points in the system. Appropriate containers that maintain proper temperature are needed to the delivery point. Remember, never break the cold chain.
Take home points:
(1) An automatic milking unit is preferred over hand milking
(2) Storage of milk should be below 40 degrees F
(3) Transport milk at below 40 degrees F

TESTING
It would be appropriate to conduct on-farm testing of the milk on a daily basis. This data should be recorded and always available for the consumer to examine. Every other month or so, milk samples should be sent to an independent lab to compare readings. If the herd is Grade A, these tests are already being carried out.

Human diseases that are associated with raw milk should be tested for. Testing the herd for tuberculosis, brucellosis, bovine leukemia virus, and Johnes before bringing new animals into the herd is advised. A closed herd is always easier to manage and less likely to harbor diseases. The farm should have a system of regular testing for mastitis (on site and by a laboratory) and maintain records of colony counts (any bacteria) and somatic counts (white cells). Also test for generic E. coli count to look for contamination from manure. To find detailed information about testing, what results mean, and what to do about the test results, contact a local veterinarian, an Extension veterinarian, or a trustworthy fellow dairyman. Records of testing should be available to the consumer upon request.

Each producer needs to develop their own protocol for the records. With the on-farm and independent laboratory results, cause needs to be established as well as needed action. It is also recommended for direct marketers to take a daily milk sample and store it in a small, well labeled, sealed container in a refrigerator. These samples should be kept for 30 days. They will be of great value in determining cause of a potential health problem.

It is suggested that a general observation of the cow’s treatment, facilities, and other condition be recorded. It is also appropriate to record any probable cause and action needed, as well as, action completed. A plan for caring for sick cows is needed. (What medicine is to be used, e.g., homeopathic/herbal or conventional?) Milk from sick cows is to be kept separate. It is not for human consumption, but it can be fed to animals. Having a closed herd is the best assurance of safety. Treat the cows humanely, with considerations for their overall well being.

Take home points:
(1) A sick cow plan needs to be developed
(2) A closed herd is easier to manage
(3) Data from appropriate milk tests should be made available to customers

Raw Milk Use and Safety Fact Sheet
Customer Module

Principles for the Consumer:
* Use common sense
* Make sure to know the farmer and are comfortable with his practices
* Know your family’s health concerns / consult professionals
* Practice safe product transportation, storage, processing and use
* Continue to educate yourself
* Follow the rules / help change the rules if changes are needed

PURCHASING
Before you purchase raw milk, educate yourself, know the facts. Before selecting the farm you desire to buy raw milk from, make a visit to the farm. Ask the right questions: How are the animals cared for? What are they fed? How are sick animals treated? What antibiotics are used and why? Are the animals wormed? If so, with
what? Also notice the sanitation conditions around the farm. Do you like what you see? Is that where you want to buy your “living food”? Are the animals fed grass and/or hay? Are they grazing outside? Is the herd free from disease? What sanitary milking procedures are used? Is there regular milk testing done? Are sick cows milked and where does that milk go? How are surfaces that come in contact with milk cleaned and what are they cleaned with?

Once you choose a farm, continue building on the relationship and learn from each other. Know your state’s rules for buying milk directly from a farm. Over half of the states allow raw milk to be picked up at the farm. Again, check with the Department of Agriculture in your state to obtain the appropriate rules. Please don’t break the rules.

Consumers should provide their own containers and lids/caps, which are labeled uniquely with a permanent pen or colored tape. Many consumers mark the date on the container with a nonpermanent pen each week. Glass containers are best because it’s easier to see when they are sparkling clean. However, milk dries almost clear, so it is not always apparent where it has not been removed. An incompletely cleaned container that has been capped for a while will give a definite odor when opened later.

Container size is important. Bottles or jars larger than 2 quarts are not recommended because it’s harder to keep the milk evenly cooled. Two-quart, wide-mouth canning jars are optimal for ease of cleaning. Use only tempered glass. A good habit to get into is to rinse emptied containers immediately. Use lukewarm water so as not to “set” the milk protein. Then wash in hot, soapy water. Rinse 3 times with water first to cut suds and then with warm-hot water to speed drying. Drain on a clean dish towel or rack, let air-dry on the counter and then cap. You can also wash in a dishwasher.

Take home points:
(1) Educate yourself, know the facts, and make sure the farm’s practices conform to the check list
(2) Know your state’s rules on buying raw milk
(3) The container needs to be very clean

TRANSPORTING AND STORAGE

For transporting fresh milk a cooler or ice chest is needed. It is helpful to have the family name on the inside and outside of the cooler. Several re-freezable blue gel packs or ice will be needed to cool empty bottles and to keep milk cold during the trip home. The milk needs to be kept at 40 degrees F or lower at all times.

When handling milk, hand washing is the most effective way to prevent contamination for the consumer also. Washing and drying hands just before filling the milk jars is important. Check the temperature of the home refrigerator to find the coldest area for storing the milk. Use the door shelf only for the bottle in current use. It may be helpful to place a container of ice in plastic quart-sized bags or re-freezable gel packs in front of or next to the containers that will be stored the longest. With care, normally milk can be stored 7 to 14 days. It is important to keep the milk COLD. Ideally milk should be held between 35 and 37 degrees F.

Do not use glass containers for freezing. Use No. 1 plastic (milk jugs) when freezing milk. Be sure to leave about one-inch of “head room” for expansion of the milk when it is frozen. Freeze as quickly as possible. To use frozen milk, thaw slowly at room temperature. Fast thawing will result in curdling and/or separation of the cream from milk. Whisking the milk may be needed to get rid of lumps of cream.

Take home points:
(1) When transporting raw milk use coolers or ice chests
(2) Once the milk is home, store the milk at 40 degrees F or lower
CONTINUING EDUCATION IS NEEDED
It is good to study the chemistry of milk. Some topics are: 1) pasteurization negates the potential benefits of raw milk; 2) improper pasteurization is dangerous; 3) milk separates so shake before use; 4) if cheese is made from raw milk legally, it needs to age for at least 60 days before sale; 5) consider making other products such as kefir; and 6) for highest quality, make butter in the spring and fall for summer and winter use.

Take home point:
(1) Keep educating yourself

Note: A National Raw Milk Use and Safety Summit was held in 2006 at Norfolk, Nebraska. This fact sheet is a result of the discussion of the issues during the 2006 Summit.

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Abbott OD, French RB, Townsend RO. Effects of Processing Upon the Nutritive Value of Milk as Evaluated with Rats, University of Florida Agricultural Experiment Station, Bulletin 485, 1951.


Beals, Peggy, RN. Guideline for the Safe Handling of Milk. Grass Lakes, MI.


Eat Wild Grass-fed Food and Facts - Jo Robinson. www.eatwild.com


Fallon, Sally and Enig, Mary. Website for Information (including sources of real milk), www.realmilk.com


Hoards Dairyman. www.hoards.com

In “Unpasteurized Milk: the Hazards of a Health Fetish” in JAMA, 1984;252(15):2049, the authors state that raw milk advocates have ‘erroneously’ cited Pottenger as having reported that disease occurred in cats fed pasteurized milk. Potter, it seems, overlooked Pottenger’s study in which he did demonstrate this, given here.


Milk Production Costs and Returns Per Hundred Weight Sold. Economics Research Service/USDA Website: www.ers.usda.gov


Nebraska Department of Agriculture. http://www.agr.state.ne.us/division/daf/dairy.htm

New Farm, The. www.newfarm.org


Northeast Organic Dairy Producers Alliance - Organic Dairy Farming and Organic Milk

On the Safety of Raw Milk (with a word about pasteurization). http://www.cfsan.fda.gov/~ear/milksafe.html

Organic Pastures Dairy Company. www.organicpastures.com


Partnership for Food Safety Education. http://www.foodsafety.gov/~dms/vlmcdavi/tsl015.htm


Porter, Dr. Charles. Milk Diet as a Remedy for Chronic Disease. 2005. God’s Whey, LLC.


Raw Milk is Good For You. http://lilipoh.com/article_issue06b.html


Stockman Grass Farmer. http://stockmangrassfarmer.net/


Virtanen et al. Cow’s milk consumption, HLA-DQB1 Genotype, and Type 1 Diabetes, Diabetes, 2000 June; 49:912-917.


Journal References

Br J Nutr 2006 Mar; 95(3):603-8
Diabetes 2000 Jun;49(6):912-7
Ann Allergy Asthma Immunol 2002 Dec;89(6 Suppl 1):33-7
Pediatr Pulmonol Suppl 1995; 11:59-60
Lancet 2002 Feb 16; 359(9306):623-4