RADIATION RISKS IN MEDICAL IMAGING

Section Editor & Contributor

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Radiologic imaging

Radiologic imaging is valuable as a diagnostic tool in medicine for diagnostic and therapeutic procedures. However, the ionizing radiation used in radiologic examination carries well-known potential risks. Radiology uses different imaging modalities such as Radiography, Computer Tomography, Ultrasound, Magnetic Resonance Imaging and Nuclear Medicine for the diagnosis and treatment of the diseases visualized within the human body.

Radiation exposure

The sources of ionizing radiation in our environment are cosmic rays from the universe, naturally occurring radioactive substances in the food and water that we eat and drink, the air we breathe, in the ground, in building materials etc, all of which contribute to our background radiation exposure.

Background radiation is most commonly given in units of millisievert (mSv), which measures and combines the radiation dose and the consequent risk delivered by an exposure.

In the early 1980s, the yearly per capita radiation dose was 3.6 mSv averaged over the U.S. population. Medical radiation contributed only 0.54 mSv to this annual dose. In 2006, medical radiation contributed 3 mSv to the annual dose, raising the per capita dose to 6.2 mSv averaged by the U.S. population.

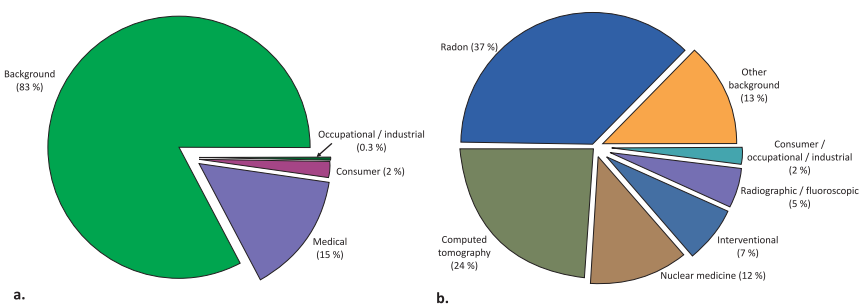


Figure 1: Average effective dose per capita to the U.S. population from major sources of exposure. (a) Effective dose (percentage of total) in early 1980s. (b) Effective dose (percentage of total) in 2006.

Fig. 2 - Mechanism

Ionizing radiation can cause tissue damage which occurs through the changes in chemical properties of molecules in the tissue following exposure to radiation. The major contributor to damage from radiation is through changing a water molecule into a new form called a “free radical”. Free radicals are chemically highly active and as such can have reactions with the cellular genetic molecules. This can cause damage to the DNA most of which is readily repaired by the cell. If not, it can result in cell death. Alternatively, if the DNA damage is repaired erroneously, it can result in an alteration of the genetic encoding leading to hereditary changes or cancer induction.

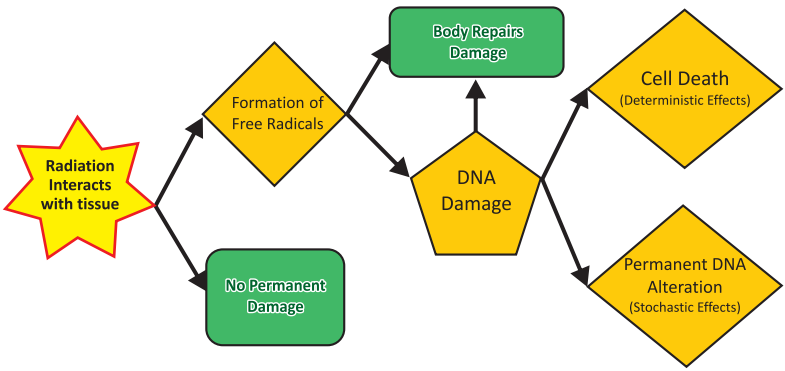


Figure 2: Mechanism of tissue damage caused by radiation.

Changes that result in cell death are termed as “Deterministic Effects”; while changes to the DNA encoding that lead to other adverse changes are termed “Stochastic Effects”.

Deterministic effect

Deterministic effects can be thought of as effects in which the outcome can be determined, i.e. they are predictable. Deterministic effects will occur if the radiation deposits enough energy in tissue to disrupt the tissue's functional subunits enough. The amount of energy required to cause these changes is different for different tissues and this is called the **threshold dose** for tissue damage.

Stochastic effect

Stochastic effects can be divided into two groups, genetic and carcinogenic effects. Based on the random nature of these effects, the production of genetic changes or induction of cancer in an individual cannot be determined for certain regardless of the amount of energy absorbed; only the probability or the likelihood can be ascertained. As such, there isn't a threshold dose above which these effects will definitely occur or below which the likelihood of these effects could be zero.

Cancer induction

Radiation effects have a latency period between the time of exposure and the onset of the effect, as seen with deterministic effects. For cancer induction, the latency period is on the order of years, with leukemia having the shortest latency period (5 to 15 years) and solid tumors having the longest (10 to 60 years).

Data Sources

Most of the knowledge regarding the risks of ionizing radiation comes from long-term studies of people who survived the 1945 atomic bomb blasts at Hiroshima and Nagasaki. Several epidemiologic studies during the past 6 decades have attempted to document the health consequences of exposure to low levels of ionizing radiation. Data sources for these studies can be divided into four categories:

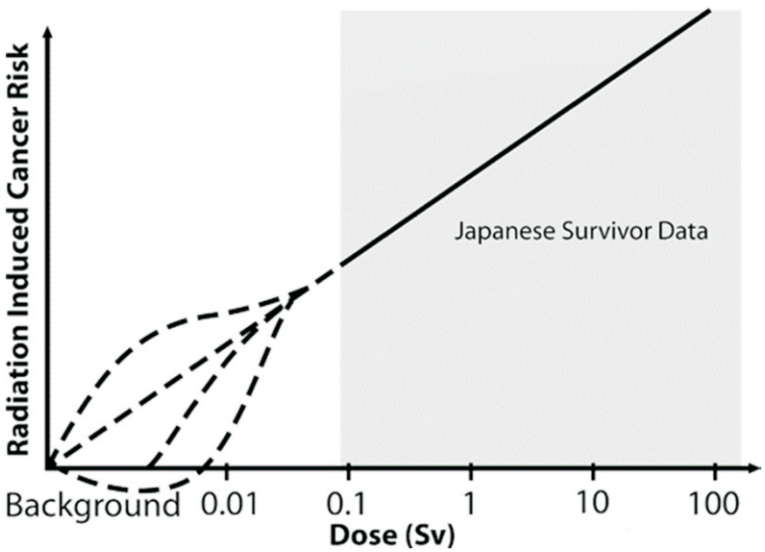
1. Atomic bomb survivors in Hiroshima and Nagasaki (Radiation Effects Research Foundation RERF) data.
2. Persons exposed to medical radiation.
3. Workers in radiation and nuclear industries and
4. Populations exposed to environmental radiation

During this 6-decade period, the U.S. National Academy of Sciences has commissioned a series of reports which are referred to as the Biological Effects of Ionizing Radiation (BEIR) reports. The latest in this series of reports (BEIR VII report) examines all four categories of data but places by far the greatest emphasis on the RERF data which form the backbone of the BEIR VII report.

Linear no threshold hypothesis

This model is not chosen because there is solid biologic or epidemiologic data supporting its use. Rather, it is used because of its simplicity and because it is a conservative approach (ie, if it is not correct, then it probably overestimates the risk of cancer induction at low doses).

Subsequent BEIR committees have extended the LNT model from mutagenesis to carcinogenesis at low.



Graph shows various models for extrapolating radiation-induced cancer risk to low doses (dashed line and curves).

Linear no-threshold (LNT) model = dashed straight line is the most commonly used one.

*Imaging procedures and their approximate effective radiation doses**		
Procedure	**Average effective dose (mSv)**	**Range reported in the literature (mSv)**
Bone density test+	0.001	0.00–0.035
X-ray, arm or leg	0.001	0.0002–0.1
X-ray, panoramic dental	0.01	0.007–0.09
X-ray, chest	0.1	0.05–0.24
X-ray, abdominal	0.7	0.04–1.1
Mammogram	0.4	0.10–0.6
X-ray, lumbar spine	1.5	0.5–1.8
CT, head	2	0.9–4
CT, cardiac for calcium scoring	3	1.0–12
Nuclear imaging, bone scan	6.3	
CT, spine	6	1.5–10
CT, pelvis	6	3.3–10
CT, chest	7	4.0–18
CT, abdomen	8	3.5–25
CT, colonoscopy	10	4.0–13.2
CT, angiogram	16	5.0–32
CT, whole body	variable	20 or more
Nuclear imaging, cardiac stress test	40.7	

**The actual radiation exposure depends on many things, including the device itself, the duration of the scan, your size, and the sensitivity of the tissue being targeted.*

+Dual energy x-ray absorptiometry, or DXA

Source: Mettler FA, et al. "Effective Doses in Radiology and Diagnostic Nuclear Medicine: A Catalog," Radiology (July 2008), Vol. 248, pp. 254–63.

Average Effective Dose in CT*		
Exam	**Relative Radiation Level**	**Range of values (mSv)**
Head	☢☢☢	0.9 – 4
Chest (standard)	☢☢☢	4 – 18
Chest (high resolution, e.g., pulmonary embolism)	☢☢☢☢	13 – 40
Abdomen	☢☢☢	3.5 – 25
Pelvis	☢☢☢	3.3 – 10
Coronary Angiogram	☢☢☢☢	5 – 32
Virtual Colonoscopy	☢☢☢	4 – 13
Calcium Scoring	☢☢☢	1 - 12
**adapted from Mettler FA, et.al. Radiology Vol 248 (1) p254-263 2008*		

Average Effective Dose in CT*		
Exam	**Relative Radiation Level**	**Range of values (mSv)**
Head/Neck angiography	☢☢☢	0.8 – 19.6
Coronary angiography (diagnostic)	☢☢☢	2 – 15.8
Coronary angioplasty, stent placement, RF ablation	☢☢☢☢	6.9 – 57
TIPPS	☢☢☢☢☢	20 – 180
**adapted from Mettler FA, et.al. Radiology Vol 248 (1) p254-263 2008*		

Average Effective Dose in CT*		
Exam	**Relative Radiation Level**	**Range of values (mSv)**
Brain (Tc99m)	☢☢☢	0.0093 – 0.0077
Brain PET (18F-FDG)	☢☢☢☢	0.019
Thyroid scan (123I)	☢☢☢	0.075 (w/15% uptake)
Thyroid scan (Tc99m)	☢☢☢	0.013
Cardiac Stress Test (depending on isotope/protocol)	☢☢☢☢	0.0085 – 0.22
Cardiac PET (18F-FDG)	☢☢☢☢	0.019
Lung Perfusion (Tc99m)	☢☢☢	0.011
GI Bleed	☢☢☢	0.007
Renal (depending on isotope/protocol)	☢☢☢	0.0049 – 0.0088
Bone	☢☢☢	0.0057
**adapted from Mettler FA, et.al. Radiology Vol 248 (1) p254-263 2008*		

Dose Descriptors

The effective dose is computed by multiplying the dose to each irradiated organ in a patient by a radiation weighting factor (unity for x-rays and gamma rays) and by a biologic weighting factor specific for the organ and summing the products for all exposed organs to yield the effective dose. **Effective dose** is defined as the dose which, if delivered uniformly to the whole body, would produce the same health consequences as those caused by a dose delivered to one or more specific organs.

Risk models

BEIR VII committee uses two risk models as the foundation for estimating the likelihood of radiation-induced cancer. These models are the ERR model and the EAR model.

ERR is the rate of disease in the exposed population divided by the rate of disease in an unexposed population minus 1.0, and EAR is the rate of disease in an exposed population minus the rate of disease in an unexposed population.

Risk factors from these models are then incorporated into a final risk model, the lifetime attributable risk (LAR) model.

Risk estimates

Estimates of radiation-induced cancer incidence and death from medical imaging are computed at times with the assumption that the age distribution of the exposed individuals resembles that of the population at large. This assumption is invalid, because older patients undergo the bulk of imaging examinations. Many patients who undergo medical imaging procedures have an illness that shortens their life expectancy. These patients are at reduced risk of cancer induction by radiation because they will not survive long enough for the cancer to materialize for several reasons, including their limited expected lifetimes.

It is essentially impossible to accurately predict cancer incidence and death in a population of individuals exposed to doses below about 100 mSv.

Virtually all imaging procedures, including CT and nuclear medicine examinations, deliver doses to patients well below 100 mSv when they are properly conducted.

The American Association of Physicists in Medicine, approved in December 13, 2011 the following statement concerning the risks of medical imaging.

The American Association of Physicists in Medicine (AAPM) acknowledges that medical imaging procedures should be appropriate and conducted at the lowest radiation dose consistent with acquisition of the desired information. Discussion of risks related to radiation dose from medical imaging procedures should be accompanied by acknowledgment of the benefits of the procedures. Risks of medical imaging at patient doses below 50 mSv for single procedures or 100 mSv for multiple procedures over short time periods are too low to be detectable and may be non-existent.

The negative health consequences of deferred imaging examinations undoubtedly far outweigh any risks of having the procedures performed.

It's important to remember three principles: to **keep radiation doses as low as reasonably achievable (or ALARA), to keep medical procedures as safe as reasonably achievable (or ASARA), and to keep medical benefits as high as reasonably achievable (or AHARA).**

Protection against radiation hazards and protection devices

The Regulatory Bodies

There are various Regulatory Bodies at the international and national level, which lay down norms for radiation protection. Each country has its national counterpart of the ICRP- NCRP The National Commission for Radiological Protection in USA and in India the AERB or the Atomic Energy Regulatory Board (AERB).

Objectives of Radiation protection

"The goal of radiation protection is to prevent the occurrence of serious radiation induced conditions (acute and chronic deterministic effects) in exposed persons and to reduce stochastic effects in exposed persons to a degree that is acceptable in relation to the benefits to the individual and to society from the activities that generate such exposure".

Role of AERB

1. Recommends and lays down guidelines regarding the specifications of medical X-ray equipment, for the room layout of X-ray installation.
2. Exercises a regulatory control on the approval of new models of X-ray equipment and the layout of any new proposed X-ray installation.
3. Regulatory authority for registration and commissioning of new X-ray equipment, inspection and decommissioning of X-ray installation.

Radiation protection actions:

The triad of radiation protection actions comprises **"time-distance-shielding".** Reduction of exposure time, increasing distance from source, and shielding of patients and occupational workers have proven to be of great importance in protecting patients, personnel, and members of the public from the potential risks of radiation.

I. ***Time:***

The exposure time is related to radiation exposure and exposure rate (exposure per unit time) as follows:

Exposure time = Exposure / Exposure rate

Or

Exposure = Exposure rate x Time

The algebraic expressions simply imply that if the exposure time is kept short, then the resulting dose to the individual is small.

II. ***Distance:***

The second radiation protection action relates to the distance between the source of radiation and the exposed individual. The exposure to the individual decreases inversely as the square of the distance. This is known as the inverse square law, which is stated mathematically as:

Exposure α I/d2

Where I is the intensity of radiation and d is the distance between the radiation source and the exposed individual. For example, when the distance is doubled the exposure is reduced by a factor of four.

III. ***Shielding***

The third radiation protection action relates to shielding. Shielding implies that certain materials (concrete, lead) will attenuate radiation (reduce its intensity) when they are placed between the source of radiation and the exposed individual.

The four aspects of shielding in diagnostic radiology include:

1. X-ray tube shielding
2. Room shielding
3. Personnel shielding
4. Patient shielding (of organs not under investigation)

1. X-ray tube shielding (Source Shielding)

The x-ray tube housing is lined with thin sheets of lead because x-rays produced in the tube are scattered in all directions. This shielding is intended to protect both patients and personnel from leakage radiation. Manufacturers of x-ray devices are required to shield the tube housing so as to limit the leakage radiation exposure rate to 0.1 R/ hr at 1 meter from the tube anode. AERB recommends a maximum allowable leakage radiation from tube housing not greater than 1mGy per hour per 100 cm^2.

2. Room shielding (Structural Shielding)

The lead lined walls of Radiology department are referred to as protective barriers as they are designed to protect individuals located outside the X-ray rooms from unwanted radiation There are two types of protective barriers.

(a) **Primary Barrier:** is one which is directly struck by the primary or the useful beam.

(b) **Secondary Barrier:** is one which is exposed to secondary radiation either by leakage from X-ray tube or by scattered radiation from the patient.

AERB has laid down guidelines for shielding of X-ray examination room and patient's waiting room which are as follows.

Patient waiting area

Patient waiting areas are provided outside the X-ray room. A suitable warning signal such as red light and a warning placard is provided at a conspicuous place outside the X-ray room and kept 'ON' when the unit is in use to warn persons not connected with the particular examination against entering the room.

3. Personnel shielding:

Shielding of occupational workers can be achieved by following methods:

(a) Personnel should remain in the radiation environment only when necessary (step behind the control booth, or leave the room when practical)

(b) The distance between the personnel and the patient should be maximized when practical as the intensity of radiation decreases as the square of distance (inverse square law).

(c) Shielding apparel should be used as and when necessary which comprise of lead aprons, eye glasses with side shields, hand gloves and thyroid shields.

The thickness of lead in the protective apparel determines the protection it provides. It is recommended that for general purpose radiography the minimum thickness of lead equivalent in the protective apparel should be 0.5mm. It is recommended that women radiation workers should wear a customized lead apron that reaches below mid-thigh level and wraps completely around the pelvis. This would eliminate an accidental exposure to a conceptus.

Other protective apparel include eye glasses with side shields, thyroid shields and hand gloves. The minimum protective lead equivalents in hand gloves and thyroid shields should be 0.5mm.

4. Patient shielding:

It has been recommended that the thyroid, breast and gonads be shielded, to protect these organs especially in children and young adults. In gonadal shielding, a lead apron is placed appropriately on the patient to protect the gonads from primary beam radiation exposure. A lead bib and collar worn over the patient's neck and thorax have been documented to effectively shield radiosensitive organs like the thyroid and the breast, and are therefore recommended for routine use in dental X-rays and head CT examinations.

Methods of Detection

There are several methods of detecting radiation, and they are based on physical and chemical effects produced by radiation exposure. These methods are:

1. Ionization
2. Photographic effect

3. Luminescence
4. Scintillation

Personnel Dosimetry

Personnel dosimetry refers to the monitoring of individuals who are exposed to radiation during the course of their work. The data from the dosimeter are reliable only when the dosimeters are properly worn, receive proper care, and are returned on time. Proper care includes not irradiating the dosimeter except during occupational exposure and ensuring proper environmental conditions.

Pocket Dosimeter

The pocket dosimeter monitors dose of radiation to the personnel. It consists of an ionization chamber with an eyepiece and a transparent scale, as well as a hollow charging rod and a fixed and a movable fiber. When x-rays enter the dosimeter, ionization causes the fibers to lose their charges and, as a result, the movable fiber moves closer to the fixed fiber. The movable fiber provides an estimate of gamma or x-ray dose rate.

Film Badge Monitoring

These badges use small x-ray films sandwiched between several filters to help detect radiation. Film badges are inexpensive, easy to use, and easy to process. Although they are useful for detecting radiation at or above 0.1 mSv (10 mrem), they are not sensitive enough to capture lower levels of radiation. Their susceptibility to fogging caused by high temperatures and light implies that they should not be worn for longer than a 4-week period at a stretch. Another major drawback to film badge monitoring is that it is an enormous task to chemically process a large number of small films and subsequently compare each to some standard test film. In India, film badges have recently been replaced by TLD badges.

Thermoluminescent dosimetry (TLD) Monitoring

The limitations of the film badge are overcome by the thermoluminescent dosimeter (TLD). Thermoluminescence is the property of certain materials to emit light when they are stimulated by heat. Materials such as **lithium fluoride (LiF), lithium borate ($Li_2B_4O_7$), calcium fluoride (CaF_2), and calcium sulfate ($CaSO_4$)** have been used to make TLDs.

Surveillance of radiation workers

AERB has recommended regular medical examination of radiation workers to assess their protection status as per the following guidelines.

-Every radiation worker prior to commencing radiation work and at subsequent intervals not exceeding 12 months shall be subjected to the following medical examinations:

1. X-ray examination of Chest.
2. All general laboratory investigations such as examination of blood and excreta.
3. Special investigations such as examination of skin, hands, fingers, nails and eyes.

Radiation Safety Officer

The NCRP has provided a brief description of the relevant qualifications and duties of an RSO. Every department should have an RSO. Who should be an individual trained in areas such as radiation protection, radiation physics, radiation biology, instrumentation, dosimetry and shielding design.

In India AERB has specified duties of the RSO. He/she shall implement all radiation surveillance measures, conduct periodic radiation protection surveys, maintain proper records of periodic quality assurance tests, and personnel doses, instruct all workers on relevant safety measures, educate and train new entrants, and take local measures, including issuance of clear administrative instructions in writing, to deal with radiation emergencies. The RSO should also ensure that all radiation measuring and monitoring instruments in his/her custody are properly calibrated and maintained in good condition, maintaining a record of all radiation surveys performed, deficiencies observed and remedial actions taken.

HYGIENE AND PUBLIC HEALTH

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Introduction

Hygiene refers to the science of preventive medicine and preservation of health — that is broad enough to incorporate concepts such as exercise and diet. Term hygiene originates from "Hygeia" the Greek goddess of health, cleanliness and sanitation. Hygiene ranges from personal hygiene, domestic hygiene to community hygiene. Good hygiene directly aids in disease prevention.

Potable water and water purification

One of the 8 essential components of primary health care outlined in Alma Ata declaration is to provide an adequate supply of safe water and basic sanitation. Potable water or drinking water is water that is safe to drink and for use in cooking, without health risks.

Water purification is the general term used for any method that aims to eliminate contaminants from water to make it safe for human being consumption. Some of these contaminants are however not harmful but are instead removed to improve the smell and taste of water. A good water purification method can eliminate near total impurities, leaving the water not only safe for human consumption but also ideal for any industrial use application.

There are several methods used to purify water:

- Filtration relies on a filter to sift out unwanted minerals and particles while allowing water to pass through. The best filtration systems can eliminate particulates sized 0.1 microns, and other microns like DNA fragments.
- Reverse osmosis systems are the best types of water purifiers that use the filtration method. Instead of relying on a filter, a reverse osmosis tool uses a porous element that acts as a unidirectional sieve to separate water from unwanted molecules.
- Distillation, is cheaper but has the disadvantage of being slow. With distillation, pure water is created once the water boils and leaves the contaminants behind. However, there are organic

substances that boil before water and creates a window that could introduce contaminants back to the water even after the distillation process.

- Biological methods of purifying water like slow sand filtration- In industries, water can also be purified via exposure to electromagnetic radiation.

Water supplies

Water is supplied to households and industries using underground pipes, that is processed and treated to meet drinking water standards. Only a little amount of municipality water is used for human consumption, rest is used for bathing, watering gardens, cleaning and cooking.

Water vendors use a range of modes of transport to carry drinking water for sale directly to consumer, including tanker trucks. Informal suppliers tend to use a range of sources, including untreated surface water, dug wells and bore wells and has been associated with outbreaks of diarrheal disease

In many places consumers purchase water from kiosks and then carry the water home in a variety of containers. Measures should be taken to protect vended water from contamination during transport as well as storage in the home, including transporting and storing water in containers that are clean, free from both fecal and chemical contamination and either enclosed or with narrow openings, ideally fitted with a dispensing device such as a spigot that prevents hand access and other sources of extraneous contamination.

2.1.2. Individual consumers: Consumers often play important roles in the collection, treatment and storage of water. Consumer actions may help to ensure the safety of water and also contribute to improvement on contamination of the water consumed by others. Installation and maintenance of household plumbing systems should be undertaken preferably by qualified and authorized plumbers or other persons with appropriate expertise to ensure that cross-connection or back flow events do not result in contamination of local water supplies.

2.1.3. Health-care facilities: Drinking-water in such facilities should be suitable for human consumption, including personal hygiene. However, it may

not be suitable for all uses or for some patients, and further processing or treatment or other safeguards may be required. Although microorganisms such as Pseudomonas aeruginosa and mycobacteria, Acinetobacter, Aeromonas and Aspergillus species may be of concern for severely immunocompromised persons.. Water used for washing medical devices like endoscopes etc may require additional processing, such as microfiltration or sterilization, depending on use. Health-care facilities may include environments that support the proliferation and dissemination of Legionella. Some equipment, such as water-cooled high-speed drills in dental surgeries, is of particular concern for both inhalation of droplets and infection of wounds. Renal dialysis requires large volumes of water that is of higher quality than drinking-water. Water used for dialysis requires processing to minimize the presence of microorganisms, endotoxins, toxins and chemical contaminants. There are special requirements regarding aluminium, which may cause dialysis dementia. Dialysis patients are also sensitive to chloramines, which needs to be considered when chloramination is used to disinfect drinking-water supplies, particularly in areas where there are home dialysis patients. All health-care facilities should have specific standard work practices as part of their infection control programme which should address issues such as water quality and treatment requirements, cleaning of specialized equipment and control of microbial growth in water systems and ancillary equipment.

2.1.4. Safe drinking-water for travelers: The most common sources of exposure to disease-causing organisms for travelers are contaminated drinking-water and food that has been washed with contaminated water. Diarrhea affects 20–50% of all travelers or about 10 million people per year. In some places tap or bottled water that has not been produced under proper conditions may not be safe, even if it is clear and colorless. It is important that travelers be aware of the possibility of illness and take appropriate steps to minimize the risks.

WHO lists the following guidelines for travelers to places with questionable water quality

1. Drink only bottled water or other beverages (carbonated beverages, pasteurized juices and milk) provided in sealed tamper-proof containers and bottled/canned by known manufacturers (preferably certified by responsible authorities). Hotel personnel or local hosts are often good sources of information about which local brands are safe.

2. Drink water that has been treated effectively at point of use (e.g. through boiling, filtration or chemical disinfection) and stored in clean containers.

3. Avoid salads or other uncooked foods that may have been washed or prepared with unsafe water.

Bringing water to a rolling boil is the simplest and most effective way to kill all disease-causing pathogens, even with turbid water and at high altitudes. The hot water should be allowed to cool without the addition of ice. If the water is turbid and needs to be clarified for aesthetic reasons, this should be done before boiling.

2.1.5. Rural Water Supplies: rural water supplies come from varied sources which include surface water, stream water, spring water, shallow wells, wells with electric pump and rain water. Since water supplies come from various sources and with limited options for water treatment, most realistic steps to ensure clean water in rural areas is to find cleanest source and keep it clean.

2.1.6. Water filters

- **Candle filters**

Water purification on a small scale such as in household purification of water can be done using following 3 methods, singly or in combination; boiling, chemical disinfection and filtration .

- **RO purification**

- As homeowners are increasingly concerned about contaminants that affect their health, as well as about non-hazardous chemicals that affect the taste, odor, or color of drinking water. Reverse Osmosis (RO) treatment of water is becoming more popular in homes .

2.1.7. R**everse Osmosis Systems**use a process that reverses the flow of water in a natural process of osmosis so that water passes from a more concentrated solution to a more dilute solution through a semi-permeable membrane. Pre- and post-filters are often incorporated along with the reverse osmosis membrane itself.

- A reverse osmosis filter has a pore size of approximately 0.0001 micron.

- Reverse Osmosis Systems have a very high effectiveness in removing protozoa (for example, Cryptosporidium, Giardia)
- Reverse Osmosis Systems have a very high effectiveness in removing bacteria (for example, Campylobacter, Salmonella, Shigella, E. coli)
- Reverse Osmosis Systems have a very high effectiveness in removing viruses (for example, Enteric, Hepatitis A, Norovirus, Rotavirus)
- Reverse Osmosis Systems will remove common chemical contaminants (metal ions, aqueous salts), including sodium, chloride, copper, chromium, and lead; may reduce arsenic, fluoride, radium, sulfate calcium, magnesium, potassium, nitrate, and phosphorous.

Although RO membranes can remove virtually all microorganisms, it is currently recommended that only microbiologically safe (i.e., coliform negative) water be fed into RO systems. Reverse osmosis will not remove all contaminants. In general is not a very effective treatment for trihalomethanes (THMs), some pesticides, solvents, and other volatile organic chemicals (VOCs).

2.1.8. V purification

Ultra Violet rays are passed in the water which kills the harmfulmicro organisms present in it but cannot purify or remove ions in water.

The ultra violet rays are used to remove or kill bacteria, virus and micro level organisms, in addition to the RO system. Thus, this system is highly purified system compared to RO alone, hence it is recommended for usage.

2.1.9. Halazone USP based Chlorine Tablets have a prominent status among water purification tablets for ensuring hygienic quality of water with its effective bactericidal activity and instant purification of water. Halazone Tablets are a powerful purifier of drinking water in small quantities. A*pplication:* It is used worldwide in army, navy, military, households, schools, hospitals for purification of drinking water.; it is very useful in case of epidemics, floods and cyclones.

2.1.10. Potability of tap water and bottled water in India. The large scale water supplies of the cities and towns use chlorine for disinfection and once disinfected at the source/water works / water treatment plant, some extra

chlorine is left as residue to act on any contamination that may happen during distribution like from leaky pipes, etc.

- Bottled water supplies, are generally considered safe, more so when purchased from reputed shops, vendors, etc. as these are unlikely to be tampered. The bottled water supplies generally use ground water and these may contain dissolved/harmful chemicals, potential carcinogens like bromates, heavy metals like Arsenic, etc. that are not noticeable routinely and need to be removed.

3. Safe food

WHO provided following tips for food safety

Buy quality food

- Buy fresh food from reliable suppliers with clean premises.
- Always check expiry dates of raw material and processed food.
- Do not buy products in damaged, dented, puffed or leaking cans and tetra packs.

Cleanliness is a must

- Wash your cutting boards, dishes, utensils and counter tops with soap and hot water before and after cooking. Use separate cutting boards for fruits/vegetables and raw meat, poultry and seafood.
- Do not use cutting boards with cracks or scars.
- Keep the refrigerator clean and dry.
- Clean the lids of canned foods before opening.
- Wash kitchen cloth towels daily with soap and hot water and dry them before using. Damp and dirty towels are breeding grounds for harmful bacteria.
- Clean kitchen sink drains thoroughly, daily as they could harbour harmful bacteria.
- Do not leave food around as it may attract insects, bacteria or vermin.
- Do not allow pets in the kitchen. Keep kitchen free of insects and pests.

Store food correctly

- Do not leave cooked food at room temperature for more than two hours.
- Always store food in covered containers in the refrigerator or freezer.
- Do not over-stuff the refrigerator or freezer. Good airflow inside the refrigerator is important for effective cooling and keeping food safe.
- Keep the refrigerator temperature at or below 5^{o}C.
- Separate raw meat, poultry, seafood and eggs from other food in your grocery bags and in your refrigerator.
- Refrigerate or freeze meat, poultry, eggs, seafood and other perishables within 2 hours of cooking or purchasing and in summers, even sooner.
- Clean and clear the refrigerated regularly to ensure that the stored food is either used or discarded.

Defrost the right way

- Never thaw food at room temperature. Defrost food in the refrigerator, cold water or in the microwave.
- Cook food immediately after thawing.
- Keep meat and seafood in the refrigerator while marinating.

Cook food thoroughly

- Always use safe water and fresh raw material to cook food.
- Cook food thoroughly to kill germs that cause food poisoning.
- If you are not sure about the quality of the drinking water, boil water for at least 5 minutes

When food is cooked

- Serve food while it is hot.
- Refrigerate leftover cooked food within two hours.
- Before consuming refrigerator food, reheat thoroughly above 75^{o}C .

- If you are unsure of how long your leftovers have been in the refrigerator, do not eat that food

Maintain personal hygiene

- Always wash hands with warm water and soap for at least 20 seconds before and after handling food. Dry with a paper towel or clean cloth.
- Wear disposable gloves if you have a cut or sore on fingers.
- Do not cook if you are suffering from respiratory illness.

3.1. Microbial contamination

Food can cause devastating impacts if contaminated with pathogenic microorganisms/microbial toxins. Safe food that is free from harmful contaminants is important for people' general health and daily life, economic and social stability.

Street foods : It is generally advised to avoid eating from road side / pavement restaurants and when inevitable avoid consuming water, iced items, raw fruits and vegetables , etc. Eat those that are freshly prepared and served hot.

3.2. Pesticidesand other hazardous substances

Pesticides are the only toxic substances released intentionally into our environment to kill living things and includes substances that kill weeds (herbicides), insects (insecticides), fungus (fungicides), rodents (rodenticides), and others.

Pesticides have been linked to a wide range of human health hazards as they are present almost everywhere ranging from short-term impacts such as headaches and nausea to chronic impacts like cancer, reproductive harm, and endocrine disruption.

The real solution to our pest and weed problems lies in non-toxic and cultural methods of agriculture Organically grown foods and sustainable methods of pest control are he key to health.

3.3. Organic foods

Organic food is that produced by methods that comply with the standards of organic farming. Standards vary worldwide, but organic

farming in general features practices that strive to cycle resources, promote ecological balance, and conserve biodiversity. Organizations regulating organic products may restrict the use of certain pesticides and fertilizers n farming. In general, organic foods are also usually not processed using irradiation industrial solvents or synthetic food additives

Foods labelled organic must be certified under the national organic program. The Indian government has developed strict guidelines and certifications procedures to keep a check on manufactures in this financially attractive market.

The amount of nitrogen content in certain vegetables, especially green leafy vegetables and tubers, has been found to be lower when grown organically as compared to conventionally. When evaluating environmental toxins such as heavy metals, the USDA has noted that organically raised chicken have lower arsenic levels. However, a 2014 review found lower concentrations of cadmium, particularly in organically grown grains.

There is not sufficient evidence in medical literature that support claims that organic food is safer or healthier than conventionally grown food. While there may be some differences in the nutrient and anti-nutrient contents of organically- and conventionally-produced food, the variable nature of food production and handling makes it difficult to generalize results. Lastly, while organic food accounts for 1–% of total food production worldwide, the organic food sales market is growing rapidly and there is an increasing publicity given to promote its consumption.

4. Air pollution

Air pollution is a major environmental health problem affecting all. It occurs due to contamination by any chemical, physical or biological agent that modifies the natural characteristics of the atmosphere. Stoves at home, tobacco smoke, motor vehicles, industrial facilities and forest fires are common sources of air pollution.

4.1. Urban and rural areas

The dangers of burning fuels like unprocessed coal and kerosene in the home should be highlighted and targets for reducing emission of health-damaging pollutants from domestic cook stoves, space heaters and fuel-

based lamps should be set. Emissions from household fuel combustion should not exceed WHO-recommended targets for PM2.5 and Carbon Monoxide (CO). WHO specifies that emissions of PM2.5 should not exceed 0.23 mg/min when unvented (i.e. without a chimney or hood) and 0.80 mg/min when vented (i.e. with a chimney or hood). Emission Rate Targets (ERTs) for carbon monoxide should not exceed 0.16 g/min for unvented devices and 0.59 g/min for vented devices.

Household use of kerosene should be discouraged. Use of clean fuels like biogas, ethanol, liquefied petroleum gas (LPG), and natural gas, along with electricity should be encouraged in order to decrease air pollution.

4.2. Face masks and Respirators

Face masks and N95 respirators are examples of personal protective equipment that are used to protect the wearer from liquid and airborne particles contaminating the face.

4.2.1. Face masks

A face mask creates a physical barrier between the mouth and nose of the wearer and potential contaminants in the immediate environment. Face masks are not to be shared and may be labeled as surgical, isolation, dental or medical procedure masks. They may come with or without a face shield.

Face masks are made in different thicknesses and with different ability to protect from contact with liquids. When worn properly, a face mask is meant to help block large-particle droplets, splashes, sprays or splatter that may contain germs (viruses and bacteria), keeping it from reaching the mouth and nose. Face masks may also help reduce exposure of your saliva and respiratory secretions to others. Face masks also do not provide complete protection from germs and other contaminants because of the loose fit between it's surface and your face.

Face masks are not intended to be used more than once. If your mask is damaged or soiled, or if breathing through the mask becomes difficult, you should remove the face mask, discard it safely, and replace it with a new one. To safely discard your mask, place it in a plastic bag and put it in the trash. Wash your hands after handling the used mask.

4.3. Respirator

A respirator is designed to protect the wearer from inhaling harmful particulate matter as in dusts, including airborne microrganisms, fumes, vapors, or gases. They range from relatively inexpensive single-use, disposable masks to more robust reusable models with replaceable cartridges, and are used by the military, private industry and the public.

There are two main categories: the air-purifying respirator, which forces contaminated air through a filtering element, and the air-supplied respirator in which fresh air is delivered alternatively.

4.4. N95 Respirators

The N95 respirator is a device designed to achieve a very close facial fit and very efficient filtration of airborne particles.

The 'N95'designation indicates that when subjected to careful testing, the respirator blocks at least 95% of very small (0.3 micron) test particles. If properly fitted, the filtration capabilities of N95 respirators exceed those of face masks. However, even a properly fitted N95 respirator does not completely eliminate the risk of illness or death.

1. N95 respirators are not designed for children or people with facial hair, because a proper fit cannot be achieved and it may not provide full protection.

5. Soil pollution

Soil pollution is defined as, "contamination of soil by human and natural activities which may cause harmful effect on living organisms. Soil pollution mainly occurs due to the following: a. industrial wastes, b. urban wastes, c. agricultural practices d. radioactive pollutants e. biological agents.

5.1. Industrial wastes – Disposal of Industrial wastes is the major problem for soil pollution

1. Sources: Industrial pollutants are mainly discharged from various origins such as pulp and paper mills, chemical fertilizers, oil refineries, sugar factories, tanneries, textiles, steel, distilleries, fertilizers, pesticides, coal and mineral mining industries, glass, cement, petroleum and engineering industries etc. These pollutants affect and alter the chemical and biological

properties of soil. As a result, hazardous chemicals can enter into human food chain from the soil or water, disturb the biochemical process and finally lead to serious effects on living organisms.

5.2. **Urban wastes** –Urban wastes comprise of both commercial and domestic wastes consisting of dried sludge and sewage. All the urban solid wastes are commonly referred to as refuse.

Constituents of urban refuse: This refuse consists of garbage and rubbish materials like plastics, glasses, metallic cans, fibres, paper, rubbers, street sweepings, fuel residues, leaves, containers, abandoned vehicles and other discarded manufactured products. Urban domestic wastes though disposed off separately from industrial wastes, can still be dangerous because they are not easily degraded.

5.3. **Agricultural practices** –Modern agricultural practices pollute the soil to a large extent. With the advancing agro-technology, huge quantities of fertilizers, pesticides and herbicides are added to increase the crop yield. Apart from these farm wastes, manure, slurry, debris, soil erosion containing mostly inorganic chemicals are reported to cause soil pollution

5.4. **Radioactive pollutants** - Radioactive substances resulting from explosions of nuclear testing laboratories and industries giving rise to nuclear dust radioactive wastes, penetrate the soil and accumulate giving rise to land/soil pollution

2. Vegetable cultivation

Wastewater is used for irrigation in treated and untreated forms, varying by geographic and economic context. Wastewater is commonly discharged into water bodies with little or no treatment due to the limited availability of treatment facilities in many countries, whichis frequently used for urban or peri-urban agriculture, comprising approximately 11% of al irrigated croplands globally. This water often contains a large range of contaminants from municipal, agricultural and industrial sources. Excreta-related pathogens, skin irritants and toxic chemicals originating from these sources pose health risks to farmers and agricultural workers, their families, communities living in proximity to wastewater irrigation, as well as the consumers of these crops.

Wastewater exposure has been linked to viral, bacterial and protozoan diseases such as salmonellosis, shigellosis, cholera, giardiasis,

amoebiasis, hepatitis A, viral enteritis and other diarrheal diseases. In particular, helminth infections such as ascariasis are commonly associated with wastewater exposure, resulting in anemia and impaired physical and cognitive development. Due to frequent contact with untreated wastewater, agricultural workers also experience skin diseases such as dermatitis and rashes. Exposure to heavy metals including arsenic, cadmium, lead, and mercury due to prolonged consumption of contaminated foods o occupational ingestion or inhalation of irrigated soil is linked to a wide range of chronic health effects.

In conclusion, It is established beyond doubt that ignorance and neglect of the laws of health and hygiene are responsible for the majority of disease to which mankind is heir. The very high death rate among us is no doubt due largely to our poverty, but i could be mitigated if the people were properly educated about health and hygiene.

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FRAILTY SYNDROME

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FRAILTY SYNDROME

Introduction

Elderly persons can become frail. **Frailty refers to a condition in which a person exhibits diminished ability to undertake essential social activities of daily living under minor environmental stressful situations.** There is a diminished reserve in the physiological function of different organ-systems of the body to carry out important daily activities and to maintain adequate homeostasis.

In such a background, any minor illness or adverse drug effects lead to disproportionate loss of function, increased risk of disability, and increased risk of death from the effects of a stressor. It must be noted that a similar amount of stress does not cause any disturbance in a physically fit individual of the same age and sex. **Thus frailty is a progressive physiological decline in multiple organ systems marked by loss of function, loss of physiological reserve and increased vulnerability to disease and death** .

Frailty is a clinical syndrome associated with increased risk of functional disability, and is a dynamic process. It is common in older adults and in those with multiple co-morbidities. The condition may be encountered independently thus differing from ageing.

Frailty and disability

Though frailty has been considered a form of pre-disability, the term should not be confused or mistaken with another entity called, disability. Disability may develop from a single pathological event leading to actual loss of function. Frailty develops from multiple pathologies.

Disability refers to an established loss of function following a condition such as stroke, poliomyelitis or fracture in an otherwise healthy individual. The person remains stable and in good health after recovery without much fluctuation in function.

In frailty there is an increased vulnerability to loss of function, and the individuals are unable to withstand minor environmental stresses of daily life. There is a marked fluctuation in response to any minor illness. Frailty and disability can coexist. In addition there may be co-morbid illnesses. When they exist together there is marked deterioration of function even with minor illness, and the patient finds an inability to cope independently. There is an increased risk for falls.

Domains in frailty

Frailty is a complex disorder characterized by impaired function in different specific domains (table 1). Each domain is assessed while making a comprehensive assessment of frailty. It must be noted that not all old persons are frail.

Table 1: Impaired domains in frailty

Musculoskeletal function
Cardio-respiratory function
Cognitive function
Neurological function
Nutritional status

Till recently, diagnosis of frailty was mostly subjective, and now objective methods for its diagnosis have been formulated. Earlier it was thought frailty is an inevitable part of old age, **now it is considered as an avoidable condition**.

The objective criteria for the diagnosis of frailty have been formulated by Linda Fried and her colleagues who proposed a clinical phenotype of frailty as a well defined syndrome with biological underpinnings. They hypothesized that the clinical features of frailty are related in a mutually exacerbating cycle of negative

energy balance, sarcopenia, and diminished strength and tolerance for exertion . **Frailty is defined as a condition having any 3 of the following 5 attributes (Table 2).**

Table 2: Criteria for the diagnosis of frailty

1. unintentional weight loss of more than 4 kg in one year
2. physical exhaustion by self report
3. muscle weakness as evidenced by grip strength
4. decline in walking speed
5. low physical activity

Frail people may develop functional decline and disability following exposure to a stressor such as an infection , fall, death of spouse or children, or addition of a new drug in the treatment regimen. These individuals do not possess the resources to respond and maintain adequate homeostasis. An early intervention may help in reversal of some of the aspects of frailty or may delay the onset of disability in elderly. As an example, a person with heart failure requires treatment of the basic condition, an exercise program to improve musculoskeletal function, balance and aerobic capacity, and nutritional support to restore the lost weight.

Aetiopathology

The development of frailty is influenced by genes, environment and life style.

Many different body systems become dys-regulated on an anatomic, molecular and physiologic level as people reach old age. Some of these systemic changes are more quickly noticeable in people who are frail. The studies have linked frailty to an increase in inflammation and blood clotting activity. There is over expression of cytokines, decline in the level of hormones, loss of muscle mass and muscle strength or sarcopaenia.

Frail patients exhibit significantly higher serum interleukin (IL)-6 levels and significantly lower levels of haemoglobin and haematocrit values than non-frail patients. Serum IL-6 level was inversely related to haemoglobin and haematocrit in frail group, but not in non-frail group. The subclinical anaemia might be related to chronic inflammatory state as evident by raised level of IL-6. IL-6 levels

correlate inversely with IGF-1 level in frail patients suggesting a potential interaction between endocrine and immune or cytokine dysregulation. There is a decline in humoral and cell-mediated immunity with advancing age.

Frail patients show increased levels of reactants linked to injury or inflammation such as C-reactive protein (CRP) and clotting factor VIII. Some patients even demonstrate increased levels of the clotting breakdown product-C dimmer.

Certain humoral changes are also noticeable in frail patients. Serum levels of insulin-like growth factor (IGF)-1 and dehydroepiandrosterone sulphate (DHEA-S) are significantly lower in frail patients than non-frail patients . DHEA-S plays an important role in suppressing inflammatory signal transduction. A decreased level in this weak androgen-steroid is likely to contribute to the increased inflammatory process.

It is yet not clear what triggers frailty in some but not in others. Certain environments, medication, age-related changes and disease make older people particularly vulnerable to become frail. There is a high prevalence of frailty in patients with chronic renal insufficiency, depression, Parkinson disease, diabetes mellitus (DM), and atherosclerosis. Frailty is encountered in persons who are inactive and malnourished. Ageing results in the loss of complexity of the physiological control system. Many older patients lose their adaptive capacity which is considered as a hall-mark of frailty.

The possible cellular changes that may result in frailty are listed in Table 3:

Table 3: Cellular changes responsible for frailty

1. increase in age-related free radical production and resulting DNA damage
2. shortening of telomere
3. changes in gene expression
4. cellular senescence

The cellular changes may contribute to dys-regulated neuroendocrine and inflammatory signaling that in turn contribute to decline in muscle, bone, cognitive and immune system functions.

Some conditions that may produce frailty are listed in table 4:

Table 4: Conditions producing frailty

Pain limiting the ability to exercise
Disease limiting cardiopulmonary function
Disease interfering with muscle function
Weight loss
Impaired executive function (depression, cognitive deterioration)

Sarcopaenia

The word sarcopaenia has been derived from the Greek roots *sarx*- for flesh and *penia*-for loss. Sarcopaenia is age-related decline in muscle mass and function that affects ambulation, mobility, nutrient intake and status and functional independence. Elderly persons with sarcopaenia, exhibit decreased lean body mass and muscle strength due to a marked uncoupling of muscle cross-sectional area and muscle fibre strength.

Sarcopaenia can be measured by bioimpedence analysis and either low muscle strength as demonstrated by hand grip or low physical performance characterized by slow gait speed. It was recognised on the basis of age, grip strength and calf circumference.

There is also accumulation of fat in the muscle (myosteatosis) which causes a decline in muscle strength leading to changes in gait and balance .

The decline in muscle mass and function affects ambulation, mobility, nutrient intake and status and functional independence . In contrast to this condition, obese persons often have a greater lean body mass than normal weight persons. However, among them a small subset exhibits sarcopaenia (sarcopaenia obese or 'fat frail'). These persons can become frail if they do not exercise adequately.

According to The European Working Group on Sarcopenia in Older People (EWGSOP)-and the European Union of Geriatric Medicine Society, the European Society for Clinical Nutrition and Metabolism and other partners, sarcopaenia

was defined as 'a syndrome characterized by progressive and generalised loss of skeletal muscle mass and strength, with a risk of adverse outcomes such as physical disability, poor quality of life and death (Fig. 1). Currently, the EWGSOP definition is widely used.

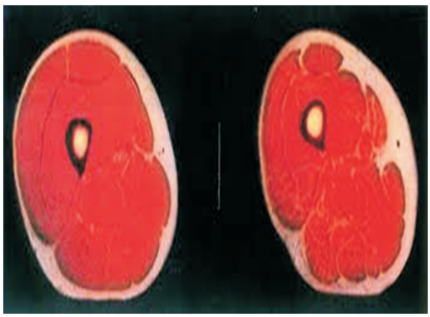

Fig.1 showing loss of muscle mass

Aetiology: There are many causes for development of sarcopaenia (table 5)

Table 5: Conditions co-incidental with sarcopania

Presence of angiotensin-converting enzyme (ACE) D allele
Age-related loss of muscle fibre
Atherosclerosis
Diabetes mellitus
Decreased physical activity
Obesity in some individuals
Decreased food intake including protein and creatine
Decreased testosterone level
Decreased intake of vitamin D
Decreased insulin-like growth factor (IGF)-1 and mechano-growth factor

Table 5: Conditions co-incidental with sarcopania

Increased cytokines (tumor-necrosis factor-alpha, interleukin-6)
Decreased motor unit acuity with a decrease in
ciliary neurotrophic factor
Loss of muscle mass and strength
Over-expression of myostatin, a transforming growth factor

Classification: Sarcopaenia may be primary or secondary .Primary sarcopaenia is age-related without any obvious cause apart from advanced age. The secondary sarcopaenia may be related to activity, disease or nutrition (table 6) .

Table 6: Causes of secondary sarcopaenia

Activity related	:	bed rest, sedentary life style, deconditioning, zero-gravity conditions
Disease related	:	advanced organ failure (heart, lung, liver, kidney or brain), inflammatory disease, malignancy, endocrine disease
Nutrition related	:	Nutrition related: inadequate dietary intake of energy and/or protein as with malabsorption, gastrointestinal disorders, use of medications that cause anorexia

In many elderly persons, the cause of sarcopaenia is multifactorial. Hence in many occasions it may not be possible to characterize exclusively primary or secondary sarcopaenia.

Pathophysiology: There is great complexity involving muscle and associated neural and hormonal regulation . Muscle tissue is not static and it exhibits a continuous process of atrophy and hypertrophy. It is a cyclical process of death and rejuvenation. Muscle proteins undergo degradation when they unfold and it leads to atrophy. The cells also undergo apoptosis. However, there is

rejuvenation of the cells following incorporation of amino acids causing synthesis of protein leading to muscle hypertrophy. There is also stimulation of stem cells leading to production of satellite cells that are capable of repairing damaged muscle.

The intake of food has to be adequate to maintain proper function of muscle. Protein and creatine play an important role. Motor unit acuity gets diminished with advancing age. There is fall in the levels of ciliary neutrotrophic factor (CNTF) and raised levels of cytokines, such as tumor-necrosis factor (TNF)-alpha and interleukin (IL)-6, all associated with decreased muscle strength. Muscle strength is decreased in diabetes mellitus. Muscle rejuvenation is affected with development of atherosclerosis as it causes a fall in blood supply to muscle.

The anabolic hormones such as growth hormone and testosterone activate insulin growth factor (ICF)-1 gene within the muscle. IGF-1 stimulates protein synthesis and muscle hypertrophy. It functions under growth hormone regulation. The production of satellite cells is activated by mechano-growth factor (MGF) leading to an increase in muscle mass. In the absence of any resistance exercise, the muscle fails to acquire strength. Growth hormone exhibits its action after the process is initiated by resistance exercise, while Ghrelin, a growth hormone secretagogue is able to increase muscle mass and food intake.

There is a fall in the concentration of testosterone in advancing age which is associated with a decrease in muscle strength and function. The level falls with aging at the rate of nearly 1% per year . There is loss of anabolic stimuli, hence the muscle mass shows atrophy . Testosterone stimulates protein synthesis and satellite cell production . The administration of large doses of this hormone is able to increase the muscle mass and strength in hypogonadal men .

Myostatin inhibits satellite cell production thus inhibiting muscle rejuvenation. A double-deletion of the myostatin gene can result in muscle hypertrophy .Vitamin D deficiency is associated with poor muscle function. There is a longitudinal change in serum 25-hydroxy vitamin D in older people as its levels appear to fall throughout the life time. The studies have shown supplementation of vitamin D in elderly result in a decreased rate of fall and reduced functional impairment . Muscle quality is maintained by adequate food intake including creatine. Often there is a decline in appetite and an inadequate intake of protein which deleteriously affects the muscle maintenance. Muscle strength decreases with a fall in the level of ciliary neurotrophic factor.

Many frail persons show certain amount of weight loss due to multiple factors persons including sarcopaenia, anorexia, dehydration, wasting, depression, disease states such as tuberculosis, cancer, congestive heart failure, COPD, chronic renal failure, and hip fracture, dietary restriction and side effects of medication. Efforts are to be made to improve the nutrition status in the elderly. Diabetes mellitus is associated with decline in muscle strength. The level of angiotensin II is elevated in diabetes which stimulates caspase 3 to cleave actinomyosin to actin and myosin. Insulin resistance facilitates fat infiltration within the muscle cells. Coexistent neuropathy causes a decrease in motor unit firing that is responsible for the maintenance of muscle quality. Anaemia has to be treated with iron supplementation or with erythropoietin or darbepoietin-alpha in chronic renal failure. Depression is often another associated condition.

Clinical features

The patient with frailty presents with a variety of vague complaints that are narrated very slowly. The clinical presentation is often atypical and late. There may be multiple co-morbid conditions. Frail elderly patients exhibit symptoms such as weight loss, weakness, fatigue, slow walking speed, and low physical activity. These manifestations interact with each other and lead to a fall in physiologic reserves which may be related to the loss of muscle mass and strength.

The patients often present with falls and unsteadiness. They often exhibit reduced perception of pain and are febrile

Fall

Unsteadiness and falls are commonly encountered. The fractured neck of femur is the most severe condition. Many conditions are associated with falls (table 7).

Table 7: Causes of falls

Accident
Tripping and slips
Age-related changes in vision, and strength
Gait and balance disorders
Syncope
Collapse from acute illness
Multiple risk factors

There can be underlying illnesses like infection, stroke, metabolic disturbances, heart failure, osteoarthropathy, postural hypotension and history of medication (sedatives, diuretics). Other presentations include infections, malnutrition, hypertension, heart failure, dizziness, and blackout, urinary incontinence, osteoarthropathy, immobility, stroke, diabetes, fluid balance disturbances, confusion and dementia.

The reserve integrative neurologic function are affected by acute illnesses such as infection, stroke, metabolic disturbances, arthritis, cardiac arrhythmias, and heart failure, to result in their inability to maintain balance. The addition of a new drug may result in deterioration. All these may result in falls.

The risk of falling increases with an increase in the number of risk factors present. The risk factors include cerebrovascular disease, Parkinsonism, deafness, visual impairment, dementia, diabetic neuropathy, postural hypotension, osteoarthritis and depression.

Clinical assessment

The history should give information on the mode of onset of the complaints and their speed of progress, medication, details of the daily activity and ability to perform them, walking and occurrence of confusion. The clinical examination should include gait, balance and stamina, nutrition, vision and hearing and mental state including cognitive function. All systems are to be examined in detail to identify the abnormality.

Frailty may exhibit the following features: 1) weight loss of 4.5 kg or more during past implying poor nutritional status, catabolic metabolism and sarcopaenia, 2) poor endurance presenting with a feeling of exhaustion, 3) weakness as demonstrated by poor grip strength, 4) slow walking with short steps, and 5) decreased physical activity.

The findings help in planning the regimen to deal with acute problem and to improve overall health and function, with an aim to reduce the likelihood of recurrence of subsequent illness and improve the quality of life. The presence of co-morbidities is to be recognized.

There are several indices and measurement techniques that are used to categorise sarcopaenia. The relative skeletal muscle index (RSMI) the appendicular skeletal muscle (derived from dual energy X-ray absorptiometry-DEXA- scanning) /height in metres squared}, fat free mass, muscle strength and loss of hand grip strength have been used to define sarcopaenia. However in clinical practice, a low body mass index (BMI) may be a useful predictor of sarcopaenia .

Diagnosis

The diagnosis of sarcopaenia is based on presence of low of muscle mass. Sarcopaenia is considered present in an elderly person >65 years if the gait speed is 0.8 m/s or less in presence of low muscle mass . Such persons should undergo further testing to determine whether they achieve the full diagnostic criteria for sarcopaenia.

Prominent muscle wasting in encountered in situations of malnutrition and cachexia, in addition to sarcopaenia. These conditions are to be differentiated as the treatment approach varies.

Malnutrition occurring due to starvation results in a loss of body fat. There is also loss of non-fat mass due to an inadequate intake of protein and energy. It should be noted that body fat in sarcopaenia is preserved. Body fat may even be increased as in sarcopaenic obesity.

Treatment

No specific treatment for frailty is available. The treatment involves the management of the precipitating acute illness and the underlying loss of function. There is also need to prevent any further loss of functions.

After treating the precipitating event, a multi-pronged approach in the management is necessary. Nutritional support is necessary to restore lost weight. Thus two factors such as physical activity and diet are readily modifiable. Pharmacological intervention is also is undertaken, though the benefits from such interventions are less evident.

Exercises are necessary to improve flexibility, strength and balance. Inactivity forms an important factor contributing to the loss of muscle mass and strength. Immobilisation induces anabolic resistance, skeletal muscle apoptosis, sarcopaenia and frailty at old age. Physical exercise strengthens the muscles and also reduces levels of inflammatory factors and increase in IGF levels to a small degree. Exercise is an important factor in therapy. Resistance or weight training is an effective counter measure to sarcopaenia, decline of muscle mass and muscle strength. Such exercises bring about an increased muscle cross sectional area (CSA) and increased mixed muscle protein synthesis rate . Muscle strength increases after a few days of training, whereas muscle mass increases 6 to 8 weeks later. It must be noted that the aerobic activity such as walking, running, cycling or jogging has not much effect on augmenting muscle mass and strength.

Exercises must be dynamic and they should target the major muscle groups of the body, that take part in lifting or pushing, and eccentric movements.

ACE inhibitors may retard the loss of muscle strength in some individuals .

Testosterone replacement may stimulate protein synthesis in hypogonadal men. This results in a moderate increase in muscle strength. However indiscriminate administration of testosterone in frail older individuals may have an increased risk of cardiovascular adverse effects.

Myostatin expressed in skeletal muscle inhibits myogenesis and promotes adipogenesis. Drugs that inhibit the effects of myostatin form a promising therapeutic approach for sarcopenia. Use of recombinant human antibodies to myostatin in healthy postmenopausal women has caused an increase in lean body mass.

Decreased food intake especially protein leads to weight loss and decreased muscle mass.. Nutritional deficiencies have to be corrected. Caloric intake has to be increased to cope with the increased demands from exercise. The elderly individuals need an increased dietary protein and amino acid. It should be more than 1.2 g per kilogram of body weight per day. Caution has to be taken to curtail the intake of protein in presence of renal insufficiency.

Leucine, an essential amino acid stimulates muscle protein anabolism in healthy elderly adults and is likely to prevent sarcopaenia . Adequate food intake, protein supplementation and supplemental creatine, and vitamin D help in maintenance of muscle quality. Creatine supplementation may be beneficial in the management of sarcopaenia but no increase in lean mass .

Often the elderly patients exhibit proximal muscle weakness due to vitamin D deficiency. Calcium and vitamin D are to be given as a prophylaxis of osteoporosis. Administration of 800 IU of vitamin D3 for a period of 2 to 12 months exhibits improvement lower extremity strength and reduces the risk of all.

The underlying disease states such as diabetes mellitus, congestive heart failure, Parkinsonism, osteoarthritis, and anaemia have to be treated. The use of ACE inhibitors is associated with an increase in lower extremity lean body mass compared to those who are using other anti-hypertensives. Loss of strength, and gait disturbances needs treatment with analgesics and physiotherapy. Visual disturbances are to be corrected.

A properly supervised exercise program if carried out for a long period of time has beneficial effect.

There is no specific medication for the treatment of sarcopaenia. Attempts are made to inhibit myostatin and manipulation of neuromuscular junction. Anabolic hormones have not shown any beneficial response.

Atherosclerosis is responsible for a fall in blood flow to muscle which in turn prevents adequate muscle rejuvenation. Anaemia has to be treated with iron supplementation or with erythropoietin or darbepoietin-alpha in chronic renal failure. Depression is often associated with frailty.

Prevention

There is no single modality of prevention of frailty. Several trials have shown that the condition can be prevented by muscle strengthening exercises, healthy diet, adequate amount of sleep, administration of hormones and growth factors, and lifestyle interventions. There is need to reduce the number of drugs taken, to train balance and gait, to correct postural hypotension by rationalizing medication, adequate hydration and use of non-steroidal anti-inflammatory drugs that cause salt and water retention, thus increasing the circulating volume, and to direct attention to those factors to reduce risk of falls .

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MONOTONY OF REPETITIVE BEHAVIOUR - AUTISM SPECTRUM DISORDER

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MONOTONY OF REPETITIVE BEHAVIOUR - AUTISM SPECTRUM DISORDER

Introduction

Autism spectrum disorder (ASD) is the name for a range of similar conditions, including Asperger's syndrome, that affect a person's social interaction, communication, interests and behaviour[1]. It includes a wide range or rather a ' spectrum' that includes varied symptoms, affects skills and results in a range of disability[2].

Definition

Autism is a neuro-developmental syndrome that is defined by deficits in social reciprocity and communication, and by unusual restricted, repetitive behaviours (American Psychiatric Association 2000). Autism is a disorder that usually begins in infancy, at the latest, in the first three years of life. It is a heterogenous condition and no two persons, children or adults have the same presentation or symptom complex.

According to the latest classification of DSM V, ASD is diagnosed based on the impairments in two domains, namely the socio-communicative and behavioural skills including fixated interests and repetitive behaviour.

Prevalence

The earliest reported systemic studies on autism were done in the 1960's.The prevalence reported at that time was 4 per 10,000 [3]. With increasing awareness, better diagnostic criteria and widening of the disease spectrum that has happened with time, the current prevalence is estimated to be 60/ 10,000 population. Data gathered in the US over the past few years between 2005- 2011 has shown a prevalence rate ranging from 45 to 110 per 10,000 population[4]. An almost four fold increase in the prevalence has been noted in the recent years. Between the years 2002- 2006, the prevalence of autism among 8 year olds has increased by 57% across all sex, races and ethnic groups. In the UK, studies of data collected by the UK General practice Research Database showed increased incidence of autism over the years, as well as recurrence in successive birth cohorts. Asian countries like Taiwan to have reported increases in diagnosis from 1.71 /10,000 individuals in 1999 to 28.72/10,000 in 2005.

This change in the prevalence may relate to the under diagnosis of the condition that occurred in the earlier years. Besides these, early diagnosis of the condition as well as the changing diagnostic criteria with the newer DSM guidelines may have contributed to the increased prevalence of the condition. The other variables, relating to the person who diagnoses the disease could also influence the prevalence rate. Studies have shown that the **school professionals are almost 6 times more likely to make an accurate diagnosis of ASD.**

Incidence

An estimate of the incidence of ASD is made possible only by the retrospective studies. The Autism and Developmental Disabilities Monitoring(ADDM) Network has reported an incidence of 1 in 110 children to be suffering from ASD[4] .Similar estimates were reported from the 2007 National Survey of Children's Health, USA which quoted 1 in 91 children between the ages of 3-17 years to be affected by autism.

Cause

The exact cause of this disease spectrum has not yet been clearly elucidated. However, it has been found to be among the most heritable developmental disorder. **Siblings of a patient have a 50 times higher risk of developing ASD** than the general population and identical twins had a 60-90% concordance compared to fraternal twins where it is 0-5%[3].

Of all the various environmental factors that have been presumed to be causative of ASD, none has been shown as a specific causative agent. An apt hypothesis could be that possible environmental triggers act on a genetic vulnerability to produce brain changes. Studies have shown that genetic linkages on chromosome 2q, 7q and 15q are frequently linked with ASD.

Conditions associated with ASD

ASD is accepted as a disorder of brain development , hence it may be associated with other brain related co-morbid conditions. Large surveys have shown that in 87.3% of children who had been diagnosed with ASD in the age range of 6-17 years, associated Attention Deficit Hyperactivity Disorder(ADHD) occurs at an estimated prevalence rate of 47.2 /100 individuals [4-].Other associated problems include anxiety problems, behavioural or conduct problems, depression or developmental delay. Almost 40-60% of the individuals also have associated

intellectual disability. Various studies have shown varying results with 29-60% of the subjects having a normal IQ.[5] Other associated genetic disorders may co-exist with ASD in a small percentage.

Epilepsy is an important associated morbidity, with rates ranging from 5-38.3%, especially in the older adolescents and adults[5]. The presence of **mental retardation** is an important predictive factor for the development of seizures, with IQ below 50 being associated with higher likelihood of seizures. Most of them had partial seizures with or without secondary generalized activity. Most develop epilepsy below the age of 2years and it is commoner in girls with autism[4]. Children with autism and epilepsy also have a higher likelihood of associated depression or an increased frequency of depression, expressed as increased behavioural disturbances, exacerbated compulsive behaviours or anxiety.

Mental retardation is found in 45-63% of the children with autism[4]. Girls tend to have more severe mental retardation . Almost 30% of the individuals had mild MR with IQ between 50-69, while 50% had severe MR with IQ< 50. Neurologic dysfunctions are common in almost 75% of the ASD cases which include dysfunctional posture and muscle tone, fine manipulative disability, mild coordination abnormalities and excessive associated movements. Girls are more likely than boys to have motor deficits.

Other associations include tics, especially in the adolescent children, schizophrenia , sleep problems, restlessness and delayed acquisition of self help skills like dressing, toileting, hygiene etc[6]

Risk factors

Although no definite cause for ASD has been elucidated, several risk factors have been thought to be associated with and increased likelihood of ASD.

1. The maternal age at the time of conception and delivery may be associated. Mothers younger than 20 years had the lowest odds of having an early diagnosis of ASD as compared with mothers over the age of 20 years. Mothers> 40 years of age had a significant risk of diagnosis of autism with an odds ratio of 2.5. Increasing paternal age also influences the likelihood of ASD. The risks are higher in case of men over 40 years had 5.75 times higher chances of ASD in their offspring compared with fathers < 30 years of age.

2. Parental education: studies have shown that mothers who were educated with 4 or more years of college education were less likely to have an autistic child compared with those who had only finished their high school. This may be only an association, but more studies need to be done to elucidate the difference.

3. The child's sex- In the USA, 75-80%of the cases of ASD diagnosed are male children. The rate of autism in boys that has been reported from Swedish Birth registry is 79.6% and 84.4% in Israel.

4. Inheritance- a genetic link has been pointed to by several studies. The relative risk of autism is 22 times greater in children with siblings diagnosed as autistic and 13 times greater when it is diagnosed as the autism spectrum disease. In families with 2 or more autistic children, the likelihood of recurrence is 35%.Monozygotic twins are more concordant for ASD compared to dizygotics, almost as high as 60%. Underlying genetic disturbances like Fragile X is often associated with ASD.

Table - 1: Genetic syndromes associated with ASD

Genetic syndromes associated with autism	
Syndrome	**Cause (if known)**
Rett syndrome [80,81]	Methyl-CpG-binding protein 2 mutation
Tuberous sclerosis [82-84]	TSC1 and TSC2 mutations
Fragile X [80, 82, 85]	FMR1 mutation creating triplet repeats on X chromosome
Neurofibromatosis [82]	
Congential Rubella syndrome [86]	
Moebius syndrome [82, 87]	Underdevelopment of cranial nerves VI and VII
CHARGE syndrome [75, 82]	CHD7 mutation
Goldenhar syndrome [75, 82]	
Down syndrome [82, 85, 88]	Trisomy 21
Prader-Willi [82, 85]	Chromosome 15 deletion inherited paternally
Angelman syndrome [82, 85]	Chromosome 15 deletion inherited paternally
Cohen syndrome [82, 89]	Mutations in COH1
Cowden syndrome [82, 90]	PTEN tumor suppressor gene mutation
Bannayan-Riley-Ruvalcaba syndrome [82, 90]	PTEN tumor suppressor gene mutation

Table - 1: Genetic syndromes associated with ASD

Genetic syndromes associated with autism	
Syndrome	**Cause (if known)**
Smith-Lemli-Opitz syndrome [82, 91]	Deficiency of final enzyme in pathway that synthesizes cholesterol
De Lange syndrome [82]	
DiGeorge syndrome [82, 92]	Chromosome 22q11 deletion
Wilms' tumor, Aniridia, Genito-urinary anomalies, mental Retardation syndrome [93]	Chromosome 11p deletion
Smith Magenis syndrome [82]	

Ref: Ped Clin Am.2012;1:27-43.

Early markers

Autism is a disorder that begins in early infancy. However, the early pointers may be too subtle and avoid detection, to be picked up only when the infant becomes more socially sophisticated[3]. Motor and sensory maturation begins at 3-6 months of age. This is the period when the infant makes and holds eye contact, coos and moves rhythmically[4]. The parents are usually excited and joyful at being able to hold conversations with their infant. Any signs of absence of these interactions should be remembered as early warning signs.

Children with ASD prefer solitary activities and prefer interactions with much younger or older people. Another characteristic of ASD is restricted , repetitive patterns of behaviour or interest, with stereotypic movements like hand flapping, finger licking etc, which may be noticed early. Repetitive speech or echolalia may be noticed as an early finding. Besides these, there is a highly restricted and fixed interest of abnormal intensity or focus together with extreme responses to specific sounds or textures, excessive smelling or touching of objects and fascination with spinning objects, lights etc.

Table - 2 : Red flags in ASD

Red Flags in Developmental Screening and Surveillance
These indicators suggest that development is seriously disordered and that the child should be promptly referred to a developmental or community pediatrician. Note : Most children do not have "red flags" and thus require quality screening to detect any problems.

Table - 2 : Red flags in ASD

Red Flags in Developmental Screening and Surveillance
POSITIVE INDICATORS (THE PRESENCE OF ANY OF THE FOLLOWING)
Loss of developmental skills at any age
Parental or professional concerns about vision, fixing, or following on object or a confirmed visual impairment at any age (simultaneous referral to pediatric ophthalmology)
Hearing loss at any age (simultaneous referral for expert audiologic or ear, nose, and throat assessment)
Persistently low muscle tone of floppiness
No speech by 18 mo, especially if the child does not try to communicate by other means such as gestures (simultaneous referral for urgent hearing test)
Asymmetry of movements or other features suggestive of cerebral palsy, such as increased muscle tone
Persistent toe walking
Complex disabilities
Head circumference above the 99.6th centile or below 0.4th centile. Also, if circumference has crossed 2 centiles (up or down) on the appropriate chart or is disproportionate to parental head circumference
An assessing clinician who is uncertain about any aspect of assessment but thinks that development may be disordered
NEGATIVE INDICATORS (ACTIVITIES THAT THE CHILD CANNOT DO)
Sit unsupported by 12 mo
Walk by 18 mo (boys) or 2 yr (girls) (check creatine kinase urgently)
Walk other than on tiptoes
Run by 2.5 yr
Hold object placed in hand by 5 mo (corrected for gestation)
Reach for objects by 6 mo (corrected for gestation)
Point at objects to share interest with other by 2 yr

From Bellman M, Byrne O, Sege R: Developmental assessment of children. BMJ 346:31-36, 2013.

Signs and Symptoms

The symptoms of ASD may be present early in infancy, but are most often overlooked. The symptoms are commonly recognized in the second year of life, when the social demands exceed the limited capacities. Those with the least severe symptoms on the spectrum may not be diagnosed till 4-6 years or older. These children usually present with delayed milestones in the core developmental areas. A working knowledge of the various milestones, especially the fine motor, communicative and speech / language skills are essential to catch them early.

Table-3: Early pointers of ASD

Social interaction and reciprocal communication behaviors

Spoken language

- Language delay (in babble or words-for example, using fewer than 10 words by the age of 2 yr)
- Regression in or loss of use of speech
- Spoken language (if present) may include unusual features, such as: vocalizations that are not speech-like; odd or flat intonation; frequent repetition of set words and phrases (echolalia); reference to self by name or "you" or "she" or "he" beyond age 3 yr
- Reduced and/or infrequent use of language for communication-for example, use of single words, although able to speak in sentences

Responding to others

- Absent or delayed response to name being called, despite normal hearing
- Reduced or absent responsive social smiling
- Reduced ro absent responsiveness to other people's facial expressions or feelings
- Unusually negative response to the requests of others ("demand avoidance" behavior)
- Rejection of cuddles initiated by parent or carer, although the child himself or herself may initiate cuddles

Interacting with others

- Reduced or absent awareness of personal space, or unusually intolerant of people entering their personal space
- Reduced or absent social interest in other, including children of his or her own age-may reject others; if interested in others, he or she may approach others inappropriately, seeming to be aggressive or disruptive
- Reduced or absent imitation of others' actions
- Reduced or absent initiation of social play with others, plays alone
- Reduced or absent enjoyment of situations that most children like-for example, birthday parties
- Reduced or absent sharing of enjoyment

Eye contact, pointing and other gestures

- Reduced or absent use of gestures and facial expressions to communicate (although may place an adult's hand on objects)
- Reduced and poorly integrated gestures and facial expressions, body orientation, eye contact (looking at people's eyes when speaking), and speech used in social communication
- Reduced or absent social use of eye contact (assuming adequate vision)
- Reduced or absent "joint attention" (when 1 person alerts another to something by means of gazing, finger pointing, or other verbal or nonverbal indication for the purpose of sharing interest). This would be evident in the child from lack of:
  - Gaze switching
  - Following a point (looking where the other person points to - may look at hand)
  - Using pointing at or showing objects to share interest

Unusual or restricted interests and/or rigid and repetitive behaviors

- Repetitive "stereotypical" movements such as hand flapping; body rocking while standing; spinning; finger flicking
- Repetitive or stereotyped play-for example, opening and closing doors
- Over focused or unusual interests
- Excessive insistence on following own agenda
- Extremes of emotional reactivity to change or new situations; insistence on things being "the same"
- Over-reaction or under-reaction to sensory stimuli, such as textures, sounds, smells.
- Excessive reaction to the taste, smell, texture, or appearance of food, or having extreme food fads

Diagnosis

It is recommended that all children receive autism specific screening at 18 mo and 24 mo of age, besides broad developmental screening at 9, 18 and 24 months [7]

ASD is diagnosed based on the criteria laid out in the fifth edition of the Diagnostic and Statistical Manual of Mental disorders. Several screening tools are available to be used for diagnosis. The Indian Scale for Assessment of Autism (ISAA) has a high sensitivity of 93.3 and specificity of 97.4 indicating a good reliability [6]. Another useful tool if the Childhood Autism Rating Scale CARS, but this has a lesser specificity and sensitivity. Besides these, a Modified Checklist for Autism in Toddlers(M-CHAT) is a free online 23-item autism screening tool for children 16-30 months is available online that can be downloaded and used.

Fig 1: Sample of ISAA Form

INDIAN SCALE FOR ASSESSMENT OF AUTISM

National Institute for the Mentally Handicapped
(Ministry of Social Justice and Empowerment Govt. of India)
An ISO 9001 : 2000 Institution
Manovikasnagar,
Secunderabad - 500 009.

Name of the child ..... Gender ..... Date .....

D.O.B. ..... Age ..... Examiner .....

Directions :

Below are given 40 statements which are divided under six domains, please tick (✓) mark the appropriate rating for each item of the scale by observing the child and by interviewing the parents in order to assess Autism.

Refer to the guidelines given in the manual for making observations and ratings.

ITEMS	Rarely Upto 20% Score 1	Sometimes 20 - 40% Score 2	Frequently 41 - 60% Score 3	Mostly 61 - 80% Score 4	Always 81 - 100% Score 5
SOCIAL RELATIONSHIP AND RECIPROCITY					
1. Has poor eye contact					
2. Lacks social smile					
3. Remains aloof					
4. Does not reach out to others					
5. Unable to relate to people					
6. Unable to respond to social/evnriomental cues					
7. Engages in solitary and repetitive play activities					
8. Unable to take turns in social interaction					
9. Does not maintain peer relationships					
EMOTIONAL RESPONSIVENESS					
10. Shows inappropriate emotional response					
11. Shows exaggerated emotions					
12. Engages in self-stimulating emotions					
13. Lacks fear of danger					
14. Excited or agitated for no apparent reason					
SPEECH-LANGUAGE AND COMMUNICATION					
15. Acquired speech and lost it					
16. Has difficulty in using non-verable language or gestures to communicate					

The chart has 40 items covering areas related to :

- social relationship and reciprocity
- emotional responsiveness
- speech- language and communication
- behaviour patterns
- sensory aspects
- cognitive components.

Each of the 40 items receives a score based on the frequency ranging from 1-5. This is categorized as occurring rarely upto 20% of the time, sometimes 21-40%, frequently 41-60%, mostly 61-80% and always 81-100%. The sum of all the scores is used to arrive at the classification of autism:

Score < 70 -No autism

Score 70-106-Mild autism

Score 107-153 Moderate Autism

Score > 153- Severe autism

This test takes 20-30 minutes to perform and is valid for 3-9 year olds.

Other investigations

A complete medical examination is recommended for all children suspected to have ASD. This includes the following

- General physical examination
- A thorough hearing screen
- A Wood's lamp examination for signs of tuberous sclerosis
- Genetic testing including a chromosomal microassay CMA. This is recommended as the standard of care for the initial evaluation of children with ASD

  Testing for Fragile X must be undertaken as it may not be detected by the CMA.

  Some of the other investigations that may be indicated include:

Table - 4: List of additional investigations

FISH test for region 15q11q13 to rule out duplications in Prader-Willi/ Angelman syndrome
Fluorescence in situ hybridization (FISH) test for telomeric abnormalities
Test for mutations in *MECP2* gene (Rett syndrome) in females DNA testing for fragile X syndrome
Metabolic testing to consider based on clinical features (emesis, hypotonia, lethargy, ataxia, coarse facial features of a storage disease, multiple organs involved)
Fasting blood glucose
Plasmsa amino acids
Ammonia and lactate
Fatty acid profile, paroxysmal
Carnitine
Acylcarnitine, quantitative
Homocysteine
Urine amino acids
Urine organic acids
Urine purine/pyrimidines
Urine acylglycine, random
Plasma 7-dehydrocholesterol (Smith-Lemli-Opitz disease screening)

Sometimes the examination of the child could point towards certain developmental disorders. These would need specialized investigations. A notable disorder if Landau –Kleffner syndrome which has characteristic eeg abnormalities associated with marked aphasia[7]. In case of suspected Rett's disorder the MeCP2 gene must be looked for[6]. In suspected Tuberous sclerosis cases, the Wood's lamp examination together with genetic testing for G-banded karytype must be elucidated.

Table 5: Additional investigations for specific condition

Medical testing to consider based on clinical features
Complete blood cell count
Liver enzymes
Biotinidase
Thyroxine, thyroid-stimulating hormone
Ceruloplasmin/serum copper
EEG if the following clinical features are noted
Clinically observable seizures
History of significant regression in social or communication functioning

Management

A structured method of management will provide the best results for the children with ASD. This should include behavioural, educational and communication interventions which would help produce a better outcome. While young children require an accurate diagnosis followed by appropriate treatment programs, the older children require on priority the sorting out of behaviour and medication issues. In adolescence, the need for vocational training and future self sufficiency plans become critical[7].

Intervention

Intervention should begin as early as possible in cases of ASD, in order to get the best benefits. An interdisciplinary team including a pediatrician, child neurologist/ psychiatrist, psychologist, occupational therapist, speech and language therapist, special educator, nutritionist and social worker, all need to be involved in the care of these children.

Several methods of intervention are available which include:

- ABA- Applied Behavior Analysis
- TEACCH- Structured teaching method- The Treatment and Education of Autistic and related Communication-handicapped children.
- Developmental/ relationship based models

- SCERTS - Social Communication, Emotional Regulation and Transactional Support - which includes a variety of treatment modes.
- Cognitive Behaviour therapy - effective to reduce anxiety and anger management

The intervention should lay emphasis on attention, imitation, communication, play and social interaction. The goals should be to enhance eye contact, social orientation, verbal and non verbal communication

- Reducing repetitive and restricted behaviour activities, interests, sensory issues an hyperactivity
- Improving joint attention
- Improving social , motor, behavioural capabilities.

Family mediated early intervention

Active involvement of the family/ caregivers is a form of co-therapy that must be encouraged. However, it must be adequately supervised, and regular training and monitoring should be on going. Parent mediated interventions are cost effective and at the same time provide a sense of empowerment to the family.

Psychopharmacologic intervention

This is useful to improve the child's functioning and ability to participate in behavioural interventions. Medications may also be needed to treat the co-morbid psychiatric or neurodevelopmental conditions or specific target behavioural symptoms that interfere with the overall functioning.

Some of the useful drugs that may be used in children with ASD are listed below[6]:

Table - 6: Medications used in ASD

DRUGS AVAILABLE FOR PHARMACOLOGICAL MANAGEMENT OF AUTISM SPECTRUM DISORDERS

Drug name	*Indications*	*Dose*	*Side-effects*
Methylphenidate	Impaired function in spite of behavioural and environmental interventions	10-40 mg each morning extended release	Sleep disturbance, decreased appetite, irritability, tics, sadness, dullness and social withdrawal
Risperidone	Ineffectiveness of stimulants and /or maladaptive behaviors	0.5 - 3.5 mg / day	Weight gain, increased appetite, fatigue, drowsiness, drooling, dizziness

Table - 6: Medications used in ASD

DRUGS AVAILABLE FOR PHARMACOLOGICAL MANAGEMENT OF AUTISM SPECTRUM DISORDERS

Drug name	*Indications*	*Dose*	*Side-effects*
Atomoxetine	Methylphenidate not tolerated	1.2 mg/kg/day	Nausea, anorexia, fatigue, early awakening
Fluoxetine	Repetitive behaviors and rigidity	2.4-20 mg/day	None significant

Management of associated co-morbid conditions

1. Sleep disturbances- which may include late sleeping, frequent waking, restlessness etc. All these may be related to the abnormal levels of melatonin, serotonin or GABA. A thorough evaluation of the sleep history including seep hygiene must be assessed, and behavioural interventions must be considered. If this does not give the desired results, melatonin may be recommended at low starting doses of 0.5- 1 mg to be administered 30 minutes before the desired sleep time, regardless of weight or age of the patient.
2. Gastrointestinal problems- are commonly associated with ASD. These have to be managed similarly as in children without ASD.
3. Anxiety- is a common finding that may lead to aggression, explosive behaviour and self injury..Cognitive behaviour therapy is an important tool for managing these patients. Sometimes, pharmacotherapy is also needed. In these cases, Buspirone, an anxiolytc drug is preferred.
4. Mood disorders- while dysregulated mood is common in children with ASD, the management of the condition is variable and difficult. Various drugs like atypical antipsychotics, SSRI's and mood stabilizing agents like lithium have been tried. However, non f these agents have been specifically tried for mood regulation specifically in children.
5. Depression- counselling and psychosocial interventions are the first line of management. However, in cases where these do not work, antidepressant drugs must be started in low doses with slow increments based on the needs. However, these drugs may produce unwanted side effects like impulsivity, silliness agitation and dis-inhibition, and an increased risk of suicide ideation.

A combination of medication with parent training is more efficacious in reducing serious behavioural disturbances as well as adaptive functioning. The overall goal of the therapy must be to facilitate the child's adjustment and improve the productivity and skills.

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