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"Micro and Nano "The Unseen Effect on Human Health.

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Abstract:-

The purpose of this study was to present data regarding the toxicity of microplastics (MPs) and nanoplastics (NPs) in mammalian bodies.

Although there are several ways for humans to be exposed to micro-and-nanoplastics (MNPs), little is known about how MNPs negatively impact diverse organ systems. The purpose of this review is to present a summary of the possible effects of MNPs on different organ systems.

According to the compiled findings, MNP exposure may cause oxidative stress, inflammation, immunological dysfunction, changes in biochemical and energy metabolism, a reduction in cell proliferation, disruptions in microbial metabolic pathways, aberrant organ development, and carcinogenicity.

NPs are quickly absorbed in the blood following a single oral dose, build up in adipose tissues, and cross the blood-brain/testis barriers. MPs' toxicokinetics in mammals is, as predicted, highly size-dependent.

The distribution, accumulation, and possible toxicity of micro- and nanoparticles are examined in this paper, along with the routes by which they enter the human body— inhalation, ingestion, and skin absorption. Special attention is paid to the possible longterm impacts of nanoparticles on organ systems like the respiratory, cardiovascular, and neurological systems, as well as their capacity to cross cellular barriers and cause inflammation, oxidative stress, and cytotoxicity. The toxicity mechanisms are also covered in the paper, including the production of reactive oxygen species (ROS), disturbance of cellular homeostasis, and inflammatory reactions brought on by nanoparticles.

Keywords –

Microparticle; Nanoparticles

Health impacts, organ systems

1.Introduction –

As the production of plastics surged to about 360 million tonnes in 2018[1], pollution from microplastics (MPs) and nanoplastics (NPs) has become a rising environmental problem. There have been reports of MPs pollution in aquatic environments ranging from the equator to the poles [2–3]. Additionally, it has been verified that MPs particles move down the food chain [4,5]. In fact, MPs particles have been discovered in processed foods and beverages such as bottle water, salt, beer, milk, and sugar , in addition to seafood [6-11]

The breakdown of MPs in the environment and some industrial or home uses, like biomedical products [12] and personal care items like toothpaste and cosmetics [13], are the sources of NPs (≤ 100 nm in diameter) pollution.

Primary microplastics (MPs) are added to commercial products, such as fertilizers and cleaning supplies, while secondary MPs are created when bigger plastic components break down[14] MPs can be broken down into nanoplastics (NPs), a subset of MPs, or they can be released from other sources, like plastics used in paints, adhesives, electronics, and other products.[15,16] . About 70–80% of the total plastic released into the environment is made up of secondary MPs and NPs, which are often created by the breakdown of macroplastics by shear forces[17] whereas primary MPs make about 15–30%.[18] Microfibers from textiles (diapers, fleeces, and disposable masks), fragments, plastic pellets and nurdles from industries, foam, and microbeads are some of the various types of MPs.[19,20] Humans are exposed to MNPs through their skin, food, and breath.

However, the European Commission Regulation (EU) 2023/2055, which has a five- to eight-year phase-in time, forbids the deliberate inclusion of microplastics in the EU [21]. People frequently come into contact with and consume different kinds of nanoplastics, including PS, PE, PVC, and polyester, through food, water, and the air, given the vast array of plastic uses and, consequently, sources of release to the environment [22]. More than 95.8% of samples of human feces tested positive for microplastics, with concentrations of pieces, films, and fibers up to 138.9 items per gram [23].

The possible negative consequences of breathed or consumed nanoplastics, such as oxidative stress, cellular damage, inflammation, DNA damage, and neurotoxicity, have already been suggested by a number of in vitro and in vivo investigations [24,25]. However, we presently know very little about the toxicokinetics—or fate of nanoplastics—in the human body.

Exposure of MNPs by various rout-

2.Exposure through diet -

The presence of MPs in human stool indicates that they were consumed through diet.Food, drinking water, and plastic food packaging are the main sources of MNPs [26,27], and exposure levels vary by age, sex, diet, and lifestyle. MNPs are also consumed by wildlife species, which puts our diets and the food chain at serious risk of contamination[28,29]. MPs have been found in a variety of seafood since they are found in n aquatic habitats[30-33]

Additionally, MPs particles have been found in zooplanktonic creatures, which suggests that MP may make its way into the food chain [34,35] . Although the risk is unknown, processed goods like milk and bottled water are susceptible to MPs added during processing and packaging.[36] Furthermore, MNPs can enter our diet through the air, mostly indoors.[37] Polyethene-terephthalate (PET), polyethene (PE), polypropylene (PP), polyvinyl chloride (PVC), polystyrene (PS), polyester (PES), polyurethane (PU), polyamide (PA), styrene acrylate, and polymethyl-methacrylate (PMMA) are the MP particles that are frequently found in foods and the environment.[28,38]

3. Inhalation-based exposure -

Another important way that people are exposed to MNPs is by inhalation. Synthetic fabrics, construction materials, road debris, plastic material abrasions, landfills, wastewater, and waste burning are the hypothesized sources of airborne MPs.[39,40,41], and [42] MPs, or 4% of indoor airborne particles, were detected in the air.[43] An human may inhale up to 130 MPs every day on average, according to some estimates.12 Industrial workers are particularly vulnerable to MP exposure; MPs can enter the respiratory system of humans and have a negative impact on health.[44,45].

The depth of particle distribution in the airways after inhalation is determined by aerodynamic size. The likelihood of a particle reaching deeper lung regions increases with particle size. Because of the increased likelihood of reaching the alveolar sacs, which are the site of gas exchange and particle transfer from epithelial to endothelial cells, inhaled particulate matter smaller than 2.5 microns in aerodynamic size is concerning.[46]

4.Contact with the skin-

There is evidence that NPs can penetrate the skin barrier, even though dermal exposure is thought to be the least significant entrance point. causes of cutaneous exposure to MNPs are microbeads in personal care items and atmospheric at point.prosynthetic fibers.[47]

However, as more and more nations outlaw microbeads in detergents and personal care items, this problem is becoming less of a concern.

MNPs' cellular uptake-

Depending on a number of variables, including the size and surface characteristics of the particles as well as the biological molecules they come into contact with, such as proteins, phospholipids, and carbohydrates, certain MPs and NPs may interact with cells after being absorbed into the body.[48] When biological fluids and tissues or organs come into touch with nanoparticles, they are exposed to protein molecules, which create a "crown" known as a protein corona.[49] Higher translocation rates are facilitated by polystyrene nanoparticles coated with a protein corona, according to in vitro experiments. This is dependent on the quantity and makeup of proteins.[50]Furthermore, protein coronas have the ability to change the shape and properties of nanoparticles in response to the cellular environment, which could intensify toxicity and cell interactions.[51] Consequently, there is a chance that the same in happen to MNPs.

5.The respiratory system

One major way that people are exposed to MNPs is by inhalation. The degree to which airborne MNPs negatively impact the respiratory system is yet unknown, though. A significant portion of the MNPs that are inhaled can be eliminated by lymphatic transport, phagocytosis, or mechanical means.[52] Chronic inflammation and fibrosis can result from the deposition of certain thin fibres in terminal bronchioles, alveolar ducts, and alveoli.[53,54]

Over an extended period of time, the inhaled dose usually determines the extent of tissue damage.[55] MPs have been found in human pulmonary tissue[56] and sputum samples[57] in recent investigations, suggesting that inhalation is a significant pathway for plastic particles to enter the body. The possible effects of MNP particles on human lung epithelial cells, a model for pulmonary toxicity, have been evaluated in a number of cell culture studies.

The way inhaled nanoparticles interact with the pulmonary surfactant (PS) coating determines their toxicological impact. According to in vitro and silicon research, hydrophilic nanoparticles migrate over the PS film rapidly, whereas hydrophobic nanoparticles become trapped and become encased in lipid protrusions.[58] According to the study, inhaled nanoparticles with various physicochemical characteristics are associated with a novel PS lipoprotein corona model.[58]

According to the study, inhaled nanoparticles with various physicochemical characteristics are associated with a novel PS lipoprotein corona model.[58] Because of variations in lipid packing and surface tension, nanoparticles may also pass through the surfactant during different breathing stages.[59] A healthy lung surfactant film depends on appropriate lipid packing and hydrophobic protein assembly, according to molecular studies.[60,61] referred to as the "corona"—in a way that seems to influence the level of toxicity.[62]

Furthermore, PS can change the characteristics of ZnO nanowires (ZnONWs) in the lung, influencing how epithelial cells internalize and process them.[63] Overall, this implies that depending on the molecules that adhere to their surface, inhaled MPs and NPs may have varying levels of absorption. The results of the aforementioned study suggest that inhaling MNPs may have an impact on respiratory health through oxidative stress and inflammatory responses, which may then lead to cellular death and the breakdown of the epithelial barrier, causing tissue damage and respiratory disease after prolonged exposure.

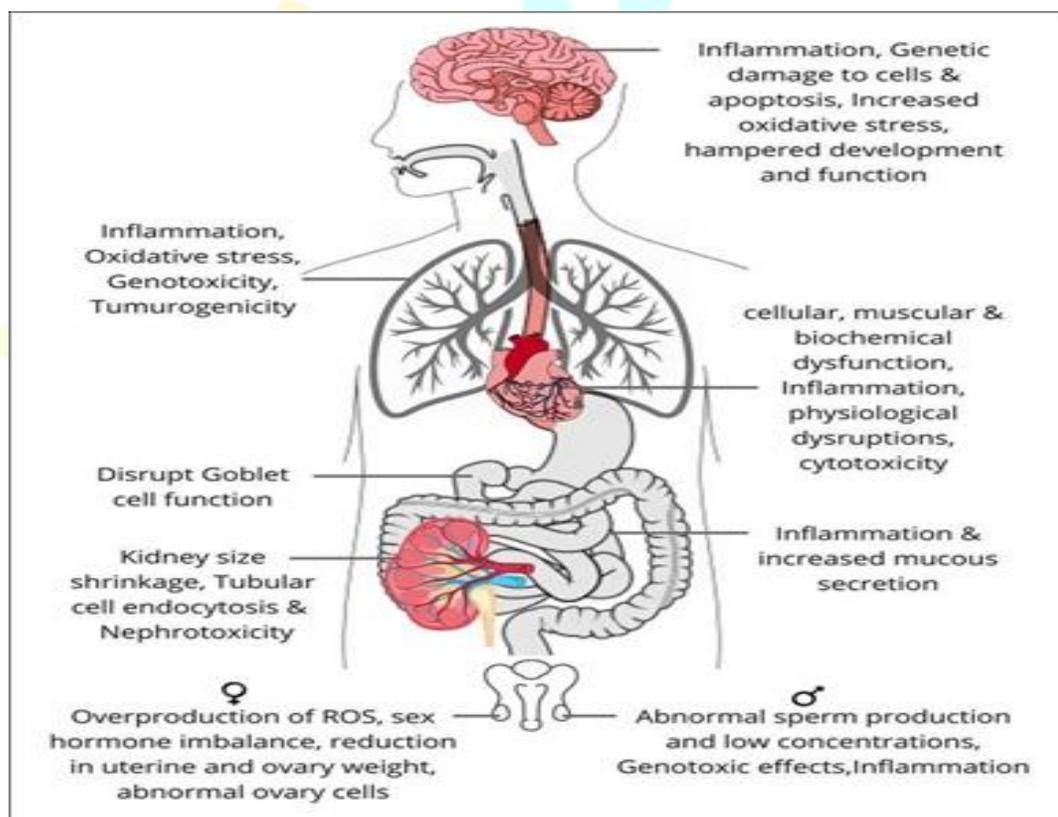According to other research, PS-NPs interact with biological elements including proteins—

Fig No:- 1 Effect of micro and nano particle on,respiratory system.

6.BBB –

The majority of foreign substances cannot enter the human brain because of the bloodbrain barrier (BBB), which is made up of a densely packed layer of endothelial cells that divides the blood components from the cerebrospinal fluid [64]. According to recent reports, metallic nanoparticles like Ag and ZnO may cross the blood-brain barrier (the latter showed the highest transport percentage, with 10.5% and 13.4% of the applied dose, respectively, moving at exposure concentrations of 1 and 2.5 mg/L), damaging brain cell membranes [65] and interfering with cholinergic neurotransmission [66]. It is possible for some metallic nanoparticles to dissolve in the cellular lysosomal environment and change into their ionic forms [67,68].

These ionic forms may use pathways designed for soluble compounds after dissolution, integrating with the body's excretory and regulatory systems and eventually being cleared [69]. They may accumulate less in biological systems as a result of this mechanism. Depending on their size, structure, and composition, Nano plastics—which are not readily biodegradable—may be at risk of building up in the brain because they seem to be able to get there a few hours after being consumed or inhaled [70,71]. Despite the possibility that PS nanoplastics could cross the blood-brain barrier, according to certain research [72,73],

7.The renal system –

A build-up of toxins and pollutants in the bloodstream due to impaired kidney function can have a negative impact on general health. MPs (PVA, PVC, PP, and PE, ranging in size from 4 to 15 µm) were discovered in human urine in a research, indicating that they can travel through the digestive system and be eliminated by biological processes.[74] MNPs are primarily eliminated via the kidney through biodegradation products in urine and the liver through phagocytosis or biliary excretion in feces.[75]

The possible effects of MNPs on kidneys were ascertained by some animal experiments and cell cultures. Human embryonic kidney cells (HEK 293) were treated to 1 µm PS-MPs (5 µg/mL) for up to 72 hours in a study by Goodman et al. (2022).[76] The findings demonstrated that PS-MPs significantly altered the kidney cells' morphology, decreased cell proliferation, and increased uptake of PS-MP particles. ROS levels were elevated in the exposed cells.[76]

In a different study, scientists exposed human kidney (HK-2) and testis (NTE) cells to fluorescently labelled PS-NPs (50 nm, 200 µg/mL for 24 hours). They discovered that the PSNPs could enter the cells through endocytosis, resulting in cellular microstructure damage and an increase in TNF-α and JNK1/2/3 expression.[77] The effects of PS-MPs (2 µm) on human HK-2 cells were investigated by Wang et al. in 2021.[78] According to the study, treatment to PS-MP (0.025–0.8 µg/mL for two hours) increased the levels of ROS and the mitochondrial protein Bad, as well as inflammatory indicators, ER stress, and the proteins LC3 and Beclin 1. PS-MPs also had an effect on the AKT/mTOR and MAPK signaling pathways.[78]

8.System of reproduction and development -

The toxicity of MNPs on reproduction and development has been documented in a few animal studies,[79,80], but human data is still few. 16 different forms of MPs were discovered in placentas and meconium samples in a Chinese investigation; the most common types were polyamide and polyurethane. IN almost 76.5% of the samples, which ranged in size from 20 to 50 μm, [81] MPs were found. The three main microbiota that were discovered were Firmicutes, Bactericides, and Proteobacteria. Additionally, a number of placenta microbiota species and the Chao index of meconium microbiota showed an adverse relationship with polyethylene, according to the study.[81] Xiao et al. (2023) discovered that PS-NPs (50 nm) can affect microstructures and penetrate testis cells via endocytosis.[77]

Proteins on cancer signaling pathways like PI3K-AKT and MAPK were discovered to be dysregulated. Testicular growth, sperm cell survival, and proliferation are all significantly impacted by the active PI3K-AKT pathway.[77] Additionally, it makes it easier for FSH and support cells to communicate, which aids in preserving male testicular stability.[82]

Research has indicated that mice exposed to PS-MPs may experience reproductive harm. For instance, male-female mice exposed to PS-MPs (5.0–5.9 μm) experienced oxidative stress, hormonal abnormalities, reproductive problems, and damage to their testicles and ovaries.[79] Additionally, following exposure to PS-MPs, fewer embryos and a lower conception rate were noted. Compared to male mice, female mice were more vulnerable to MPs exposure.[79] Exposure to PS-MPs has been demonstrated to induce ovarian inflammation and reduce oocyte quality in female mice, indicating reproductive harm.[83]

In a different study, male mice given PS-MPs (5.0–5.9 μm) in saline solution for six weeks showed decreased serum testosterone levels, decreased sperm motility and count, and increased sperm deformity rate. MNPs may potentially be harmful to reproduction and upset the energy balance. Since testicular histology was not examined, it is uncertain whether the effects on testicular function are directly related to exposure to the test materials.[84] Defects in the epididymis may also be the cause of the effects on sperm.
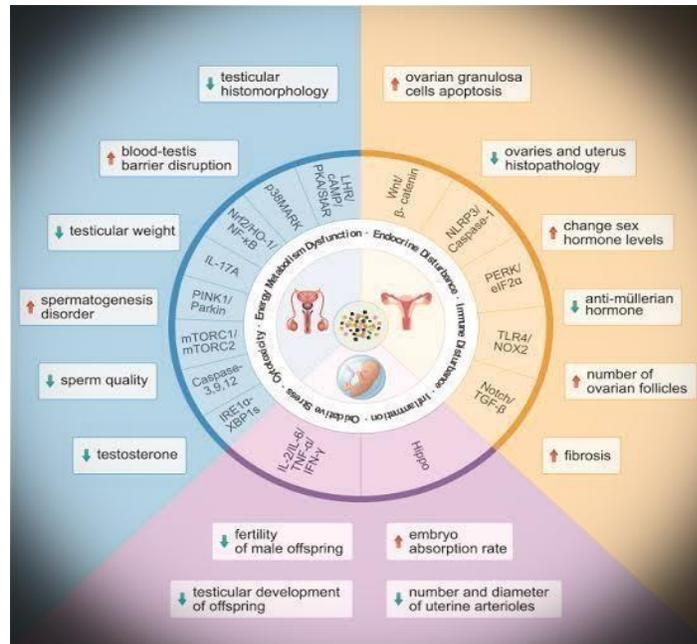
Fig No :-2 Effect of micro and nano particale on,system of reproduction and development.

9.The muscular system

Fewer research have evaluated MNPs' impact on the muscular system than on other organs. As of right now, there is no concrete proof that MNPs build up in human muscle tissue. According to a study, eating fish and other shellfish causes MPs to build up in the muscular tissue of northern fulmars.[85] Nevertheless, there was no discernible association with muscle injury.[86,87] PS-MPs (1–10 µm and 50–100 µm) exposure disturbed muscle fiber regeneration and the equilibrium between myogenic and adipogenic development, according to a study conducted in a mouse model.[88] Additionally, treatment to PS-MPs changed the p38 MAPK and NF-κB pathways and caused satellite cells to produce too many ROS.[88]

Additionally, treatment to PS-MPs changed the p38 MAPK and NF-κB pathways and caused satellite cells to produce too many ROS.[88]

10.The endocrine system –

MPs include a number of substances that are regarded as endocrine-disrupting chemicals (EDCs), including phthalates and bisphenol A (BPA). The regular operation of the endocrine system may be hampered by certain EDCs. During crucial developmental phases, such as the perinatal period, EDCs can enter the body and alter hormonal balance as agonists or antagonists, resulting in neuroendocrine impacts.[89] According to a study, PS-MPs (0.1 g/L) can change the pathways by which decabrominated diphenyl ether (BDE-209) is broken down and increase the toxicity of the thyroid gland and endocrine system in aquatic creatures.[90] A single dose of BPA (10 µg/kg) in an in vivo investigation quickly raised plasma insulin levels, which in turn decreased glycaemia.152

According to reports, BPA may raise the risk of type 2 diabetes when combined with other EDCs as phthalates,[91,92] . According to a study by Jin et al. (2021), male mice's testosterone levels can drop, testicular inflammation can occur, and the blood-testis barrier can be disrupted by oral gavage of PS-MP (0.5 μm, 4 μm, and 10 μm) at a dose of 10 mg/mL for 28 days.[93].
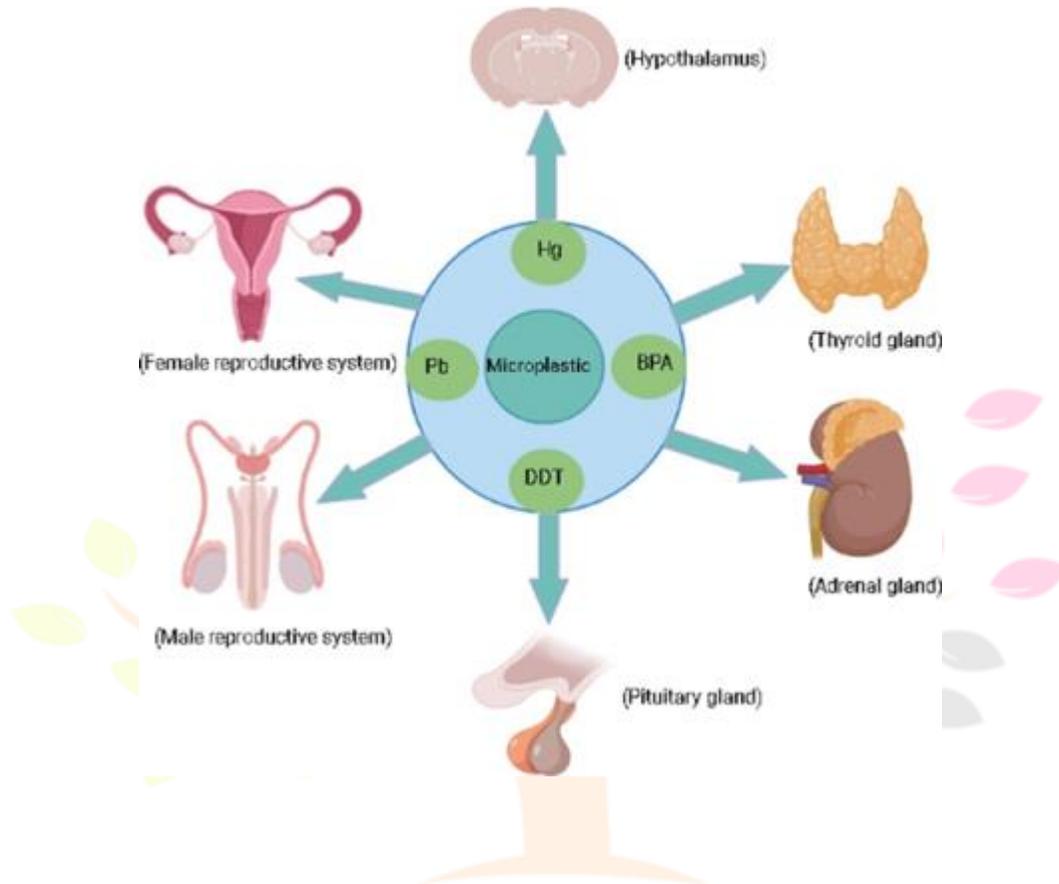

Fig No:-3 Effect of micro and nano particales on mascular system.

11.The nervous system –

Human central nervous systems are extremely vulnerable to environmental contaminants, particularly while they are developing in the womb.[94] Consequently, oxidative stress brought on by exposure to micro- and nanoplastics may harm cells and make people more susceptible to neurological conditions.[95] MNPs have the potential to be more neurotoxic than MPs because of their size.[96] MP exposure can alter glutamate, γ-aminobutyric acid, and acetylcholine, which can have an impact on the central nervous system.[97] Neurological problems can result from an excessive build up of acetylcholine caused by impaired AChE action.[97]

Using a 3D model of cortical spheroids, Hua et al. (2022) investigated the effects of PS-MPs (1 µm and 10 µm, 5, 50, and 100 µg/mL for 4–10 days and 4–30 days) on the human brain.101 Long-term exposure reduced cell viability, while short-term exposure increased Nestin, ATF4, PAX6, SOD2, and HOXB4 gene expression and cell proliferation. Additionally,

PS-MPs impacted brain tissue patterning and DNA damage gene expression.101 MP 1 µm is expected to be taken up and internalized by neural progenitor cells via mechanisms such endocytosis or phagocytosis.[98]

Fluorescent PS-MPs (5 µm and 20 µm) administered orally to male mice in an animal investigation resulted in decreased AchE activity, altered cholinergic neurotransmission efficiency, neurotoxicity, and oxidative stress (91, 148).Exposure to 91 MPs resulted in a decrease in phenylalanine, a precursor to neurotransmitters, and an increase in threonine, aspartate, and taurine levels in the blood. The possible effects of MNPs on the neurological system necessitate more research despite the lack of appropriate data.
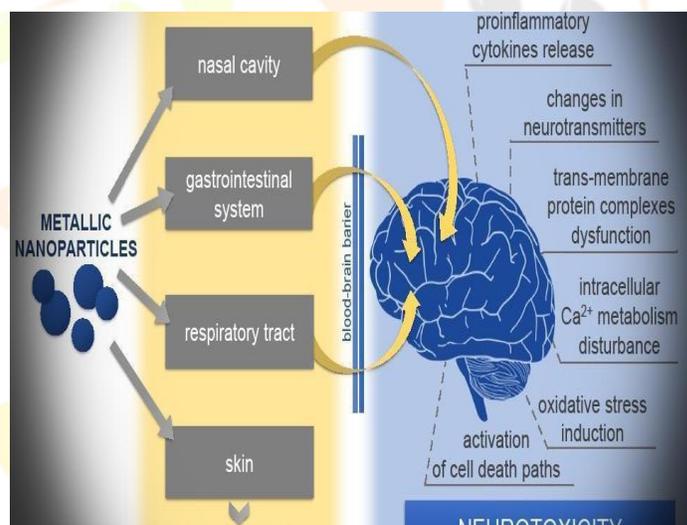

Fig No:-4 Effect of micro and nano particales on nervous system.

12.The immune system -

Depending on how they spread, exposure to toxins can cause either local or systemic immune responses. However, just environmental exposure may disrupt the immune system's normal function in cases of genetic predisposition, favoring autoimmune disorders or immunosuppression.[99] Immune cells that

have been exposed to MP strongly alter the transcription of enzyme levels that result in the release of cytokines.

Immune cells significantly alter several transcriptional levels, such as enzyme levels and cytokine production, in response to MP exposure. In order to examine the possible impacts of ingested MPs, such as 50–500 μm MP polymer representing tire wear and polyolefins at concentrations 823.5–1380.0 μg/cm2. Lehner et al. (2020) created an in vitro 3D intestinal model using human intestinal epithelial cell lines Caco-2 and HT29-MTX-E12, human dendritic cells, and blood monocyte-derived macrophages. [100]

The results indicated minor alterations in the barrier integrity and inflammatory cytokine levels (IL-8, TNFα, and IL-1β), although these changes were not statistically significant.[101] When exposed to 60 nm PS-NPs, human bronchial epithelial cells (BEAS-2B) and murine macrophages (RAW 264.7) demonstrated severe toxicity and autophagic cell death in a different in vitro investigation. Through the Akt/mTOR and AMPK pathways, NH2-PS induced autophagic flux and triggered the autophagic cell killing process.[102] According to Han et al. (2020), human immune cells exhibited an immunological response after being exposed to polyvinyl chloride (PVC) and acrylonitrile butadiene styrene (ABS) for four to five days.[103]

According to the study, ABS and PVC both increased the release of TNF-α and IL-6 while suppressing the release of histamine. The study hasn't looked into the possibility that prolonged exposure could result in a stronger immunological response.[104] It has been demonstrated that polypropylene MPs (PP-MPs, size ∼20 μm and 25–200 μm) can trigger the production of pro-inflammatory cytokines such IL-6, TNF alpha, and histamine in a size and concentration-dependent way, thereby inducing local immunological responses.[105]

In the mouse model, PE-MPs (10–150 μm) at high doses (600 μg/day) changed the intestinal microflora's composition and variety and triggered inflammatory responses by upregulating TLR4, AP-1, and IRF5 expression.83 Following MPs exposure, Th17 and Treg cells in CD4+ T cells were reduced, and the blood level of IL-1α was also markedly raised.83 Although there is some indication that MNPs have an impact on the immune system, the majority of research has only looked at the innate immune response. It is yet unclear how MNPs affect the adaptive immune response.
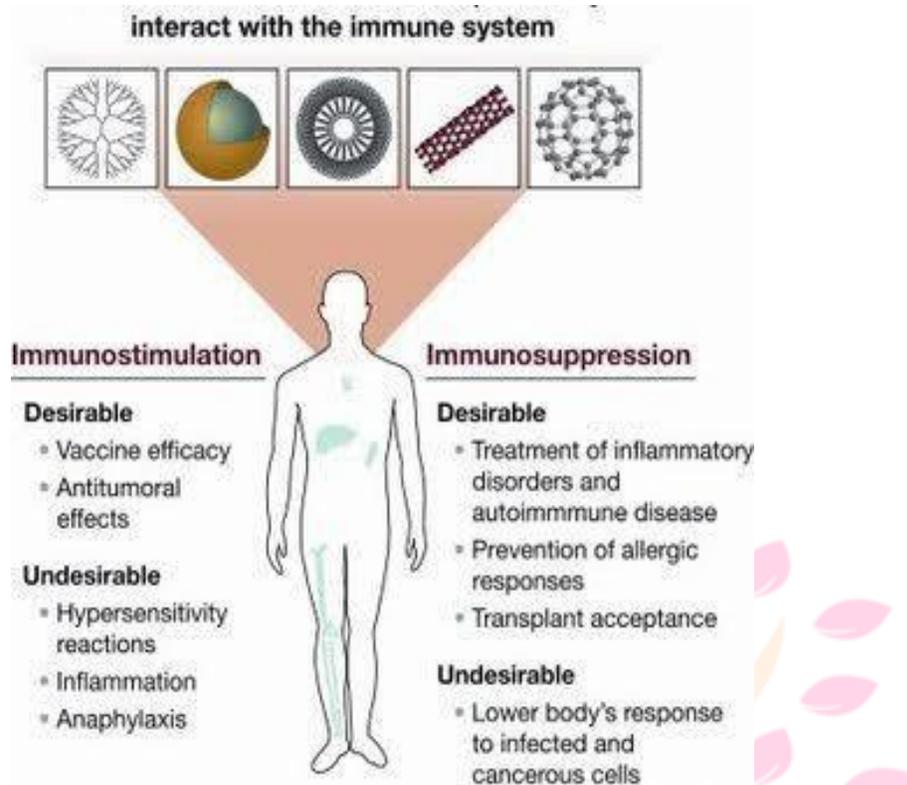
Fig No:-5 Effect of micro and nano particale on immune system.

14.Additional impacts MNPs -

It can have genotoxic, metabolic, biochemical, and carcinogenic effects in addition to impacts on particular organs. As was previously mentioned, MNPs can result in hepatic dysfunction and intestinal inflammation. It is unclear, therefore, if liver and intestinal inflammation and damage can result in the onset of serious illness. Mice given tiny MPs (1 μm in diameter, 10,000 μg/L in drinking water) in a recent study had higher fasting blood glucose and insulin levels, indicating a liver-gut metabolism interaction that resulted in insulin resistance and the development of diabetes.[106]

These findings point to the need for a larger cohort research to evaluate insulin resistance following exposure to MPs. Hs27 cell lines obtained from the foreskin were subjected to spherical PS-NPs (100 nm) in a different investigation.[107] The findings demonstrated that DNA damage was caused, which led to a rise in the development of nuclear buds and micronuclei.[108]

Conclusions-

The environment is full of MNPs, and people are regularly exposed to them from a variety of sources. There is mounting evidence that exposure to MPs and NPs may have negative impacts on several organ systems in humans. According to the literature compiled here, exposure to MNPs may result in oxidative stress, inflammation, immune system impairment, changes in cellular and energy metabolism, changes

in biochemical parameters, tissue degeneration, aberrant organ development and dysfunction, and even genotoxicity and carcinogenicity.

The fundamental mechanisms of MNPs' detrimental biological impacts on human health remain unclear, despite the fact that several animal and cell culture studies have demonstrated these effects. It is also necessary to look into whether prolonged exposure to MNPs is linked to an increased risk of developing a disease. The possible negative health effects of MNPs in humans and the associated processes require more observational research. Future research must also quantify the pathophysiology of MNPs and their effects on human health. This will fill in any research gaps and help to summarize what is currently known.

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