Environmental and Health Impacts of Pesticides and Fertilizers and Ways of Minimizing Them

Envisioning A Chemical-Safe World



# Environmental and health effects of fertilizer use

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## About

In December 2017, Resolution 4 of the 3rd Session of the United Nations Environment Assembly (UNEA 3) requested "the Executive Director to present a report on the environmental and health impacts of pesticides and fertilizers and ways of minimizing them, given the lack of data in that regard, in collaboration with the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and other relevant organizations by the fifth session of the United Nations Environment Assembly". In response to this request, UNEP published a *Synthesis Report on the Environmental and Health Impacts of Pesticides and Fertilizers and Ways to Minimize Them*[1] in February 2022 (United Nations Environment Programme [UNEP] 2022).

The overall goal of the synthesis report is to provide the information base to enable other advocacy actions to be taken by stakeholders to minimize the adverse impacts of pesticides and fertilizers. Specific objectives of the synthesis report are to:

- Update understanding of current pesticide and fertilizer use practices;
- Present major environmental and health effects of pesticides and fertilizers, during their life cycle, and identify key knowledge gaps;
- Review current management practices, legislation and policies aimed at reducing risks in the context of the global chemicals, environmental and health agenda;
- Identify opportunities to minimize environmental and health impacts, including proven and innovative approaches.

This chapter on "Environmental and health effects of fertilizer use" is the 9th in a series of 12 chapters that make up a comprehensive compilation of scientific information. The chapters were developed to both inform and further elaborate on the information provided in the synthesis report. Please note that the disclaimers and copyright from the synthesis report apply.

1 The Synthesis report is available at https://www.unep.org/resources/report/environmental-and-health-impacts-pesticides-and-fertilizers-and-ways-minimizing.

# Environmental and health effects of fertilizer use

9

## 9.1 Overview

Fertilizers are included among the sources of air, water and soil contamination and pollution.

There is an overall lack of adequate data on the environmental and health effects of fertilizers. Estimating these effects is hampered by, for example, the difficulty of quantifying the effects of diffuse sources of contaminants and pollutants.

Greenhouse gas (GHG) emissions comprise methane ($CH_4$) and nitrous oxide ($N_2O$) emissions from crop and livestock activities and carbon dioxide ($CO_2$) emissions from land use and land use change (Tubeillo *et al*. 2015). The crop and livestock sources of $CH_4$ are mainly enteric fermentation, rice cultivation and manure management, while those of $N_2O$ are manure, inorganic fertilizers, and emissions from crop residues (Tubeillo *et al*. 2013). [Chapter 9.2.1]

GHG emissions occur during the manufacture of fertilizers (Zhang, W. *et al*. 2013). Fertilizer production is also reported to contaminate the environment with trace elements, for example cadmium and arsenic during the production of phosphate fertilizer (Mirlean and Roisenberg 2006). [Chapter 9.2.1] The application of nitrogen fertilizers has been associated with $N_2O$ emissions (Albanito *et al*. 2017). These emissions are higher in the case of soils to which both inorganic and organic fertilizers have been applied (Charles *et al*. 2017). Efficient fertilizer use can help reduce such emissions (Thapa *et al*. 2016). [Chapter 9.2.1]

Ammonia is the main $PM_{2.5}$ precursor from agricultural activities, emitted from heavily fertilized fields and livestock waste, it combines with other precursors to form particulate matter (Li, X. *et al*. 2015; Bauer, Tsigaridis and Miller 2016; Wu, Y. et al. 2016). It can contribute to nutrient imbalances, and eutrophication (Organisation for Economic Co-operation and Development [OECD] 2013; Royal Society and Rand Europe 2018). Ammonia is also a key acidifying pollutant that contributes to soil acidification and acid rain (or acid deposition), which damages vegetation including crops and forests, causes further acidification of soils, lakes and rivers, and has adverse effects on biodiversity (FAO 2002; OECD 2013; Royal Society and Rand Europe 2018; United States Environmental Protection Agency [US EPA] 2020a). [Chapter 9.2.1]

Fertilizers can have a negative impact on soil's physical and chemical properties (e.g., soil acidification), as well as on soil organisms (e.g., microorganisms, invertebrates and other animals) and plants (FAO 2015; Wall, Nielsen and Six 2015; Humbert *et al*. 2016; Midolo *et al*. 2019). They may contain pathogens and contaminants such as toxic concentrations of trace elements, and endocrine disrupters. Applying contaminated fertilizers to soil could introduce these contaminants into the environment (Gionfa 2018; Rodríguez Eugenio, McLaughlin and Pennock 2018). Nitrogen fertilization can affect soil biodiversity, contributing to the decomposition of soil organic matter and crop residues (Li, X.G. *et al*. 2017) which may lead to degradation of soil quality (FAO *et al*. 2020). [Chapter 9.2.2]

Microplastics, which are among the contaminants present in fertilizers, are reported to affect soil's biophysical properties. The sources of microplastics in soils include sewage sludge (biosolids), controlled-release fertilizers, compost, and wastewater used for irrigation (Gionfa 2018; He et al. 2018; Weithmann *et al*. 2018; Guo, J. et al. 2020). [Chapter 9.2.2]

Pollution of the aquatic environment by nitrogen and phosphorus contributes to eutrophication and affects the dynamics of the aquatic food web. This pollution has adverse effects on coral reefs, algae, aquatic invertebrates, amphibians and fish (Egertson and Downing 2004; Díaz *et al*. 2012; Rabalais *et al*. 2014; Jeppesen *et al*. 2016; Zieritz *et al*. 2016; Garriga, Montori and Llorente 2017; Khan *et al*. 2018). [Chapter 9.2.3]

Fertilizes are best known for their contribution to food security. The systematic reviews carried out for this report identified a data gap. There were no reports found directly linking responsible and efficient fertilizer use with human health effects or quantifying the contribution of fertilizers to these effects. Where the use of fertilizers was suspected to be the cause of certain illnesses, studies have been inconclusive, or data are lacking. Due to the lack of adequate data, studies that are not specific to fertilizers are considered in this chapter (e.g., those on contaminants that can potentially be from fertilizers). In some of these studies contaminants that could come from fertilizers were associated with adverse environmental and health effects. [Chapter 9.3]

Any negative health effects that can be attributed to inorganic or organic fertilizers are likely to be due mainly to nutrient losses before application (e.g., ammonia [nitrogen] losses during storage of manure) or after application (e.g., leaching of nitrates from the soil to groundwater).

Adverse health effects can also be attributed to the contaminants present in fertilizers (e.g., potentially toxic trace elements) and pathogens (Udeigwe *et al*. 2015; Rodríguez Eugenio, McLaughlin and Pennock 2018). [Chapter 9.3] Direct effects of fertilizers on human health can occur through contact, inhalation (e.g., exposure to ammonia in fertilizer factories or to manure in livestock production systems, exposure to particulate matter [$PM_{2.5}$], exposure to dusts from manure) (US EPA 2016) or explosions during transportation or storage (US EPA 2015; Laboureur *et al*. 2016; Guglielmi 2020). [Chapter 9.3.1] Indirect effects can occur through ingestion. For example, toxic trace elements in fertilizers can contaminate drinking water (Shukla and Saxena 2018; Jin *et al*. 2019) or enter the food web through their application to the soil, uptake by plants, and ingestion of contaminated food by humans or of contaminated feed by animals (Gall, Boyd and Rajakaruna 2015; Wiggenhause *et al*. 2019). [Chapter 9.3.2]

The links between fertilizer use and both environmental and health effects can be complex. Some of the effects could be gender or age specific. For example, dietary exposure to non-lethal toxic doses of nitrates has been associated with methemoglobinemia in infants, pregnancy loss, birth defects and infant mortality, among others (Gupta, Gupta and Gupta 2017). Manure can be contaminated by environmental oestrogen, and some studies have suggested a relationship between environmental oestrogen and breast cancer (Adeel *et al*. 2017). [Chapter 9.3.2]

Links between fertilizers and human health remain largely unknown. A systematic review of epidemiological studies showed that the outcomes with the largest number of studies were cancers for inorganic fertilizers and infections for organic fertilizers (Box 9.3-2). An appraisal of published systematic reviews and/or meta-analyses of potential associations between exposure to cadmium (small amounts of which are found in phosphorus fertilizers) with human health-related outcomes included kidney disease, cancers, endocrine disorders and cardiovascular disease. Some reported findings were significant and others were not significant or inconclusive. Fertilizers were mentioned in some publications, but no study assessed fertilizer use as a source of cadmium exposure (Box 9.3-2). [Chapter 9.3.2]

Antimicrobial resistance (AMR) in humans has been associated with the presence of manure and contact with livestock (Huijbers *et al*. 2014; Huijbers *et al*. 2015; Muloi *et al*. 2019). Antimicrobial resistant bacteria, which have been detected in manure and sewage sludge (biosolids), end up in water and soil (Huijbers *et al*. 2015). [Chapter 9.3.4]

The environmental effects of fertilizer use can have an adverse impact on human health and nutrition. For example, degradation of the terrestrial and aquatic environments affects the sustainability of food production.

Studies have suggested that changes in human diet can affect the environment and health. For example, it has been proposed that increased adoption of plant-based diets would have positive effects on the environment and health. Greater intake of more plant-based foods would likely reduce the amounts of fertilizers used (Marlow *et al*. 2009; Sabaté and Soret 2014). [Chapter 9.4]

While there are indications that fertilizer use (especially when it is excessive, inefficient or irresponsible) may have adverse effects on the environment and health, some of the potential impacts of these effects remain unknown. [Chapter 9.5]

## 9.2 Adverse environmental effects of fertilizer use

Fertilizer use is related to air pollution, as well as to the contamination of terrestrial and aquatic environments. Air pollution related to fertilizer use includes the contribution of their use to anthropogenic greenhouse gas (GHG) emissions, ammonia emissions and particulate matter ($PM_{2.5}$) (Chapter 9.2.1). Contaminants from fertilizers in the terrestrial and aquatic environments include nutrients (e.g., from excessive application of fertilizers), metals (e.g., cadmium), endocrine disrupters and antibiotics (Chapters 9.2.2 and 9.2.3).

Excess nutrients from applied fertilizers may be transported to nearby water bodies (e.g., streams and lakes) by means of rainwater, erosion, tile drains and other drainage systems, irrigation channels and seepage, and on to underground water supplies through leaching. Contaminants in fertilizers (e.g., trace elements and pathogens in biosolids) can also pollute soils and water bodies.

### 9.2.1 Air

#### The contribution of fertilizers to greenhouse gas emissions

GHG emissions from crop and livestock activities, forestry and land use mainly comprise methane ($CH_4$) and nitrous oxide ($N_2O$) emissions from crop and livestock activities and carbon dioxide ($CO_2$) emissions from land use and land use change (Tubeillo *et al*. 2015).

In 2017 global emissions from crop and livestock activities and agricultural land use (largely deforestation and peatland degradation) were about 20 per cent of carbon dioxide equivalent ($CO_2$eq) emissions from all human activities, with crop and livestock activities contributing about 11 per cent (FAO 2020) (Figure 9.2-1). However, the contribution of crop and livestock activities and agricultural land use to global emissions has been declining, for example from 29 per cent in 1990

Figure 9.2-1 **Agriculture's shares of regional and global carbon dioxide equivalent ($CO_2$eq) emissions in 2017.** FAO (2020).

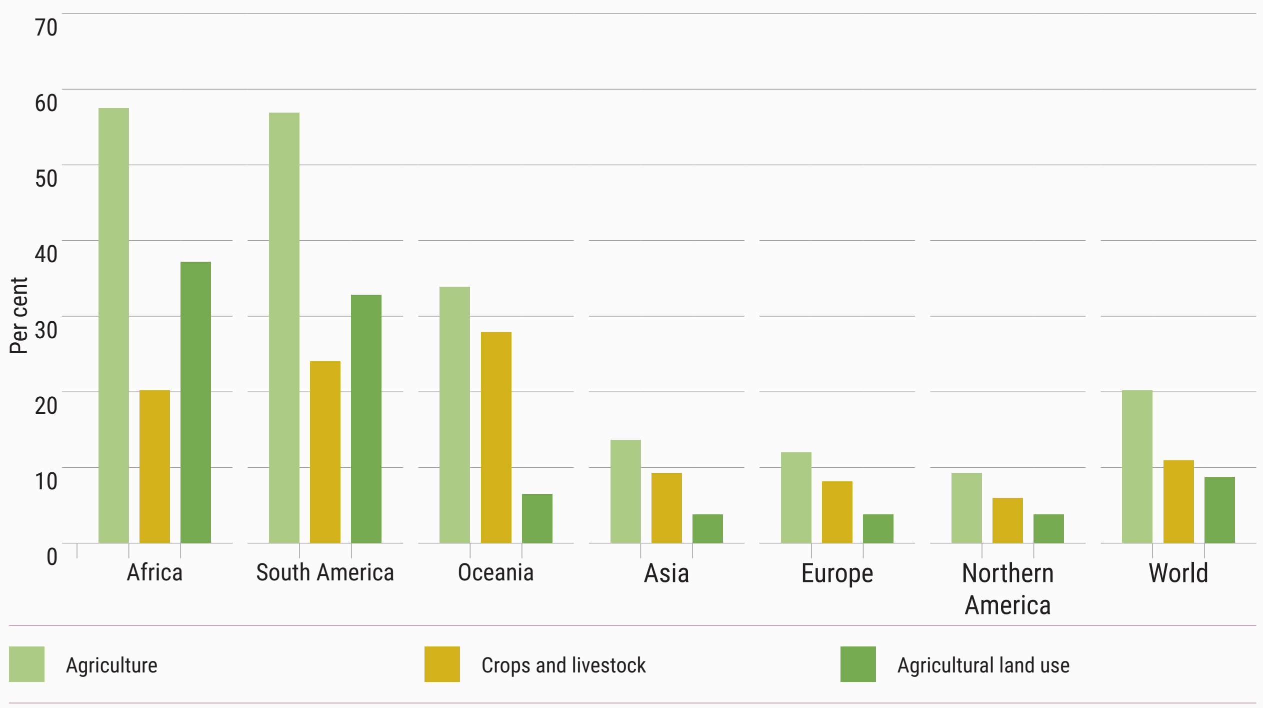
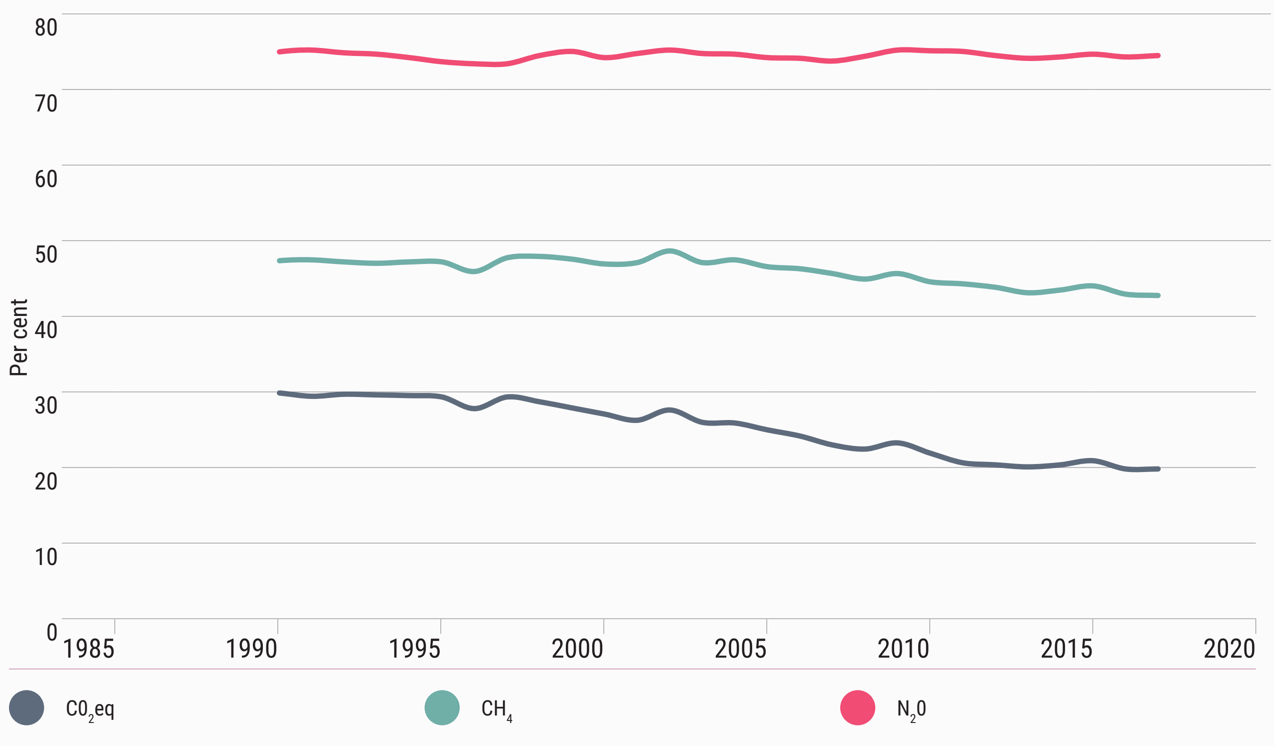
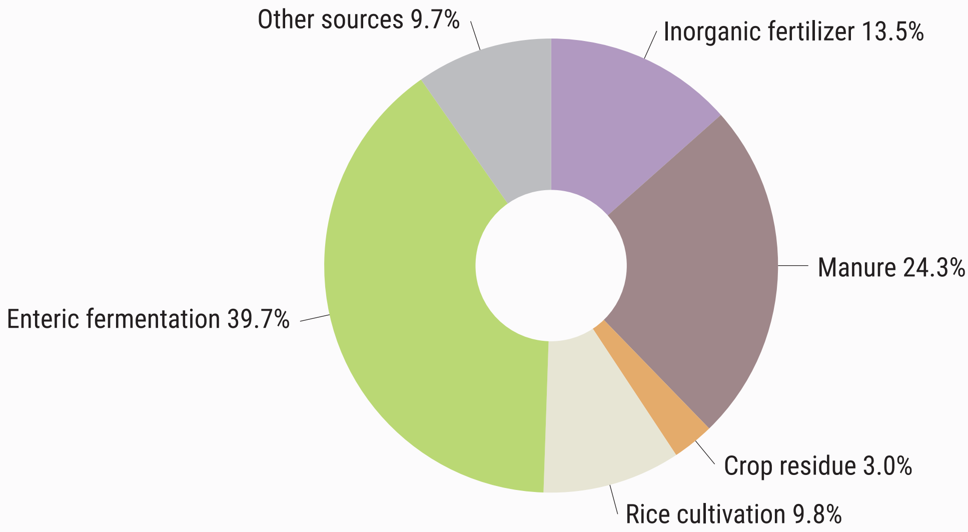



Figure 9.2-2 **Agriculture's shares of methane ($CH_4$), nitrous oxide ($N_2O$) and carbon dioxide equivalent ($CO_2$eq) emissions, 1990-2017.** FAO (2020).




to 20 per cent in 2017 (Figure 9.2-2). The decline is partially due to a decrease in agricultural land use emissions (from 6.9 to 5.0 gigatons [Gt] $CO_2$eq between 1990 and 2017). It is likely that the contribution of crop and livestock activities did not change much during this period.

**Figure 9.2-3 Contribution of different sources of agricultural emissions from crop and livestock production (per cent).** Tubiello *et al*. (2013).




Crop and livestock activities, forestry and land use accounted for 47 per cent and 74 per cent of total $CH_4$ and $N_2O$ emissions, respectively, in 1990 and 42 per cent and 75 per cent of these emissions in 2017; $CH_4$ and $N_2O$ emissions were largely from crop and livestock activities within the farm gate (FAO 2020). A 2021 study by UNEP also reported that approximately 40 per cent of $CH_4$ emission come from Crop and livestock activities (UNEP and Climate and Clean Air Coalition 2021)

Crop and livestock sources of $CH_4$ are mainly enteric fermentation, rice cultivation and manure management, while those of $N_2O$ are manure, inorganic fertilizers, and emissions from crop residues (Tubeillo *et al*. 2013). Livestock production is a key contributor to agricultural emissions (Figure 9.2-3).

Studies have reported differences in estimates of GHG emissions among the various tools used to produce these estimates. For example, GHG emissions estimated for 2006 in the Republic of Indonesia were close to 500 million metric tons (Mt) and 1,400 Mt of carbon dioxide equivalent per year ($CO_2$eq $yr^{-1}$), according to the National Reducing Emissions from Deforestation and Degradation Agency (BP REDD+) 2015 and the Indonesian National Carbon Accounting System (INCAS) 2015 inventories, respectively (Austin *et al*. 2018).

The refinement of the 2006 Intergovernmental Panel on Climate Change (IPCC) Guidelines on National Greenhouse inventories, published in 2019, takes into consideration the climate and sources of nitrogen in estimating emissions, for example by including separate default values for organic nitrogen inputs and inorganic nitrogen fertilizers in wet climates instead of a single default value for both these nitrogen sources (Hergoualc'h et al. 2019). This suggests that GHG emissions could be over- or underestimated in some regions.

GHG emissions also occur during the manufacture of fertilizers. For every ton of nitrogen fertilizer produced and used in China, GHG emissions have been estimated to be 5.1, 0.9 and 5.2 tons of $CO_2$eq, respectively, during ammonia synthesis, conversion of ammonia to fertilizer products and application of fertilizer in fields (Zhang, W. *et al*. 2013). In addition, fertilizer production has been reported to contaminate the environment with trace elements, for example cadmium and arsenic during production of phosphate fertilizer in Brazil (Mirlean and Roisenberg 2006).

The application of nitrogen fertilizers has been associated with $N_2O$ emissions (Albanito *et al*. 2017). These emissions are higher in the case of soils to which both inorganic and organic fertilizers have been applied rather than organic fertilizer alone (Charles *et al*. 2017). Between 2007 and 2016, global $N_2O$ emissions from natural and anthropogenic sources were estimated to be about 17.0 MT of nitrogen per year, of which anthropogenic sources contributed about 43 per cent (7.3 million tons of nitrogen per year), according to a study by Tian *et al*. (2020). The authors reported that anthropogenic emissions from nitrogen additions to land under crops (including manure left on pastures) contributed about 48 per cent (3.5 MT of nitrogen/year) of anthropogenic emissions while manure management contributed about 3 per cent (0.2 MT of nitrogen/year).

Efficient fertilizer use can help reduce these emissions. Based on a meta-analysis carried out to evaluate the effectiveness of enhanced efficiency fertilizers in reducing $N_2O$ emissions in cereal production systems, Thapa *et al*. (2016) reported that nitrification inhibitors, double inhibitors (DIs: urease plus nitrification inhibitors) and controlled-release nitrogen fertilizers consistently reduced $N_2O$ emissions compared with conventional nitrogen fertilizers across soil and management conditions. However, the effectiveness of nitrification and urease inhibitors was reported to depend on environmental factors and management practices (Abalos *et al*. 2014). In addition, $N_2O$ fluxes were influenced more by the amount of nitrogen added than the nitrogen source (fertilizer, legume biomass or animal manure), but in coarse soils $N_2O$ emissions from manure tended to be higher than those from inorganic nitrogen fertilizers (Han, Walter and Drinkwater 2017).

GHG emissions are the most important driver of human-induced climate change (Jantke *et al*. 2020). In January 2020, 11,000 scientists from throughout the world signed a letter (Ripple *et al*. 2019) in which they highlighted the urgent need to increase action to reduce GHG emissions, which are rising rapidly with increasingly damaging effects on the Earth's climate.

The Intergovernmental Panel on Climate Change (IPCC) (2018) has presented four illustrative model pathways for achieving the net emission reductions needed to limit global warming to 1.5°C above pre-industrial levels, with no or limited overshoot. One of these pathways (designated P2), which has a "broad focus on sustainability", includes global reductions of $CH_4$ emissions from agriculture in 2030 by 48 per cent relative to 2010 and of $N_2O$ emissions from agriculture by 26 per cent in the same year, also relative to 2010. The other three pathways include smaller reductions of these agricultural emissions, or the actions they describe are projected to be able to achieve the overall net emission reductions required even if there are slight increases in these $CH_4$ and $N_2O$ emissions (IPCC 2018).

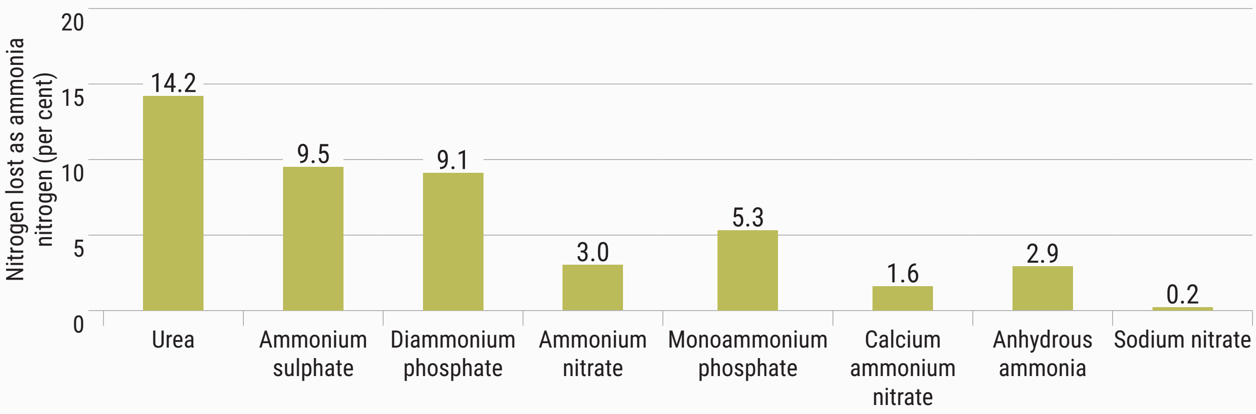
### Ammonia emissions and $PM_{2.5}$

Ammonia is the main $PM_{2.5}$ (fine particles with aerodynamic diameters ≤2.5 μm) precursor from agricultural activities (Bauer, Tsigaridis and Miller 2016; Wu, Y. *et al*. 2016). The gas is emitted from heavily fertilized fields and livestock waste. It then combines with other precursors (mainly nitrogen oxides and sulphates) to form particulate matter. Other precursor gases include sulphur dioxide, nitrogen oxides and volatile organic components (VOCs) (Li, X. *et al*. 2015).

Particulate matter (PM) refers to solid particles and liquid droplets in the air. These particles can be from direct emissions (primary particles) or be formed from precursors (secondary particles). Primary particles are emitted directly from anthropogenic sources (e.g., industry, power plants, vehicles) or natural ones (e.g., outdoor biomass burning, dust storms). In the European Union (EU) agriculture was estimated to contribute 4 per cent of $PM_{2.5}$ (European Environment Agency [EEA] 2017). In Europe, parts of the United States and China about 50 per cent of precursors from anthropogenic sources have been estimated to be from agriculture (Bauer, Tsigaridis and Miller 2016). $PM_{2.5}$ associated with agriculture has largely been attributed to the use of nitrogen fertilizers and animal husbandry.

According to a EU report (Amann 2017), application of inorganic fertilizer contributed approximately 20 per cent of total ammonia emissions in the EU-28 region and manure management about 75 per cent. In the United

**Figure 9.2-4** **Amount of nitrogen lost as ammonia, as a percentage of nitrogen applied, for major inorganic fertilizers.** Hergoualc'h *et al*. (2019).




States, about 80 per cent of ammonia emissions are from agriculture, of which 58 per cent from livestock manure, according to a US EPA report cited by Rotz (2020).

Based on data from two meta-analyses and other studies, the amount of nitrogen from fertilizers lost as ammonia, as a proportion of the total nitrogen applied, was estimated to be about 14 per cent for urea and ranged from 0.2 per cent to 9.5 per cent for other fertilizers (Figure 9.2-4) (Hergoualc'h *et al*. 2019). Increased use of nitrogen fertilizers has contributed to an increase in ammonia emissions, with South Asia accounting for more than 50 per cent of total global emissions (Xu, R. *et al*. 2019).

$PM_{2.5}$ among others causes reduced visibility in the air and when deposited on the ground or water. It can cause acidification, alter nutrient balance and affect ecosystem diversity (US EPA 2020b; US EPA 2020c; WHO 2018).

For the adverse health effects of $PM_{2.5}$, see Chapter 9.3.3.

### Ammonia emissions and pollution

Apart from contributing to fine particulate matter in the atmosphere, ammonia is a key acidifying pollutant, for example contributing about 30 per cent of total emissions of acidifying pollutants in OECD countries (OECD 2013). Ammonia can contribute to nutrient imbalances, soil acidification and eutrophication when deposited in an ecosystem (OECD 2013; Royal Society and Rand Europe 2018). It also contributes to acid rain (or acid deposition), which damages vegetation (including crops and forests), causes acidification of soils, lakes and rivers, and has adverse effects on biodiversity (FAO 2002; US EPA 2020a).

## 9.2.2 The terrestrial environment

Fertilizers can have adverse environmental effects. For example, a negative impact on soil's physical and chemical properties, soil organisms (e.g., microorganisms, invertebrates and animals) and plants. For the positive environmental effects of fertilizers see Chapter 10.3.4.

Fertilizers may contain contaminants such as toxic concentrations of trace elements, pathogens and endocrine disrupters (this list is not exhaustive) (Chapter 9.3.2). For example, municipal biosolids have been found to be a sink for many pharmaceuticals and the chemicals in personal care products (Rodríguez Eugenio, McLaughlin and Pennock 2018). Applying contaminated fertilizers to soil may introduce these contaminants into the environment, possibly causing harm to beneficial organisms (Rodríguez Eugenio, McLaughlin and Pennock 2018).

Sources of microplastics in soils include sewage sludge (He et al. 2018; Weithmann *et al*. 2018; Guo, J. et al. 2020), controlled-release fertilizers, compost, and wastewater used for irrigation (Gionfa 2018). In addition, plastics used in intensive agriculture (e.g., in greenhouses or as mulching material) can fragment to microplastics (Steinmetz *et al*. 2016).

### Fertilizers and soil quality/properties

Excessive or inefficient use of fertilizers can contribute to soil acidification. Human-induced acidification of agricultural soils is primarily associated with product removal (e.g., the removal of all harvestable materials) or increases in nitrogen and sulphur inputs (e.g., through excessive use of fertilizers) (FAO 2015). For example, in China the acidification of agricultural soils is largely associated more with nitrogen fertilization than with acid deposition (Guo, J. *et al*. 2010). A meta-analysis of 106 studies estimated that nitrogen addition reduced soil pH by 0.26 on average globally (Tain and Niu 2015). Moreover, acidification may contribute to further soil pollution through the mobilization of toxic trace elements (Rodríguez Eugenio, McLaughlin and Pennock 2018).

Nitrogen fertilization can affect soil biodiversity, contributing to the decomposition of soil organic matter and crop residues (Li, X.G. *et al*. 2017) and may lead to degradation of soil quality (FAO *et al*. 2020).

Sewage sludge may contain toxic trace elements (Mortvedt 1996). Deposition and accumulation of these elements in the soil can influence the relative availability of nutrients to plants. For example, increased concentrations of zinc in the soil can lower the accumulation of lead in wheat grain (Nan *et al*. 2002).

Other contaminants which can be found in fertilizer, and which are increasingly considered important, include endocrine disruptors, organic contaminants and microplastics (also see Chapter 9.3.2). Not much is known about the effects of these contaminants on soil properties. However, microplastics have been reported to affect soil's biophysical properties (de Souza Machado *et al*. 2019).

### Soil microorganisms

Beneficial microorganisms in agriculture include microorganisms that break down dead organic matter, mycorrhizal fungi that contribute to improved retention of nutrients and water in the soil and facilitate root penetration leading to improved nutrient use by plants, and nitrogen-fixing rhizobia (FAO *et al*. 2020).

On the other hand, some soil-borne microorganisms can cause diseases in humans (Rodríguez Eugenio, McLaughlin and Pennock 2018). See Chapter 9.2 on the adverse human health effects of fertilizer use for additional information.

Excess fertilizer applications typically reduce the abundance of mutualistic soil biota, which enables an increase in pathogenic microbiota and pests (Wall, Nielsen and Six 2015).

The application of nitrogen fertilizer has been associated with reduced microbial biomass, and excessive amounts of nitrogen applied over a long period have been associated with declines in the abundance of microbes and fungi (Treseder 2008). The relative abundance of different types of microorganisms within groups can also be affected. For example, in a study by Dai *et al*. (2018) nitrogen fertilizer reduced the abundance of Acidobacteria and increased the relative abundance of Proteobacteria and Actinobacteria. In addition, Liu, P. *et al*. (2017) demonstrated that changes in bacterial communities can differ with type of fertilizer. A study by de Graaff et al. (2019) reported that the effects of nitrogen fertilizer on different groups varied. For example, the authors found that inorganic nitrogen fertilizer can have negative and positive impacts on the diversity of arbuscular mycorrhizal fungi and bacteria, respectively.

Tillage, sometimes used to incorporate fertilizers into the soil, can have adverse effects on soil microorganisms. This practice can contribute to increased mineralization of soil organic matter due to greater exposure to microbial decomposers and optimal moisture and temperature (Dhaliwal et al. 2019).

A number of studies have demonstrated or reported that contaminants, that is, potentially toxic trace elements (Chu 2018; Mishra, Singh and Arora 2017), endocrine disrupters and pharmaceuticals (Frková *et al*. 2020) potentially present in fertilizers can interfere with microbial biomass and diversity (Rodríguez Eugenio, McLaughlin and Pennock 2018). However, although they may be present in fertilizers, fertilizers are not the only source of these contaminants in soil (Shi *et al*. 2019). For example, toxic concentrations of trace elements in soil can result in adverse effects on soil microbial diversity and activity (Xie *et al*. 2016; Srivastava et al. 2017); however, there are indications that organic inputs, particularly those from waste streams, probably pose greater risks with respect to soil pollution than inorganic fertilizers (Lugon-Moulin *et al*. 2006; Pizzol, Smart and Thomsen 2014). For examples of contaminants in fertilizers, see Chapter 8, Table 8.4.1.

In experiments by Kuzikova *et al*. (2019) nonylphenol, an endocrine disrupter which has been reported in sewage sludge, for example by Mao *et al*. (2012), was associated with reduced diversity of microbial species when added to the soil. Pharmaceuticals, which can affect the diversity of the soil community (Pino-Otín *et al*. 2017), have been detected in manure (Cycoń, Mrozik and Piotrowska-Seget 2019). Despite an absence of studies on the adverse effects of fertilizers on soil microorganisms, the studies presented here suggest that fertilizers, especially untreated organic fertilizers, have the potential to adversely affect soil microorganisms.

### Soil invertebrates

Beneficial soil invertebrates in agriculture include invertebrates that accelerate litter decomposition and nutrient cycling, improve soil aggregation and porosity, and aid in the control of plant pathogens (FAO *et al*. 2020). These invertebrates can also regulate the activity or composition of soil microbial communities.

The global decline in insect populations has been partially attributed to the use of pesticides and inorganic fertilizers (Sánchez-Bayo and Wyckhuys 2019).

Fertilizers have also been reported to have positive and negative effects on invertebrate biodiversity and populations for some types of soil invertebrates. For example, increased soil fertility, or application of nitrogen, has been associated with increased the populations of soil mites (Cole, Buckland and Bardgett 2005), increased growth of nematodes (Liu, T. *et al*. 2015), increased earthworm populations (Edwards and Lofty 1982) and increased abundance of dipterans and beetles (Lemansk and Scheu 2015). However, Minor and Norton (2004) reported that predatory mites (Mesostigmatid) benefited from the application of biosolids, while saprophagous and mycophagous mites (Oribatida) were adversely affected. Adverse effects of the use of excessive fertilizers have also been reported in the case of other invertebrates. Nitrogen application resulted in reduced species richness for nematodes (Liu, T. *et al*. 2016) and the use of excessive amounts of sludge produced adverse effects in earthworms (Edwards and Lofty 1982).

The negative effects of nitrogen inputs on soil organisms could be partly due to acidification. In a study on nitrogen inputs by Chen, Lan and Bai (2015), reduced bacterial, fungal and nematode biomass was mainly associated with soil acidification. Earthworms have also been reported to be affected negatively by soil acidity (Solomou *et al*. 2013).

High concentrations of toxic trace elements in soil can contribute to reduced earthworm density and diversity (Tovar-Sánchez *et al*. 2018; Wang, K. *et al*. 2018), although it is likely that these effects rarely occur as a result of normal fertilization practices.

There are indications that endocrine disrupters can have adverse effects on soil invertebrates. For example, in a study on the effects of bisphenol A (BPA) on earthworms, the authors concluded that observed changes in gene expression could have such effects on earthworm populations (Novo *et al*. 2018).

Studies have associated microplastics in soil with the health of soil organisms (Helmberger, Tiemann and Grieshop 2019). For example, an increase in concentrations of microplastics in litter was associated with reduced growth of earthworms

(Lwanga *et al*. 2016). The review by Helmberger, Tiemann and Grieshop (2019) demonstrates that this a new and growing area of research and that much is still unknown.

Some studies have compared the effects of inorganic and organic fertilizers on soil invertebrates. Organic fertilizers increased the total abundance of soil fauna, whereas low level inorganic fertilizers caused increases in four- and nine-year-old poplar stands but not in 20 year-old stands (Wang, S. 2016).

### Vertebral Animals

Vertebral animal poisoning from drinking water contaminated with cyanobacteria has been reported (Svirčev *et al*. 2019). Effects of oral exposure of animals to cyanotoxins include lesions in the small intestine and hepatic system and damage to the DNA in intestines (Kubickova *et al*. 2019).

Contaminants in fertilizer can enter the food chain and can have adverse effects due to , the intake of contaminated feed.

Perchlorate, an endocrine disruptor of concern to human health (Chapter 9.3.2), has been shown to interfere with iodine uptake by the thyroid gland in amphibians, leading to retardation of metamorphosis and reduced growth rates (Miyata and Ose 2012). The thyroid effect of the chemical has also been reported in fish (Matthiessen, Wheeler and Weltje 2018)

Fluoride, an impurity in phosphatic fertilizer, was generally found to accumulate in the upper soil profile following long-term application of superphosphate fertilizer in pastures (McLaughlin *et al*. 2001). Although the risk of fluorosis in grazing animals was reported to be low, continued applications could increase this risk. In New Zealand a model estimated that ingestion of soil during grazing could cause chronic fluorosis in sheep and cattle during the winter (Cronin *et al*. 2000). Actual cases of fluorosis have been reported. Chronic fluoride toxicosis (with up to 15 per cent of a herd going lame) was reported in an extensive beef cattle herd in northern Australia, where large quantities of fertilizer-grade phosphate were fed to animals as part of a mineral supplement (Jubb et al. 1993).

### Plants

Studies on the effects of fertilizer use on plant biodiversity have mostly focused on grasslands and natural plant communities. Several studies indicate that the use of inorganic nitrogen fertilizer can influence plant biodiversity. A systematic review concluded that plant biodiversity in mountain grasslands is reduced by nitrogen addition (Humbert *et al*. 2016). A meta-analysis of studies assessing the effects of nitrogen addition on terrestrial natural and semi-natural plant communities by Midolo *et al*. (2019) concluded that applying nitrogen fertilizers reduced plant species richness and abundance. A study on the impacts of 120 years of inorganic fertilizer and manure use in grassland by Kidd *et al*. (2017) showed that there could be differences in plant species richness and abundance depending on nutrient sources. For example, in the study yearly application of manure and inorganic nitrogen fertilizer were both associated with fewer plant species than the control (no inorganic fertilizer or manure).

Plants exposed to toxic trace elements in the soil show reduced growth and reduced yields (Srivastava *et al*. 2017). Exposure to toxic trace elements can also contribute to reduced produce quality. For example, in a wheat study it was associated with decreased protein content in plant parts and increased concentrations of these elements in grain (Athar and Ahmad 2002). Exposure to excessive amounts of trace elements can influence plant populations. For example, plant diversity and population sizes were affected negatively in grassland polluted by trace elements (Hernández and Pastor 2008).

The application of compost made from plant material can result in increased crop disease, especially if fertilizers are not well composted (University of Nebaska-Lincoln 2020). Crop residues are potential sources of disease spores (Pizolotto *et al*. 2019) and insects for the next crop. Hence, if such residues are partially composted and applied to the soil as fertilizer, disease infections and insect pest infestations can affect the next crops.

Endocrine disrupters have been shown to affect biological nitrogen fixation in legume plants by interfering with communication between plants and soil bacteria (Fox *et al*. 2001) and to reduce leaf chlorophyll content and plant growth (Kim, Kwak and An 2019).

Plants have been reported to take up antibiotics present in manure (Kumar 2005) and to take up AMR genes from antimicrobial-spiked manure (i.e., dairy manure fortified with individual antimicrobial compounds belonging to the sulfonamide and tetracycline classes; Mullen *et al*. 2019), indicating that such contaminants can pose a risk to humans and animals through the food chain.. Manure application could enhance the prevalence and stimulate the propagation of antibiotic resistance in agricultural soils (Pérez-Valera *et al*. 2019; Wu, N. *et al*. 2020). However, the risk may not increase with increased use of manure (Peng *et al*. 2018). For example, in a study by Liu, P. *et al*. (2017) the abundance of soil antimicrobial resistance genes increased after manure fertilization but gradually returned to normal.

### The terrestrial ecosystem and food webs

An increase in mineral nitrogen and phosphorus from polluting sources (e.g., atmospheric deposition and run-off water), and in agroecosystems due to excessive use of mineral fertilizers, have consequences for plant growth and microbial decomposition that can cascade to soil food webs. This causes nutrient imbalances (typically carbon:nitrogen [C:N], carbon:phosphorus [C:P] or nitrogen:phosphorus [N:P]) between consumers and their resources, strongly constraining nutrient cycling and limiting consumer reproduction and growth (Maaroufi and De Long 2020). The effects of nutrient imbalance on soil organisms and food webs can be direct (in the case of organisms such as bacteria and fungi that take up nutrients directly from the soil solution) or indirect, via alterations of the nutritional content of primary producers and their litter inputs, with cascading consequences for both green and brown food webs.

Interactions exist between soil invertebrates and soil microorganisms Soil invertebrates prey on soil microorganisms. They also compete with them for resources (Scheu, Ruess and Bonkowski 2005). In addition, they are involved in the mixing and breakdown of plant residue inputs to soil (Chamberlain *et al*. 2006) and therefore make organic matter accessible to microorganisms (Bray and Wickings 2019). It is likely that some practices affect both soil invertebrates and soil microorganisms, but not necessarily in the same manner. It is also likely that, as with soil microorganisms, the effects of inorganic and organic fertilizers on soil invertebrates can be positive.

### 9.2.3 The aquatic environment

Nutrient pollution in the aquatic environment contributes to eutrophication and affects the dynamics of the aquatic food web. For example, it has adverse effects on coral reefs, algae, aquatic invertebrates, amphibians and fish. It also has an impact on water quality and the value of water bodies and waterfront properties (Chapter 10.2.2) and can affect human health (Chapter 9.3.2).

Protecting, restoring and monitoring water quality can have positive effects on both terrestrial and marine ecosystem health, as well as, for example, reducing the costs of drinking water treatment. According to the United Nations summary progress update for Sustainable Development Goal (SDG) 6 ("Ensure availability and sustainable management of water and sanitation for all"), there are currently insufficient country data to estimate global status or trends with regard to meeting this SDG. Of the 48 countries that reported in both 2017 and 2020, 21 are on track to improve water quality; urgent action is therefore needed globally to improve monitoring systems for surface water and groundwater and to define water quality standards (UN-Water 2021).

Some data exist on regional and national clean-up initiatives. In North America, harmful algal blooms and hypoxia in Lake Erie (Barbiero *et al*. 2018; Sgro and Revie 2018; US EPA 2020d) and Chesapeake Bay (Chesapeake Bay Foundation 2019; US EPA 2020e) have threatened ecosystem and human health for a number of years.

This problem is being addressed through cooperation between national, state and other bodies, and progress is reported (Governments of Canada and Ontario 2018; US EPA 2020f; Chesapeake Bay Foundation 2021). For farmers, proposed measures to reduce agricultural inputs of nutrients to both Lake Erie and Chesapeake Bay include following the 4Rs of nutrient stewardship (right time, right place, right rate, and right source), conservation tillage, and growing cover crops (US EPA 2018; Chesapeake Bay Program 2019).

### Eutrophication

This section discusses eutrophication at the global level, with its causes and the process involved and elaborates on the effects of aquatic pollution on coral reefs, algae, aquatic invertebrates, amphibians and fish. It should be noted that no relevant reports on ecotoxicological field studies were found.

Since the 1960s the number of water bodies in which hypoxia associated with eutrophication has been reported has been increasing (Díaz *et al*. 2012; Rabalais *et al*. 2014; Breitburg, Gregoire and Isensee 2018; Breitburg *et al*. 2018). There were about 10 documented sites in 1960 (Figure 9.2-5); the number increased to 762 by 2013, with 479 experiencing hypoxia, 55 having once experienced hypoxia but improving, and 228 experiencing other symptoms of eutrophication including algal blooms, species loss, and impacts to coral reef assemblages (World Resources Institute 2013).

Eutrophication is triggered by a change in the quantity, relative proportions or chemical forms of nitrogen and phosphorus entering aquatic systems. It is influenced by environmental factors such as temperature and light. Sources of nutrients include agriculture, human sewage, urban run-off, industrial effluent, and fossil fuel combustion (Selman *et al*. 2008; Díaz *et al*. 2012; Le Moal *et al*. 2019).

Attempts have been made to estimate contributions from various sources. Between 1900 and 2000 global nutrient delivery to streams increased from 34 to 64 Mt nitrogen and from 5 to 9 Mt phosphorus per year (Beusen *et al*. 2016). The contribution of agriculture to nutrients in surface water increased by about five times for nitrogen (6 to 33 Mt N/year, which is 19 per cent to 51 per cent of the total) and slightly more than doubled for phosphorus (2 to 5 Mt P/year, which is 35 per cent to 56 per cent of the total). Apart from food production, another key contributor could be non-food items (clothing, goods for shelter, services and other manufactured products), which were estimated to account for 35 per cent of global marine eutrophication and 38 per cent of the global freshwater eutrophication in 2011 (Hamilton *et al*. 2018).

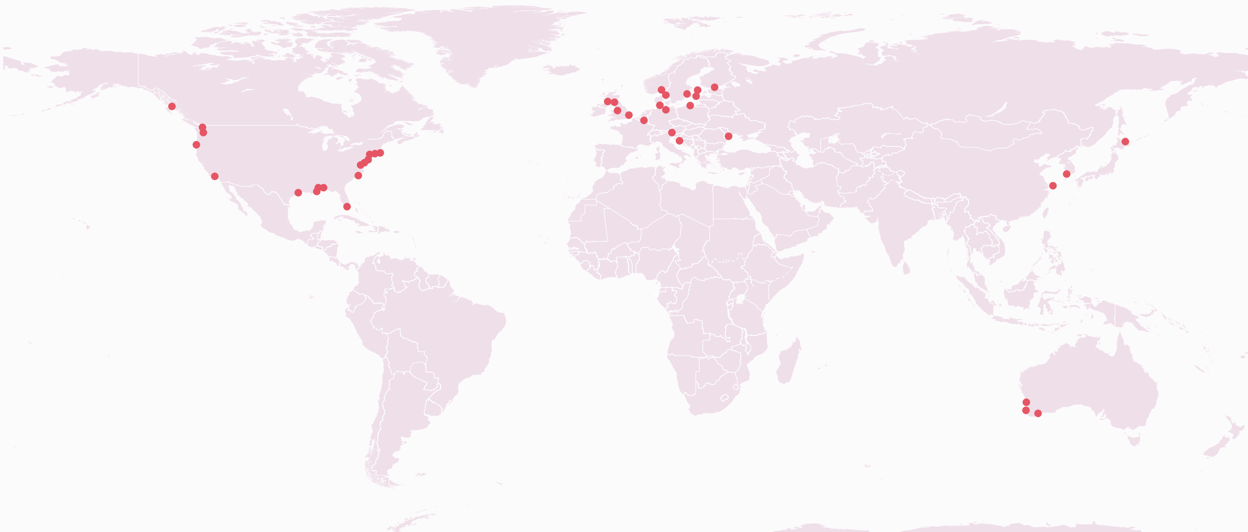
The increase in nutrients in aquatic ecosystems contributes to an increase in plant biomass and surface blooms of cyanobacteria (blue-green algae) (Khan *et al*. 2018). The death and decomposition of these undesirable aquatic plants reduces penetration of light in the water and causes depletion of oxygen levels in the water body, with extreme depletion of oxygen leading to the death of aquatic organisms and the formation of hypoxic zones (Khan *et al*. 2018). The formation of hypoxic zones has also been linked to climate change, which is driving losses of nutrients. Rising global temperatures are contributing to decreased oxygen in the water, and hence to the formation of hypoxic zones (Brietburg *et al*. 2018; Delgado 2021).

### Coral reefs

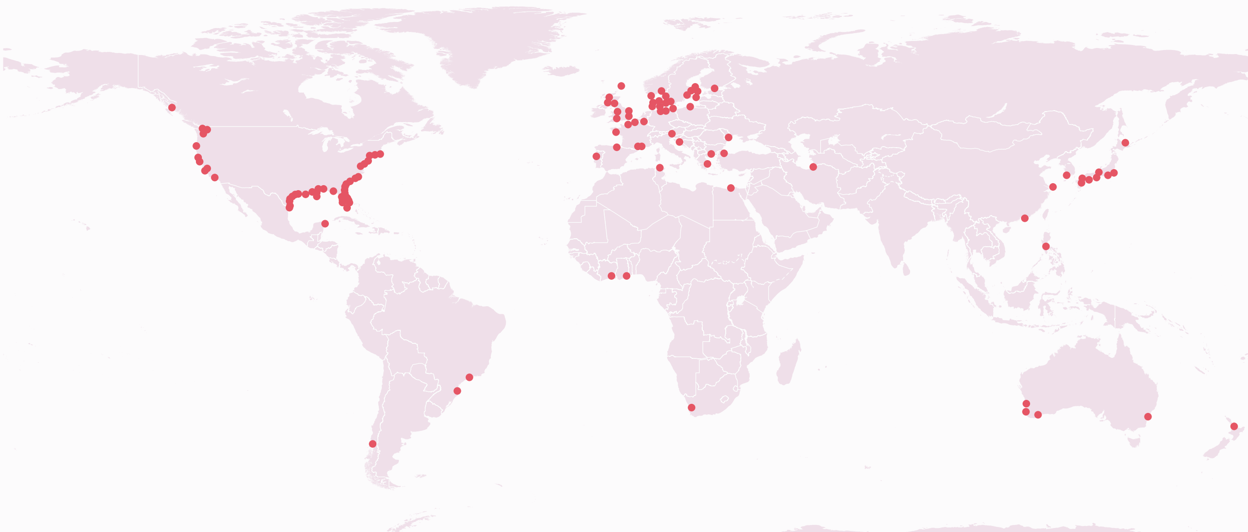
The world's coral reefs are under threat from local activities such as overfishing and destructive fishing, coastal development, climate change, ocean acidification, watershed-based pollution, and marine-based pollution (Wear 2016; Hoegh-Guldberg *et al*. 2017). About 50 per cent of coral reefs have been lost in the past 20 years, and it is feared that 70-90 per cent will disappear during the next 20 years as a result of climate change and pollution; rising sea surface temperatures and acidic waters could eliminate nearly all existing coral reef habitats by 2100 (American Geophysical Union 2020). Anthropogenic land uses (e.g., agriculture and urban development) can contribute to declines in coral cover, diversity, colony size and structural complexity (Carlson, Foo and Asner 2019). Pollution from agriculture has been identified as a threat in at least 25 per cent of coral reefs globally (Burke *et al*. 2011).

**Figure 9.2-5** **Global distribution of documented cases of hypoxia related to human activities. Each case is represented by a dot. The number of hypoxic areas is cumulative for the successive time periods.**
Rabalais *et al*. (2010) as reproduced in Díaz *et al*. (2012).

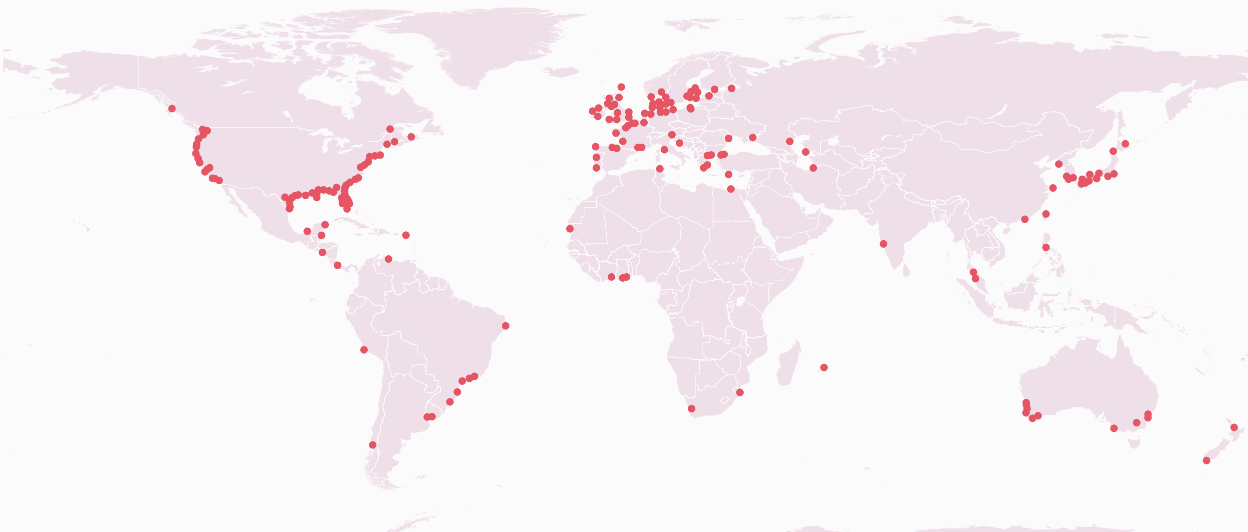
**Up to 1969**



**Up to 1989**



**Up to 2009**



A well-known example of a coral reef adversely affected by human activities is the Great Barrier Reef (GBR) in Australia. Studies have reported reductions in coral cover and seagrasses and animal species (Kroon *et al*. 2016). The decline has been partially attributed to nitrogen and phosphorus nutrient loads in rivers in the catchments draining into the GBR (Thorburn, Wilkinson and Silburn 2013). As pointed out by the authors of that study, a key source of nitrogen and phosphorus is the application of substantial amounts to crops. Several measures have been taken to manage the GBR. They include establishing targets to reduce nutrient loads from key catchments, enacting regulations, and setting up a reef trust (Department of Agriculture, Water and Environment of Australia 2020). Scientists have warned that saving coral reefs globally will require more aggressive actions from countries (Gibbens 2020).

### Algae

Anthropogenic sources have been related to abundance of algae (Berthold *et al*. 2018). Nutrient supplementation with fertilizers increases algae productivity (Boyd 2018). With excessive nutrient loading, the initial impacts are excessive growth of phytoplankton, microalgae (e.g., epiphytes and microphytes) and macroalgae (i.e., seaweed), which leads to reduction of light; inhibition of coral growth because the algae outcompetes coral larvae for available surfaces to grow; a shift in phytoplankton species and composition; and creation of favourable conditions for the development of nuisance, toxic, and otherwise harmful algal blooms (Selman *et al*. 2008). Harmful algal blooms are mainly the result of cyanobacteria, and some types of harmful cyanobacterial algal blooms produce toxins called cyanotoxins which can affect aquatic ecosystems (Graham, Dubrovsky and Eberts 2017).

Algae are eaten by microscopic animals (zooplankton) and insects, both of which are then eaten by small fish which may in turn eaten by larger predatory fish (Watson and Cichra 2013). However, water quality tends to deteriorate with an increase in nutrient input, subsequently affecting production negatively (Boyd 2018). The onset of oxygen-deficient conditions can greatly alter the community structure of water-column phytoplankton (Gauns *et al*. 2020). According to Ger *et al*. (2016), cyanobacteria compete with other phytoplankton for resources and these other phytoplankton decline during blooms. This study also reports that cyanobacteria are a poorer food source for zooplankton than some other phytoplankton. Hence, feeding on cyanobacteria affects zooplankton growth.

### Fish

Reports on fertilizers' effects on fish are largely based on data collected in eutrophic water bodies. Common carp increased and sport fish decreased with an increase in lake trophic status in Canada (Egertson and Downing 2004). Hypoxia had a negative impact on fish survival (Jeppesen *et al*. 2016) and reduced the growth rate of sea bass larvae (Vanderplancke *et al*. 2014). "Taste-and-odour compounds" produced by cyanobacteria may accumulate in fish and make them unpalatable to humans (Graham, Dubrovsky and Eberts 2017). However, a study on algal bloom in 2011 in Lake Erie in North America (the largest bloom in history) did not identify any decline in the value of commercial fishing as a result of this bloom while the weight and value of the fish harvest were above typical values (International Joint Commission 2014).

Inorganic and organic fertilizers are sometimes used to promote algal growth in aquaculture (e.g., in fish and shrimp farming) (Boyd 2018). A World Bank report has suggested that effluents could be used as a source of nutrients in fisheries (White 2017).

### Amphibians

Increased nutrients in water can reduced or increased tadpole survival and growth (Mann *et al*. 2009). In experiments the growth of tadpoles was reduced when they were exposed to ammonia and nitrate fertilizers (Garriga, Montori and Llorente 2017) and metamorphosis was delayed upon exposure to nitrates (Wang, M. *et al*. 2015).

### Aquatic invertebrates

Acidification and nutrient pollution are among the most important anthropogenic factors threatening freshwater mussel diversity in Peninsular Malaysia (Zieritz *et al*. 2016). Hypoxia and toxins, from eutrophication, affect reproduction and growth of invertebrates. According to a meta-analysis of impacts of hypoxia in invertebrates, hypoxia reduces reproduction and growth is not as sensitive (Galic, Hawkins and Forbes 2019). Hypoxia was also reported to reduce the growth of oysters (Jeppesen *et al*. 2016). In addition, toxins released upon the death of algal blooms may accumulate in aquatic invertebrates (Bownik 2016)

Elevated nitrogen concentrations in aquatic environments can increase vector populations. For example, the number of mosquitos in rice fields increased with the use of inorganic fertilizer rather than organic manures (Victor and Reuben 2000). Moreover, mosquito survival rates were higher in water with than without ammonium nitrate fertilizer (Muturi *et al*. 2016). In another study Culex mosquitoes laid more egg clutches in nutrient-rich containers than in containers without nutrients (Reiskind and Wilson 2004). Still, Johnson *et al*. (2010) have argued that the effects of environmental nutrient enrichment on disease are complex and multifaceted, varying with the type of pathogen, host species and condition, attributes of the ecosystem, and the degree of enrichment; some pathogens increase in abundance, whereas others decline or disappear.

## 9.3 Adverse health effects of fertilizer use

Fertilizes are best known for their contribution to food security. Few studies demonstrate that fertilizers have adverse effects on human health. However, they have been identified among the sources of contamination and pollution of air, water and soil and hence can potentially affect human health. For example, nitrates in drinking water have been associated with negative health effects although fertilizers are not their only source. Nitrate sources for humans can be exogenous (e.g., from food and water) and endogenous (the body can make nitrates).

There are reports that inorganic and organic fertilizers are among the sources of pollution (such as increased nitrate concentrations in groundwater and drinking water) that can affect human health (de Paz *et al*. 2009; Ward *et al*. 2018; Yu, G. *et al*. 2020). However, during the systematic review carried out for this report, there were no reports found of fertilizers directly causing human health effects when applied in a responsible and efficient manner or quantifying the contribution of fertilizers to such health effects. For some illnesses, where fertilizer use was suspected to be the cause, studies have been inconclusive or data are lacking.

Based on the existing literature, it seems likely that any negative health effects which can be attributed to inorganic or organic fertilizers are mostly due to nutrient losses before application (e.g., ammonia [nitrogen] losses during storage of manure) or after application (e.g., leaching of nitrates from the soil to groundwater). When fertilizers are handled and used responsibly, these losses are minimized and benefits are maximized (Chapter 10.3).

The perceived, actual and potential links between fertilizers and human health effects are presented in Figure 9.3-1. However, the relationships between these links are simplified in the figure. In real life the pathways connecting fertilizer contaminants/emissions to human health effects are not so distinct and can be rather complex.

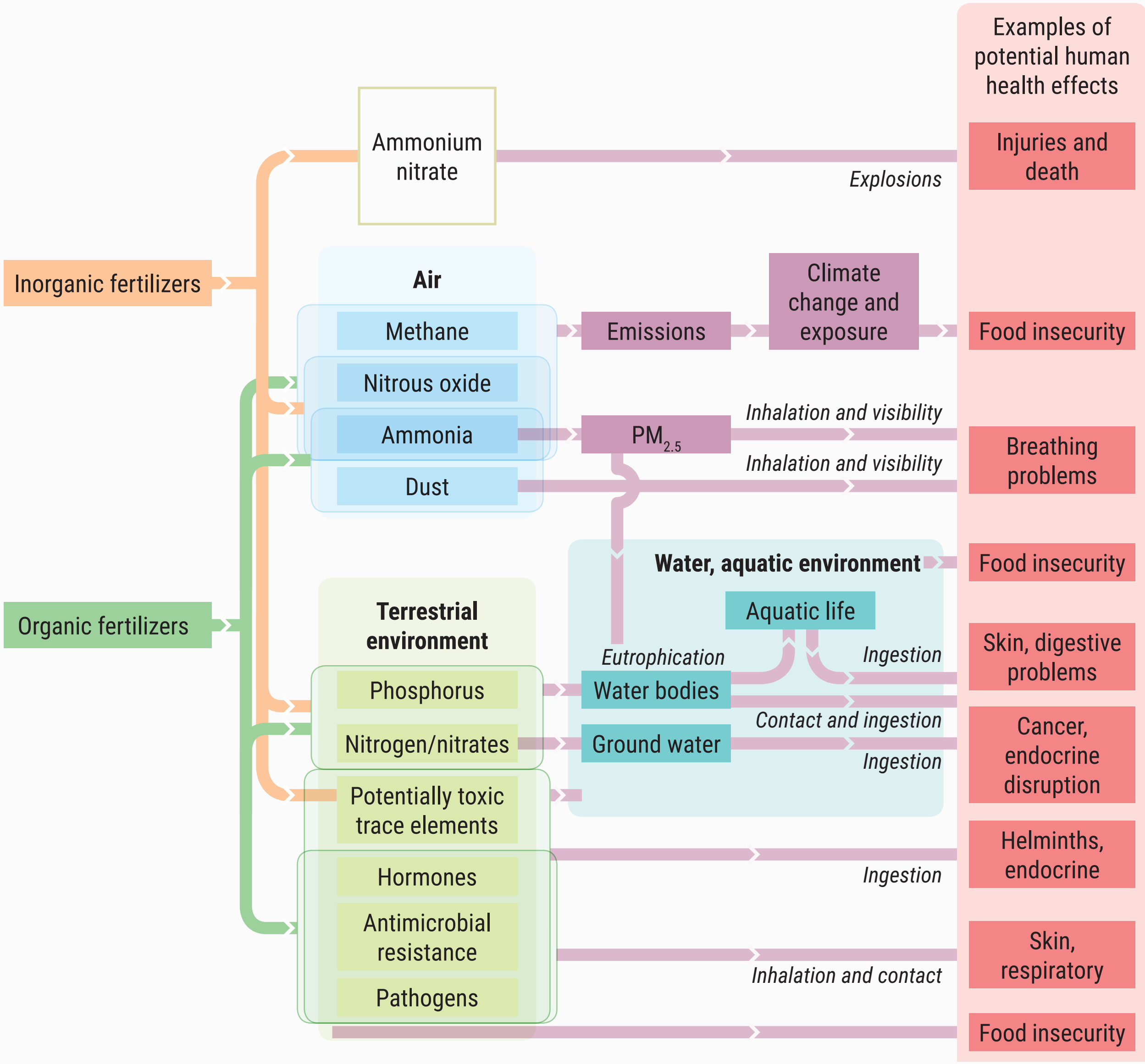
### 9.3.1 Adverse effects of occupational exposure

The reported adverse effects of occupational exposure to fertilizers mainly concern contact or inhalation of ammonia from fertilizers and manure (US EPA 2016). Another hazard associated with fertilizers is explosions and fires in storage settings involving (reactive) nitrogen fertilizers (US EPA 2015; Laboureur *et al*. 2016; Guglielmi 2020).

#### Ammonium nitrate and explosions/fires

Incidents involving ammonium nitrate fertilizers, including disasters in which many lives were lost,

Figure 9.3-1 Simplified generic schematic diagram of connections between fertilizers and human health issues.




have been documented (US EPA 2015; Laboureur *et al*. 2016; Guglielmi 2020; European Commission [EC] n.d.). Additional information about these accidents is provided in Chapter 10.2.1 and Figure 10.2-1.

Guidelines and advice on the transport, storage and handling of ammonium nitrate fertilizer (Chapter 7.2) have been developed based on reviews of these incidents (Pittman *et al*. 2014; US EPA 2015). Accidents can be prevented by using fertilizer formulations which reduce the potential for uncontrollable fires and detonation, and safety measures which provide assurance against uncontrollable fires (Gyenes and Wood 2015; Babrauskas 2016; Babrauskas 2017).

### Exposure to ammonia

Major sources of ammonia gas include leaks and spills during commercial synthesis, production, storage, processing or transporting of ammonia; refrigeration equipment failure; decaying manure from livestock; application of fertilizers; sewage or wastewater effluent; burning of coal, wood or other natural products; volcanic eruptions; forest fires; and the decomposition of nitrogenous compounds (US EPA 2016). Ammonia is also found naturally in the environment. It is a component of the global nitrogen cycle and is one of the main precursors of particulate matter ($PM_{2.5}$) from agricultural activities.

### Acute toxic effects

Short-term inhalation exposure to high levels of ammonia in humans can cause irritation and serious burns in the mouth, lungs and eyes (US EPA 2016).

In case reports of injury following acute exposure, changes in lung function have been observed. Respiratory effects have also been reported in some, but not all, controlled human exposure studies conducted on volunteers, according to the literature reviewed in US EPA (2016).

### Chronic toxic effects

Chronic exposure to airborne ammonia can increase the risk of respiratory irritation, cough, wheezing, tightness in the chest, and impaired lung function in humans (US EPA 2016).

In fertilizer factories respiratory effects following inhalation exposure to ammonia have been reported, according to a toxicological review

**Table 9.3-1** Respiratory effects in humans from inhalation exposure to ammonia in fertilizer factories.
Based on US EPA (2016).

| Place/country | Description | Effects | References |
|---|---|---|---|
| Urea plant and ammonia plant in a urea fertilizer factory, Bangladesh | Exposures to ammonia and acute respiratory effects were determined for workers in both plants<br>Workers at the ammonia and urea plants were classified as low and high exposure groups, respectively<br>The two groups were compared to controls (from the administration building) | Urea plant workers had higher mean exposure to ammonia and prevalence of acute respiratory symptoms, than ammonia plant workers<br>The symptoms with highest prevalence in the urea plant were chest tightness and cough | Rahman *et al.* (2007) as cited in US EPA (2016) |
| Two urea fertilizer factories, Saudi Arabia | Study to determine the prevalence of respiratory symptoms and disease among workers chronically exposed to ammonia gas<br>The factories were classified as high and low exposure factories; both factories were compared to controls (administration staff) | Increased prevalence of respiratory symptoms (i.e. bronchial asthma, chronic brochities in high exposure factory than in low exposure factory | Ballal *et al.* (1998) |
| Ammonia factory, Saudi Arabia | Workers exposed to ammonia divided into two groups (high and low cumulative exposure); both groups were compared with controls | Decreased lung function with greater cumulative ammonia concentration | Ali *et al.* (2001) |
| Fertilizer chemical plant, India | Workers exposed to irritants in diammonium phosphate (DAP), urea and ammonia plants vs. controls | Decreased lung function in workers from the three plants; DAP workers most affected, followed by ammonia, and urea workers were least affected | Bhat and Ramaswamy (1993) |

by US EPA (Table 9.3-1). In a study on healthy humans during ammonia exposure in an exposure chamber, symptoms related to irritation and central nervous effects were reported (Sundblad *et al*. 2004). Fertilizer was among the irritants reported to induce dermatitis in farmers in Poland (Kieć-Swierczyńska, Krecisz and Swierczyńska-Machura 2003).

In a study on rats, ammonia was reported to damage the respiratory system (Perkins *et al*. 2017).

#### Other contaminants

Dusts in pig housing were found to contain antibiotics (Hamscher *et al*. 2003) and endotoxins (Shin et al. 2019). In a systematic review of the literature (Farokhi, Heederik and Smit 2018) several studies showed a significant relationship between airborne endotoxins and human respiratory health.

Lam *et al*. (2015) reported that occupational health risks associated with wastewater and excreta management in Southeast Asia included diarrhoea, skin infection, parasitic infection, bacterial infection and epilepsy.

The use of phosphate rock, which contains small amounts of naturally occurring radionuclides, in the production of fertilizers generates a by-product called phosphogypsum. Phosphogypsum maintains nearly 80 per cent of its original radioactivity due to $^{238}$U decay products such as radon, $^{226}$Ra, and polonium, $^{210}$Po (Rodríguez Eugenio, McLaughlin and Pennock 2018). World production of this waste is currently around 200 million tons per year (Chernysh *et al*. 2021). Phosphogypsum waste disposed of in water or on land can be a threat to the environment and human health (Saadaoui *et al*. 2017; US EPA 2020g; Chernysh *et al*. 2021). Nevertheless, the literature associating this waste with environmental and human health effects does not appear to be extensive.

### 9.3.2 Adverse effects of dietary exposure

This section discusses the adverse effects of trace elements, particularly cadmium; adverse effects of nitrates; and adverse effects of urea and pathogens in organic fertilizers. It also covers endocrine disrupters in fertilizers and toxins in eutrophic water bodies, as well as the effects of fertilizers on food quality.

#### Potentially toxic trace elements

Potentially toxic trace elements can be ingested through food and water intake (Gall, Boyd and Rajakaruna 2015). In the literature both leafy and non-leafy vegetables are reported to be good accumulators of trace elements when grown in contaminated soil (Khan *et al*. 2015). A review of the literature on the abiotic inorganic contaminants in foods by McLaughlin, Parker and Clarke (1999) considered arsenic, cadmium, mercury, lead and selenium to be the most important elements in terms of food chain contamination. According to FAO's report on soil pollution by Rodríguez Eugenio, McLaughlin and Pennock (2018), the fertilizer industry is considered a source of potentially toxic trace elements such as mercury, cadmium, arsenic, lead, copper and nickel and natural radionuclides like $^{238}$U, $^{232}$Th and $^{210}$Po. Livestock manure and sewage sludge are among the sources of trace elements such as chromium, copper, nickel, lead and zinc.

#### Cadmium

Cadmium is released by natural and anthropogenic sources to the atmosphere, aquatic environments and terrestrial environments (UNEP 2010). According to the literature, over 90 per cent of cadmium released to the environment is from anthropogenic sources (Khan *et al*. 2017). Industrial processes (e.g., smelting of non-ferrous metal ores, fossil fuel combustion, ferrous metal production) are the main sources of atmospheric cadmium; atmospheric deposition contributes to the build-up of soil cadmium (WHO 2019a). Production of rechargeable nickel-cadmium batteries accounts for most global cadmium consumption. Other uses include alloys, anticorrosive coatings, pigments, polyvinyl chloride stabilizers, and semiconductors for solar cells (United States Geological Survey 2020).

Major contributors to cadmium levels in agricultural soils appear to be atmospheric deposition, phosphate fertilizers, sewage sludge and animal manure (UNEP 2010). Recent studies on the actual contributions of different sources globally were not found. However, according to a recent EU report on the total annual input of cadmium to agricultural soils in Europe (Smolders 2017), phosphate fertilizers contributed about 58 per cent, atmospheric deposition about 25 per cent and manure, sludge and lime about 17 per cent; the annual input from these sources was slightly less than 0.2 per cent of the current stock of cadmium in the soil. Cadmium emissions in the EU fell by about 65 per cent between 1990 and 2016 (EEA 2018). High cadmium concentrations in soil have been associated with industrial activities in several world regions. For example, high concentrations have been reported in rice grown in soils contaminated by industrial discharges in Asia (Chaney 2012) (Box 9.3-1).

Phosphorus fertilizers contain small amounts of cadmium, as this metal occurs naturally in phosphate rock (Roberts 2014). In a study in New Zealand cadmium concentrations in the topsoil were some seven to eight times greater than in deeper horizons; cadmium, phosphorus and uranium were highly correlated, consistent with a common source which was most likely phosphate fertilizer (Salmanzadeh *et al*. 2016). Another study reported that in many New Zealand territorial authorities there were no farms with soil cadmium concentrations beyond the range that naturally occurs in that country (Abraham *et al*. 2016).

A wheat study in which phosphorus fertilizer was labelled with a radioisotope revealed that 6.5-15 per cent of the cadmium in the shoot was from the fertilizer and that most of fertilizer cadmium (>97per cent) remained in the roots and soils (Wiggenhause *et al*. 2019). According to the authors, a limitation of this study was that source tracing with stable isotopes overestimated the proportion of cadmium in plants derived from the fertilizer because the isotope ratios of the sources were not sufficiently distinct from those of the soils. The fact that use of phosphate fertilizers can contribute to the uptake of larger quantities of cadmium in plants has been known for at least half a century (Schroeder and Balassa 1963). To minimize soil pollution from fertilizers, many countries (e.g., in the EU) have threshold values for cadmium in fertilizers.

Cadmium uptake in plants has been associated with soil properties such as soil pH, per cent carbon, soil zinc (Smolders 2001), soil salinity (Li, Chaney and Schneiter 1994; McLaughlin *et al*. 1994), soil cadmium concentrations, precipitation during the growing period (Eriksson *et al*. 1996) and plant species (Hatch, Jones and Burau 1988). High cadmium levels have been reported in some crops, for example cocoa in the Latin America and Caribbean region (Meter, Atkinson and Laliberte 2019) and rice and vegetables in China (Chen *et al*. 2018). A study by John (1973) compared cadmium concentrations in edible plant parts. It reported that higher cadmium levels were found in leafy vegetables (i.e., lettuce and spinach leaves) compared with non-leafy plant parts (brassica tops, radish and carrot tubers, pea seeds and oat grains). Tobacco is among the non-food crops known to hyperaccumulate cadmium (Suman *et al*. 2018). Food is the main source of exposure to cadmium in general, but for smokers tobacco is another important source as tobacco plants (like other plants) take up cadmium from the soil (WHO 2019a). Absorption via the lungs is higher than via the gastrointestinal tract. Cadmium exposure from drinking water is relatively unimportant compared with exposure from diet (UNEP 2010).

The FAO and WHO Joint Expert Committee on Food Additives has established a provisional tolerable monthly intake (PTMI) for cadmium, based on meta-analysis of epidemiological studies on the relationship between urinary cadmium and beta-2-microglobulin (a marker of renal tubular effects; WHO 2019a). According to a report by the European Food Safety Authority, health-based guidance values for oral intake could be exceeded by children and adults at the 95th percentile of exposure (European Food Safety Authority [EFSA] 2012). It should be noted, however, that the tolerance level proposed by EFSA is lower than that proposed by the FAO/WHO Joint Expert Committee (2.5 vs. 5.8 µg/kg of body weight per week) (European Union [EU] 2020).

### Adverse health effects of cadmium

#### *Acute toxic effects*

According to UNEP's Final Review of Scientific Information on Cadmium (UNEP 2010), acute cadmium poisoning in humans as a result of occupational exposure to airborne cadmium is characterized by irritation of the respiratory tract and lung damage.

#### *Chronic toxic effects*

Chronic toxic effects in humans include damage to the kidneys (proteinuria) and skeletal damage, with the former an early effects indicator. Lung cancer has also been associated with occupational inhalation of cadmium (UNEP 2010; Vacchi-Suzzi *et al*. 2016).

As noted in the UNEP report, cases of cadmium poisoning have been reported in farming households and by industry workers. In Japan after the Second World War, bone and kidney effects were linked to consumption of rice irrigated with water polluted with cadmium combined with a low-calcium diet. The major source of pollution was a mine located upstream (UNEP 2010). Among workers, concentrations of cadmium in blood and urine have been associated with ambient cadmium concentrations. Hence, for occupational effects the main route of exposure reported in workers is via inhalation (UNEP 2010; Vacchi-Suzzi *et al*. 2016). Chronic exposure matters more than acute (one-time) exposure, as cadmium has a long biological half-life of 15-20 years in humans and the effects manifest themselves mainly in older people (>50 years) (Smolders 2017). While dietary exposure to cadmium is recognized as a potential threat to human health (Box 9.3-1), no studies have assessed fertilizer use as a source of exposure, according to an epidemiological review carried out for this report (Box 9.3-2).

Effects in mammals are similar to those seen in humans. In addition, in animal experiments, cadmium has been reported to have reproductive effects such as interference with production of hormones and skeletal effects (e.g., disturbance of the accumulation of bone mass) (UNEP 2010; Vacchi-Suzzi *et al*. 2016). Cadmium mainly

**Box 9.3-1** China: Dietary cadmium could be a threat to human health

Cadmium intake by the population is increasing in China. In a study on dietary exposure to cadmium by Song *et al.* (2017), cadmium uptake was estimated to be above the general provisional tolerable monthly intake established by the Joint FAO/WHO Expert Committee on Food Additives in at least 5 per cent of the study group. The estimated dietary cadmium intake for some subsistence rice farmers in southern China is comparable to that of people in the region of Japan where Itai-Itai disease (UNEP 2010; WHO 2019a) was first reported (Wang, P. *et al.* 2019).

Studies have reported that mining is the main pollution source for cadmium contamination of soils (e.g. Liu. X. *et al*. 2016), for example when rice is irrigated with water contaminated by mining and smelting (Wang, P. *et al*. 2019). In addition, increased application of fertilizer nitrogen was associated with an increase in cadmium concentration in the soil solution (Mitchell *et al.* 2020) and excessive use of nitrogen fertilizers has been associated with increased cadmium in food crops (Wang, P. *et al*. 2019). Soil pH has declined in the major Chinese crop production areas, which has been partially attributed to high rates of soil application of nitrogen fertilizers (Guo, J. *et al*. 2010). Lower soil pH can contribute to increased cadmium concentrations in plants (e.g. see Dai, H., Wei and Skuza 2020). High intake of dietary cadmium has also been associated with food choice. Rice has a comparatively high cadmium concentration compared to other cereals, and per capita consumption of rice is high in China as in some other Asian countries (Wang, P. *et al.* 2019).

According to the literature on cadmium reviewed in the FAO report on soil pollution (Rodríguez Eugenio, McLaughlin and Pennock 2018), measures that can reduce crop uptake of cadmium include addition of lime (to raise soil pH) and zinc (to reduce cadmium absorption and accumulation). In addition, the method of application and type of fertilizer used can influence uptake of cadmium by plants. For example, Fan *et al.* (2017) reported that split applications of ammonium or urea resulted in significantly lower cadmium concentrations in Chinese cabbage grown in soil contaminated by cadmium compared with single applications. However, no such difference was observed when nitrate was used as the source of nitrogen.

**Box 9.3-2 General findings of two epidemiological reviews on fertilizers ("fertilizers and human health", "cadmium case study") carried out for this report.[1]**

The first of two reviews carried out for this report was a systematic review of epidemiological studies linking fertilizer use and human health effects. Few studies were identified for final inclusion (47 for inorganic fertilizers, 17 for organic ones). The outcomes with the largest number of studies were cancers for inorganic fertilizers and infections for organic ones. The studies reported significant, not significant or inconclusive findings for the outcomes studied. Although this epidemiological review highlighted several limitations of the studies (e.g. study design, poor exposure assessment) it concluded that this is an emerging evidence base.

The second was a review and appraisal of published systematic reviews and/or meta-analyses on potential associations of cadmium exposure with human health-related outcomes. Among the assessed publications, the outcomes studied included kidney disease, cancers, endocrine disorders and cardiovascular disease. Significant, not significant or inconclusive findings were reported. Fertilizers were mentioned in some publications, but no study assessed fertilizer use as a source of cadmium exposure.

The findings of the two reviews are a clear indication of the existing data gap with regard to the health effects of fertilizers.

1 The full reviews are presented as an annex to this report. "Epidemiological Evidence Report: Exposure to pesticides and fertilizers and human health".

bioaccumulates in the kidneys and liver of vertebrates; it can also accumulate in aquatic invertebrates and algae.

Several studies (Cheng *et al*. 2019; Guo, J. *et al*. 2021) have demonstrated that there could be a link between cadmium and the spread of AMR. Relationships have been observed between tolerance to potentially toxic trace elements like cadmium and AMR among bacteria (Wales and Davies 2015; Singer *et al*. 2016; UNEP 2017; Cheng *et al*. 2019). Furthermore, the addition of cadmium to soil has been reported to increase the abundance and translocation of antibiotic resistance encoded genes in the soil and in lettuce (Guo, H. *et al*. 2021). Cheng *et al*. (2019) argue that although much remains unknown about direct transmission of AMR through the food chain to humans, the risk should not be neglected.

### Uranium

An important use of uranium is as nuclear fuel to generate electricity in nuclear power stations. Uranium occurs naturally in mines (uranium ores), but is also found in industrial wastes and as a by-product of the copper and phosphoric acid industries, in areas affected by nuclear power plant accidents, and in phosphate rock (Kiegiel, Gajda and Zakrzewska-Kołtuniewicz 2017). Currently, obtaining uranium from rich uranium ores is considered cheaper than recovering it from secondary sources (Kiegiel, Gajda and Zakrzewska-Kołtuniewicz 2017). However, since uranium is a finite resource there may be a need in the distant future to recover it from secondary sources.

Phosphate rock contains some uranium, and some of this uranium remains in the final fertilizer product during mineral processing (Haneklaus *et al*. 2017). In the EU-28 it has been estimated that the amount of uranium extracted from imported phosphate rock could have been up to 334 tons in 2017 (Tulsidas *et al*. 2019). However, according to that study, recovery of uranium from phosphate fertilizers is constrained by low uranium prices. Liesch, Hinrichsen and Goldscheider (2015) reported that the range and spatial distribution of uranium and occasional peak values in drinking water appeared to be related to geogenic sources, and that agricultural land use generated a measurable but low background of uranium in groundwater. According to the literature, ingestion of uranium can affect human and animal health (Schnug and Lottermoser 2013).

### Nitrates in drinking water

#### Sources of nitrates in drinking water

Nitrates in drinking water are from anthropogenic and geogenic sources. Inorganic and organic fertilizers are reported to be among the largest anthropogenic source of nitrates in groundwater (Shukla and Saxena 2018; Jin *et al*. 2019). Studies in India have identified increased nitrate concentrations in surface and groundwater with sewage percolation, and use of excessive amounts of inorganic fertilizers, among the sources of nitrates in drinking water (Gupta, Gupta and Gupta 2017). In the United States nitrogen inputs (inorganic fertilizer, manure) have been among the factors associated with increased violations of the allowable limit for nitrates in drinking water (Pennino, Compton and Leibowitz 2017).

The results of a bibliometric analysis carried out to provide insights into research activities and tendencies with regard to global drinking water from 1992 to 2011 (Fu, Wang and Ho 2013) show that arsenic, nitrates, fluoride, lead and cadmium were the most researched water contaminants. This study reported that in 1992 the number of articles about arsenic, nitrates, fluoride, lead and cadmium was below 50 for each contaminant, but by 2012 there were more than 250 articles about arsenic and nitrates, close to 200 about fluoride, and fewer than 200 about lead and cadmium. Although no such analysis was found for the period after 2012, nitrates in drinking water have continued to be an area of interest for researchers.

#### Evidence of high nitrate concentrations in drinking water

The guideline values for nitrates in drinking water for human consumption are set at 11 mg/litre for nitrate nitrogen and 50 mg/litre for nitrate ion in the WHO guidelines for drinking water quality (WHO 2016; WHO 2017a).

Nitrate contamination of groundwater is a global problem (Zhou 2015; Ward *et al*. 2018 ). However, global and national documentation on the extent and seriousness of this problem is scarce. The literature suggests that nitrates in drinking water could be affecting the health of a substantial proportion of the global population.

According to Mateo-Sagasta, Zadeh and Turral (2018), nitrates in groundwater have been reported to be a major problem in Europe, the United States, and South and East Asia. In Europe, nitrate drinking water limit values had been exceeded in around one-third of the groundwater bodies for which information was currently available (Mateo-Sagastra and Burke 2010). In India studies have reported a continuous increase in nitrate concentrations and nitrate concentrations above permissible levels in many states (Gupta, Gupta and Gupta 2017). Other examples are shown in Table 9.3-2.

#### Sources of nitrates in humans

Approximately 80 per cent of dietary intake of nitrates is from vegetables, with the remainder

**Table 9.3-2** Evidence of high nitrate concentrations in water in selected countries.

| | Study description | Conclusions | Reference |
|---|---|---|---|
| Australia | Quality of water in 1,054 wells | Data identified fertilizer as the main nitrate source in ≈50 per cent of wells with high nitrate concentrations | Thorburn *et al.* 2003) |
| China | Quality of water in monitored rivers | Standards for drinking or bathing not met in 70 per cent and 28 per cent of rivers in 2001 and 2015, respectively | Cassou, Jaffee and Ru (2017) |
| Switzerland | Quality of underground water | Concentration > the allowable limit in > 10 per cent of the sites and in ≈ 40 per cent of samples from a highly populated, intensively farmed plateau | Federal Office for the Environment of Switzerland (2019) |
| United States | Violations of the allowable limit of nitrate in drinking water | Among the factors positively related to violations were fertlizer purchases and nitrogen inputs (animal manure, inorganic fertilizer), soil organic matter and population density | Pennino, Compton and Leibowitz (2017) |

coming from other foods and drinking water (Blekkenhorst *et al*. 2018). Nitrates are also produced in the body. This endogenous synthesis of nitrate complicates the risk assessment of nitrate (WHO 2003).

### Adverse health effects of nitrates

#### *Acute toxic effects*

According to the literature cited by the World Health Organization (WHO 2003), fatalities have occurred following a single intake of 4-50 grams of nitrate (equivalent to 67-833 mg of nitrate per kilogram of body weight) and toxic doses have ranged from two to nine grams.

#### *Chronic toxic effects*

Exposure to non-lethal toxic doses has been associated with methemoglobinemia, also known as blue baby syndrome, in infants up to six months of age; it has also been associated with pregnancy loss, birth defects and infant mortality, cardiorespiratory issues (e.g., asthmatic attacks), gastrointestinal issues (e.g., diarrhoea in children), cancer, thyroid disruption and other health disorders (Gupta, Gupta and Gupta 2017).

Some health effects have been reported in populations. For example, according to literature cited by Gupta, Gupta and Gupta (2017), in India ingestion of water with high concentrations has been associated with diarrhoea, acute respiratory infection, early onset of hypertension, and increased blood pressure in school children.

An additional effect reported in animal experiments is kidney damage. Increasing kidney damage in rabbits was associated with intake of water with increasing concentrations of nitrates (Gupta *et al*. 2010).

There is, however, a lack of consensus among studies on the health effects of nitrates. A meta-analysis by Bahadoran *et al*. (2015) reported no significant association between nitrate exposure and the risk of thyroid cancer, hyper- and hypothyroidism, and a significant association between higher exposure to nitrite and the risk of thyroid cancer. In addition, Powlson *et al*. (2008) concluded that there was no consensus on links between nitrates and either blue baby syndrome or cancer of the digestive tract. Furthermore, a meta-analysis by Song, Wu and Guan (2015) associated high nitrate intake with a reduced risk of gastric cancer. Studies quantifying the contribution of fertilizers to nitrates in drinking water or groundwater are lacking. Some studies have suggested a possible relationship between fertilizer use and kidney disease, but other possible causes of that disease have been proposed (Box 9.3-3).

**Box 9.3-3** Chronic kidney disease of unknown origin

Reports of chronic kidney disease of unknown origin (CKDu) are increasing globally, including in rural agricultural communities in Central America and other regions (Lunyeara *et al*. 2016; Singh *et al*. 2020).

A review of epidemiological studies from Central America concluded that, among other risk factors, there is a positive relationship between high (versus low) drinking water intake and CKDu (Gonzáles-Quiroz *et al.* 2018). In remote Australian Aboriginal communities where there is a high incidence of CKDu, levels of nitrates and uranium greatly exceed officially recommended levels. Most of these communities rely on raw groundwater to supply their domestic needs. They may be ingesting high levels of both nitrates and uranium, probably including uranyl nitrates (Rajapakse *et al.* 2019).

Possible causes of CKDu in different parts of the world continue to be examined. For example, a recent report based on the existing literature concluded that in Central America epidemiological patterns could not be explained by non-occupational risk factors, and that occupational heat stress was likely the main driver of the CKDu epidemic in that region (Wesseling *et al*. 2020). However, the review of epidemiological studies by Gonzáles-Quiroz *et al.* (2018) found no significant associations between heat stress and reported cases of CKDu in Central America. Their meta-analysis showed positive associations for males (versus females), family history of CKD and lowland altitude, as well as water intake. In addition to heat stress, there were no significant associations with pesticide exposure, non-steroidal anti-inflammatory drugs intake or alcohol consumption.

### Urea

Very few incidents involving urea appear to be mentioned in the literature. The Toxicological Review of Urea by the United States Environmental Protection Agency (US EPA 2011) mentions a report by Steyn (1961) on accidental poisoning of 80 farm workers presumed to be exposed to a fertilizer containing 98 per cent urea. Symptoms reported were nausea, vomiting, excitement and convulsions accompanied by urination. According to the review, symptoms reported in other studies include decreased platelets adhesiveness in humans and reduced growth and negative effects on liver and kidney in animals.

### Pathogens in organic inputs

Several studies have reported negative human effects of pathogens found in manure and sewage sludge/biosolids (Udeigwe *et al*. 2015). Livestock (e.g., cattle, pigs and chickens) can be carriers of pathogenic bacteria, protozoan parasites, helminthic worms and viruses (Goss, Tubeileh and Goorahoo 2013). A review by Delahoy *et al*. (2018) identified Salmonella, Lassa virus, Cryptosporidium and Toxoplasma gondii as important pathogens that could potentially be transmitted in animal faeces. Other pathogens which can potentially be transmitted through animal manure include Escherichia coli and Enterococci (Stocker *et al*. 2015). Use of raw sewage was associated with the presence of Giardia (a protozoa) and Ascaris (a helminth) in vegetables (Amahmid, Asmama and Bouhoum 1999). Helminths can be transmitted by eggs present in human faeces, which can contaminate the soil (WHO 2020a). The pathogens infect humans through oral intake, for example consumption of contaminated food and water or inhalation (Udeigwe *et al*. 2015) and dermal contact (Ercumen *et al*. 2017).

### Livestock ownership

In a systematic review by Penakalapati *et al*. (2017) livestock ownership was associated with childhood diarrhoea, but was also protective against diarrhoea or was unrelated to it. The relationship between livestock ownership and child growth was also inconsistent with regard to reported positive, negative and no associations. Children who slept in the same quarters (or rooms) as animals were more likely to suffer from environmental enteric dysfunction than those sleeping away from animals.

### Unrefined vs. refined organic fertilizers

The risk of contamination differs among organic fertilizers. Organic inputs processed before use will most likely have less pathogen contamination than those used before processing. Industrial organic inputs can present fewer risks, in relation to pathogens and contamination, than organic inputs produced and recycled within the farm. There are regulations targeting the quality of organic inputs. Chapters 8.4.2 and 8.5.2)

Pathogen populations in manure can be reduced by improving food and housing hygiene for livestock, storing manure at high temperatures, composting, avoiding the use of fresh manure, and applying manure early in the season to allow maximum time between application and harvesting (Hoagland *et al*. 2018). Some pathogens in manure can survive up to 120 days; persistence is longer in cold than in warm soil (Goss, Tubeileh and Goorahoo 2013).

In a study aimed at reducing pathogen survival by composting pig manure (McCarthy *et al*. (2011) the derived compost complied with EU regulations for processed manure products, as E. coli and Enterococcus were below limits and it was Salmonella-free. However, even when regulations are in place some products may be below standards. For example, in a study carried out in the United States by Brinton, Storms and Blewett (2009) some of the composts sold had pathogen concentrations above US EPA standards at the point of sale,

### Endocrine disruptors

The International Programme on Chemical Safety (IPCS) has defined an endocrine disruptor as "an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations" (IPCS 2002; Bergman *et al*. 2013). The same report defines a potential endocrine disruptor as “an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism, or its progeny, or (sub)populations”.

Cadmium and nitrates (discussed earlier in this chapter) and perchlorate and steroid hormones are included among potential endocrine disrupters.

Potential endocrine disrupters have been reported in animal manure. Manure from pigs was found to contain endocrine disrupting compounds (Combalbert *et al*. 2012). These compounds can reach humans through contaminated water used for drinking, recreation or fishing (Goss, Tubeileh and Goorahoo 2013).

### Perchlorate

According to a statement by the European Commission, perchlorate occurs naturally in the environment although other sources include nitrate and potash deposits and the manufacture, use and disposal of rocket propellants, explosives, fireworks, flares and air bag inflators (EC 2015). Water, soil and inorganic fertilizers were suspected to be relevant contributors of perchlorate found in fruits and vegetables in the EU, and Member States were requested to investigate sources of perchlorate in food.

Perchlorate is a competitive inhibitor of iodine uptake by the thyroid. It can interfere with thyroid function due to iodine shortage (Kabir, Rahman and Rahman 2015). Inhibition is reversible, as perchlorate does not bind to the thyroid and is rapidly excreted (FAO and WHO 2011). This concern is addressed in the 2019 EU Regulation on Fertilising Products, where the limit value for perchlorate in an inorganic macronutrient fertilizer was set at 50 mg/kg dry matter (EU 2019).

EU Member States have a harmonized enforcement approach to perchlorate, including harmonized guidance on perchlorate levels as a reference for trade within the EU aimed at protecting the health of consumers (EC 2015). In 2019 definitive limits were proposed and were favourably reviewed on the technical level by Member States in 2019 (EC 2019). In a 2020 amendment to Regulation (EC) No. 1881/2006, a section on maximum perchlorate levels in selected foodstuffs was added (EC 2020, p. L 160/5).

### Steroid hormones

Groundwater is susceptible to contamination by steroid hormones from livestock facilities (Kolok et al. 2018). Application of manure to agricultural land is a route for oestrogens into terrestrial environment, and oestrogens have been detected in groundwater (Adeel *et al*. 2017). Steroid hormones have been detected in the roots of Chinese cabbage grown in soil treated with compost (Zhang, J. et al. 2019). Some studies have suggested a relationship between environmental oestrogens and breast cancer, but more data are required to confirm the presence or absence of such a relationship (Adeel *et al*. 2017). Overall, evidence on the contribution of fertilizers to endocrine disruptors and the impact of this contribution on human health is lacking.

### Organic contaminants

Organic contaminants are persistent and include organochlorines (OCs), polychlorinated dibenzo-p-dioxin (PCDD), polychlorinated dibenzofurans (PCDF) and poly- and perfluoroalkyl substances (PFAS) (Rodríguez Eugenio, McLaughlin and Pennock 2018). These contaminants have been detected in sludge (Venkatesan and Halden 2013) and reported in soils with a history of sludge application (Weber *et al*. 2018). They can be taken up by plants, leading to dietary exposure (Brambilla *et al*. 2018). Their occurrence in soil is localized around industrial and urban areas and is not widespread (Rodríguez Eugenio, McLaughlin and Pennock 2018).

Evidence concerning the contribution of fertilizers to organic contaminants in soil and the effects of this contribution on human health is lacking.

### Microplastics

Global plastic production continues to increase (PlasticsEurope 2019; Research and Markets 2021). At the same time, plastic pollution is growing rapidly (Meijer *et al*. 2021;

Silva *et al*. 2021). Microplastics are solid plastic particles, generally defined as 5 millimetres (mm) or less in size, which come from a variety of sources including the fragmentation and degradation of larger pieces of plastic litter (Anderson *et al*. 2016). Nanoplastics can be defined as solid plastic particles less than 1 micrometre (μm) in size which originate from engineered material or are produced unintentionally through the degradation and fragmentation of larger plastic objects, including microplastics (Jakubowicz, Enebro and Yarahmad 2021). Despite widespread concerns, little is yet known about the human health and environmental risks of microplastics and nanoplastics (WHO 2019b). Moreover, "what is known is surrounded by considerable uncertainty" (Science Advice for Policy by European Academies [SAPEA] 2019, p. 108).

"Primary microplastics" are produced intentionally (UNEP 2019). Very small plastic pellets used in manufacturing, and the microbeads added to cosmetics and personal care products (an application banned in some countries) are well known examples of primary microplastics. A European Chemicals Agency report (European Chemicals Agency [ECHA] 2019) describes the intentional use of microplastics in controlled-release fertilizers and fertilizer additives as follows: "Polymers in fertilizing products are primarily used to ensure the following functions: controlled release of nutrients over a period of up to 18 months through micro-encapsulation; anti-caking, prilling and other preservative functions; as fertilizer additives; reduced dust formation during application of fertilizers; [and] reduced run-off of fertilizers" (ECHA 2019, p. 104).

The ECHA report estimates that the total amount of microplastics intentionally used in the EU was estimated at 51,500 tons per year, of which the controlled-release fertilizers and fertilizer additives contributed about 29 per cent. Coated seeds and controlled plant protection products were found to have contributed around 25 per cent and household cleaning products and cosmetics about 31 per cent of total microplastics intentionally used in the European Economic Area per year (ECHA 2019).

Routes of human exposure to microplastics, whatever their sources, include ingestion, inhalation and dermal contact (Prata *et al*. 2020). Microplastics have been detected in foodstuffs, including eatable fruits and vegetables (Conti *et al*. 2020), as well as in human stool (Schwab *et al*. 2019) and in human placentas (Ragusa *et al*. 2021). Estimates by Cox *et al*. (2019) of annual dietary consumption of microplastics in the United States increased when inhalation was considered; individuals who drank bottled water ingested more microplastics than those who drank tap water. Microplastics have, however, been detected in both tap and bottled water, as well as in marine water, freshwater and wastewater. As emphasized by WHO (2019b), the quality and quantity of data vary across these water types.

According to the WHO report on microplastics in drinking water (WHO 2019b), absorption and distribution of very small microplastic particles, including nanoplastics, in the human body may be higher than in the case of larger particles. The WHO report adds that chemicals may arise from the production and degradation of microplastics, and that microplastics have the potential to accumulate hydrophobic persistent organic pollutants (POPs). A limited number of studies in freshwater indicate that microplastics could possibly enable long-distance transport of pathogens and increase the transfer of antimicrobial resistant genes between microorganisms.

The WHO report found that, despite substantial knowledge gaps, "the potential risks from microplastic-associated microorganisms are far lower than the well-established risk posed by the high concentrations and diversity of pathogens present in human and livestock wastes in drinking-water sources. In addition, in terms of providing surfaces for attachment and transport of microorganisms including pathogens, the concentrations of microplastics reported in drinking-water sources are far lower than concentrations of non-plastic particles that contribute to normal turbidity in water" (WHO 2019b, p. 48). However, it emphasized the need to better understand the sources and occurrence of microplastics in fresh water and drinking water; the efficacy of different treatment processes and combinations of processes; and the significance of the potential return of microplastics to the environment from treatment waste streams, including the application of sludge biosolids to agricultural land (WHO 2019b).

Among the potential human health and environmental risks of microplastics being assessed by scientists, it has been suggested that they could contribute to the enrichment of antibiotic resistant bacteria (ARB) and the spread of AMR (WHO 2019b; Zhang, Y. *et al*. 2020; UNEP 2021).

#### Eutrophication

The extent and causes of eutrophication are discussed in Chapter 9.2.3.

##### Toxins

Toxins from harmful cyanotoxins have been reported in eutrophic waterbodies on all continents (Laybourn-Parry and Pearce 2007; Graham, Dubrovsky and Eberts 2017; Kubickova *et al*. 2019; Svirčev *et al*. 2019). Toxins produced by harmful cyanobacterial blooms can affect not only humans, but also fish and other animals. These toxins can enter the food chain through contaminated food sources. They have been found in fish muscles (Poste, Hecky and Guildford 2011). Humans may be exposed to them through oral, respiratory and dermal routes, as well as through haemodialysis if the dialysate is contaminated with cyanotoxins (Chorus and Welker 2021). They can affect the nervous system, lungs, liver, kidney, immune system and digestive system (Kubickova *et al*. 2019). Symptoms reported in humans include abdominal pain, vomiting, headache and diarrhoea (US EPA 2020h).

##### Adverse health effects

*Acute toxic effects*

Acute toxic effects resulting from eutrophication have been reported in humans. Some case studies provide evidence that exposure to cyanobacterial toxins in drinking water and recreational exposure to freshwater cyanobacteria can lead to illness (Chorus and Walker 2021).

At a haemodialysis clinic in Brazil, 116 (89 per cent) of 131 patients experienced visual disturbance, nausea, vomiting and muscle weakness following routine haemodialysis treatment; thereafter 100 patients developed acute liver failure (Azevedo *et al*. 2002). These effects were associated with the presence of cyanobacteria in the water supply reservoir, as cyanotoxins were found in patients' serum and liver tissue.

##### Chronic toxic effects

According to a literature review by Kubickova *et al*. (2019), chronic exposures to drinking water contaminated with cyanobacterial compounds, in some instances in combination with other factors, have been associated with increased incidence of liver cancer or chronic liver damage and increased incidence of colorectal or small intestinal cancer. However, according to Chorus and Welker (2021), it is impossible to show causation or to derive concentration-response data from the epidemiological studies available to date.

#### Nutrient dilution

Yield increases due to intensification have been related to the "dilution" of some nutrients (Cakmak and Kutman 2018). In wheat, nitrogen application reduced the essential amino acid index (EAAI) and protein digestibility-corrected amino acid score (PDCAAS) in grain (Zhang, P. *et al*. 2017). It is therefore possible that unbalanced fertilizers could affect the quality of food derived from plants. Balanced nutrition may reduce protein dilution as yield increases (Duncan *et al*. 2018).

### 9.3.3 Adverse effects of residential exposure

The section covers the adverse health effects of atmospheric $PM_{2.5}$ on human health.

For the adverse environmental effects of $PM_{2.5}$, see Chapter 9.2.1.

**Epidemiology**

Adverse health effects

For health effects this report relies on the recent Policy Assessment for the Review of the National Ambient Air Quality Standards for Particulate Matter by the United States Environmental Protection Agency (US EPA 2020b). That document reviews currently available evidence on health effects and exposure/risk information, among other topics. Some of its conclusions on health are presented below:

*Acute and chronic toxic effects (short-term and long-term, respectively)*

From agricultural activities ammonia is the main precursor for $PM_{2.5}$ (Bauer, Tsigaridis and Miller 2016; Wu, Y. et al. 2016). The Policy Assessment (US EPA 2020b) concludes that:

a causal relationship exists between long-term exposure to $PM_{2.5}$ and both mortality and cardiovascular effects.

there is likely to be a causal relationship between $PM_{2.5}$ and respiratory effects for both short and long-term exposure duration.

long-term exposure to $PM_{2.5}$ is likely to have a causal relationship with cancer and nervous system effects.

evidence suggests, but is not sufficient to infer, that a causal relationship is likely to exist between $PM_{2.5}$ and metabolic effects (e.g., diabetes, alterations in glucose and insulin homeostasis), reduced fertility, reduced chances of pregnancy, reduced foetal growth, low birth weights and preterm babies for both short- and long-term exposure.

### 9.3.4 Fertilizers and antimicrobial resistance

There is a risk that AMR will be transmitted from livestock systems to humans through direct contact or via the food chain (Huijbers 2016; WHO 2017b; Bandyopadhyay and Samanta 2020; Bennani *et al*. 2020).

AMR bacteria, which have been detected in manure, end up in water and soil (Huijbers *et al*. 2015). AMR in humans has been associated with the presence of manure (Muloi *et al*. 2019) and contact with livestock (Huijbers *et al*. 2014).

Since similar antimicrobials are provided to humans and animals (Tang *et al*. 2017), it is difficult to quantify the contributions of the livestock sector to AMR resistance in human beings. Still, the large amounts of antimicrobials used in livestock production could pose a large AMR risk if it is not already having a significant impact on human health. Interventions that restrict antibiotic use in food producing animals have been associated with a reduced antimicrobial resistance in animals, but studies on the effects of such interventions on AMR in humans remains scarce (Tang *et al*. 2017; Scott *et al*. 2018). However, it is likely that such interventions can result in reduced antimicrobial resistance in humans (Scott *et al*. 2018)

There are ongoing AMR surveillance programmes in Europe, but the results are difficult to compare due to differences in methodologies used in data collection (Schrijver *et al*. 2018).

For pesticides and AMR, see Chapter 4.4.7.

## 9.4 Links between the environmental and health effects of fertilizers

The environmental effects of fertilizer use can have negative effects on human health and nutrition. For example, degradation of the terrestrial and aquatic environments affects the sustainability of food production, and hence human health and security.

Changes in insect vector populations due to fertilizer use can affect the spread of communicable diseases. Townsend *et al*. (2003) hypothesized that increasing nutrient availability could often favour disease-causing organisms. They suggested that vector-borne diseases like malaria and West Nile virus may be affected by elevated nitrogen in aquatic environments. Although studies linking fertilizers to diseases transmitted by such vectors appear to be lacking, the fact that studies have demonstrated a positive relationship between fertilizer use and vectors indicates that fertilizer use can increase incidences of some vector-borne diseases in humans.

Studies have suggested that changes in human diet can affect both the environment and human health. For example, Sabaté and Soret (2014) proposed that increased adoption of plant-based diets would have positive effects on the food supply, as well as on the environment and human health. Increased intake of more plant-based foods would likely reduce the amounts of fertilizers used. For example, in a study by Marlow *et al*. (2009) non-vegetarian diets required 13 times more fertilizer than vegetarian ones.

## 9.5 Key data gaps: environmental and health effects of fertilizers

To a large extent, risk assessment involves the use of scientific principles and methods to conceptualize, assess and manage risks (Aven 2016). The knowledge generated can be used to guide decision-making, e.g., in determining policies.

While there are indications that fertilizers can have adverse effects on the environment and health (Chapters 9.1 and 9.2), some of the potential impacts of these effects may be unknown. The epidemiological reviews carried out for this report bear this out (Box 9.3-2). For example, according to the review of studies linking fertilizer use and health effects, studies were few; they reported either significant, not significant or inconclusive findings for the outcomes studied; and they had limitations (e.g., in regard to study design, poor exposure assessment).

Other reports have highlighted the lack of adequate data on adverse effects for use in decision-making. As pointed out in the FAO publication Soil Pollution: A Hidden Reality (Rodríguez Eugenio, McLaughlin and Pennock 2018), in the case of fertilizers, risk assessment is constrained by, for example, large gaps in available information on health effects as well as in toxicological data. According to plans for the implementation of the EU Fertilizer Regulation (EU 2019), the European Commission shall by 2026 submit to the European Parliament and to the Council a report which shall include "any new relevant scientific information as regards the toxicity and carcinogenicity of contaminants that becomes available, including the risks from uranium contamination in fertilizing products".

Estimating the risks posed by contaminants and pollutants from diffuse sources is difficult. Moreover, for many of those in the environment that could be from fertilizers, fertilizers are not the only source and the contribution of fertilizers to adverse environmental and health effects is difficult to estimate. This problem could partly explain why literature on risk assessment studies for fertilizers is scarce. According to a review of the types of risk in agriculture (Komarek, de Pinto and Smith 2020), a large share of studies has been devoted to production and markets and very few to health issues. Since farmers must cope with and manage different types of agricultural risks, with compounding effects, the authors suggest a shift in the focus of research towards analysing multiple contemporaneous types of risks, including those related to the environmental and health effects of overuse or inappropriate handling of inorganic fertilizer.

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