

Review Article

Poultry Manure and its Contribution to Inflammation and Cancer Progression

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ABSTRACT

Indiscriminate manure disposal has been highlighted as a significant cause of environmental contamination due to the presence of various biological and chemical irritants. It includes pathogens, antibiotics, and organic pollutants, all of which have the potential to harm not only the environment but also human health. Several incidents have been reported, most notably among farmers and those living near the farms, as a result of air and water pollution caused by manure losses. Acute and chronic exposure to these hazards may result in a variety of health issues, including infection, inflammation, and even cancer. Despite this, humans are

constantly exposed to these risk agents due to a lack of awareness of proper disposal methods and knowledge of the risk agents' associations with diseases. Thus, the review discusses the potential health risk or diseases linked to poultry manure and recommends future measures to minimise the hazards to farmers' health and the environment posed by their existing practices.

Keywords: Cancer, infection, inflammation, pathogenic bacteria, poultry manure

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INTRODUCTION

The growing demand for food products, whether proteins, carbohydrates, or fibre, has rapidly increased over the last decade, in lockstep with the world's population growth. The global population was 7.9 billion in 2022 (Population Matters, 2023), expected to reach 9.7 billion by 2050. On the other hand, population growth will undoubtedly increase the demand for poultry production for human consumption. According to the United Nations Food and Agriculture Organization (2021), poultry meat production increased from 9 to 132 million tonnes worldwide between 1961 and 2019, accounting for nearly 39% of global meat production. Additionally, global broiler meat production reached approximately 83.2 million metric tonnes in 2012 and is expected to reach approximately 102 million in 2021 (<https://www.statista.com/aboutus/our-research-commitment/1239/m-shahbandeh>). In Malaysia, the yearly per capita consumption of poultry meat increased from 41.9 kg in 2012 to 53.1 kg in 2022 (Organisation for Economic Co-operation and Development, 2022).

While modern agricultural technology has increased production efficiency and safety, the risks to the human population posed by these industries have remained relatively constant. It is because as poultry farming becomes more popular, the production of poultry waste will increase, endangering humans and contributing to environmental contamination. It has been established that poultry excrement contains a variety of contaminants, including veterinary antimicrobials, heavy metals, and pathogens. These contaminants can enter surface water, groundwater, and agricultural soil during storage and disposal, posing direct or indirect threats to public health (Gbotosho & Burt, 2013).

Poultry manure is the faeces of poultry (chicken, turkey, duck, and geese), which is frequently used as an organic fertiliser to increase the soil's nitrogen, phosphate, and potassium levels. However, it is a major source of pathogens that can harm humans. For example, *Listeria*, *Salmonella*, *Staphylococcus*, *Actinobacillus* and *Campylobacter* are just a few pathogens that have been prevalent in poultry wastes and have been linked to adverse effects on human health and the human food chain (Kyakuwaire et al., 2019). These pathogens may be spread from poultry wastes to water sources through run-off, which humans may consume or ingest as a source of water or marine-based food (Kyakuwaire et al., 2019).

Additionally, due to easier market access, most poultry industries are massive and concentrated in urban areas. However, this location is frequently near critical areas such as rivers and drainage systems that provide water to nearby residents (Taiwo & Arowolo, 2017). Inadequate waste management increases their risk of contracting infections, which can cause life-threatening conditions (Food and Agriculture Organization of the United Nations, 2013). Exposure to these zoonotic pathogens, which are pathogens that have spread from animals to humans, has been shown to cause a variety of infectious diseases in humans, including Listeriosis, Salmonellosis, and Campylobacteriosis (Kyakuwaire et

al., 2019). Thus, appropriate and preventive strategies must be implemented at all levels of agriculture to mitigate health risks (Food and Agriculture Organization of the United Nations, 2013). Additionally, this approach would contribute to sustainable agriculture without the risk or concern of zoonotic pathogen contamination (Garcia et al., 2020).

CURRENT MANAGEMENT OF POULTRY MANURE AND ITS DISADVANTAGES TO HUMANS

Poultry manure contains thirteen essential nutrients required for plant growth and development, including Nitrogen (N), calcium (Ca), phosphorous (P), sulphur (S), copper (Cu), chlorine (Cl), iron (Fe), molybdenum (Mo), potassium (K), magnesium (Mg), manganese (Mn), zinc (Zn), and Boron (B) (Singh et al., 2018). These nutrients are frequently derived from poultry feed, medications, supplements, and drinking water. The abundance of nutrients in poultry manure can be regarded as one of the best fertilisers as it fulfils the main plant growth requirements (Singh et al., 2018).

Reused Poultry Manure as Bedding Material

Poultry litter usually consists of bedding material mixed with manure, feathers, spilt water and waste feed accumulated during the production cycle. Although poultry litter is often used as an excellent fertiliser for enhancing the growth of vegetable crops, it also has been extensively re-used as bedding materials for subsequent batches of broilers due to the high cost and demand for high-quality wood shaving bedding, the primary component of litter (Redding, 2011). This re-used practice is prevalent in several countries, including the United States of America (Macklin et al., 2006) and Australia (Runge, 2007).

Unfortunately, this practice will promote certain food-borne pathogens such as *Salmonella* and *Campylobacter*, which are commensals in poultry, increasing the risk of human contamination via direct contact with food crops or spray irrigation (Kyakuwaire et al., 2019). Despite concerns about the spread of harmful pathogens into the environment, this practice of reusing bedding material is expected to grow in the future due to limited supplies of suitable bedding material. Nevertheless, Bucher et al. (2020) found the benefit of using reused poultry litter to deter the growth of *Salmonella*. It contradicts ideas probably due to the environmental stressors or alteration of physiochemical parameters disrupting the normal mechanism that regulates the complex interplay between bacterial members of the community, driving the lower abundance of *Salmonella* in reused bedding.

Source of Energy Production

Additionally, as poultry manure is a complex source of organic components, these wastes could be utilised for energy production. Among the common methods for converting poultry litter to energy is fluidised bed combustion (FBC) technology. The heat produced from this

method can then be used to produce energy or to provide heating for buildings or poultry houses (Choudhury et al., 2020). Nevertheless, the main concern with this technique is the number of gases produced, such as carbon dioxide (CO₂), methane (CH₄) and nitrous oxide (N₂O), all of which is known as greenhouse gases (GHG) contributor, and particulates that are being released and polluting the air. Exposure to these particles may promote several cardiovascular and respiratory consequences for humans, including cardiac arrhythmias, asthma attacks, and bronchitis (Manisalidis et al., 2020).

Stockpiled of Poultry Manure

In some countries, surplus poultry litter is also openly stockpiled in the environment. Normally, poultry stacking generates heat, which kills any pathogens present in the litter (Wilkinson et al., 2011). However, it may cause pathogen run-off into adjacent rivers and creeks, particularly during heavy rain or flooding (Kyakuwaire et al., 2019). Although certain measures were implemented to ensure the effective use of poultry manure while minimising its negative impacts, there is still a risk to the environment and human health if it is not correctly managed.

ROUTE OF HUMAN EXPOSURE TO POULTRY MANURE

Inhalation

It is common knowledge that poultry farms generate excessive dust from bedding materials, feed, dried faeces, and feather particles. Dust may contain microorganisms, including endotoxins, fungi, and bacteria, affecting living things when inhaled. Dust-containing living organisms are referred to as bioaerosol, and they can spread throughout the environment and food chain, causing numerous diseases such as pulmonary disease, infection, and skin irritation (Jerez et al., 2014).

Salmonella, *Listeria*, and *Campylobacter* are among the pathogens known to be released from the internal environment of poultry facilities (Hakeem & Lu, 2021) (Figure 1). After poultry have been transported or eliminated, the broiler house is contaminated to varying degrees, increasing the likelihood of their release into the environment. In order to prevent infections in large-scale poultry farms, it is required to disinfect the housing. Disinfection can minimise or eliminate potential pathogenic bacteria in the home and prevent their spread across batches. Infectious diseases in poultry houses can be effectively controlled by selecting the most appropriate disinfectants, disinfection procedures, and strategies (Jiang et al., 2018). Some pathogens released into the environment can adapt to harsh environmental circumstances, allowing them to grow, breed, infect other hosts, and produce toxic compounds that may damage human health (Mokhtar et al., 2022). Among the potentially produced toxic compounds are listeriolysin O (LLO), a pore-forming toxin

encoded by the *hly* gene of *Listeria monocytogenes* (Churchill et al., 2006) and *Salmonella* cytolethal distending toxin (S-CDT), a toxin that can cause DNA damage in eukaryotic cells, produced by *Salmonella enterica* serotype Typhi (Miller et al., 2018).

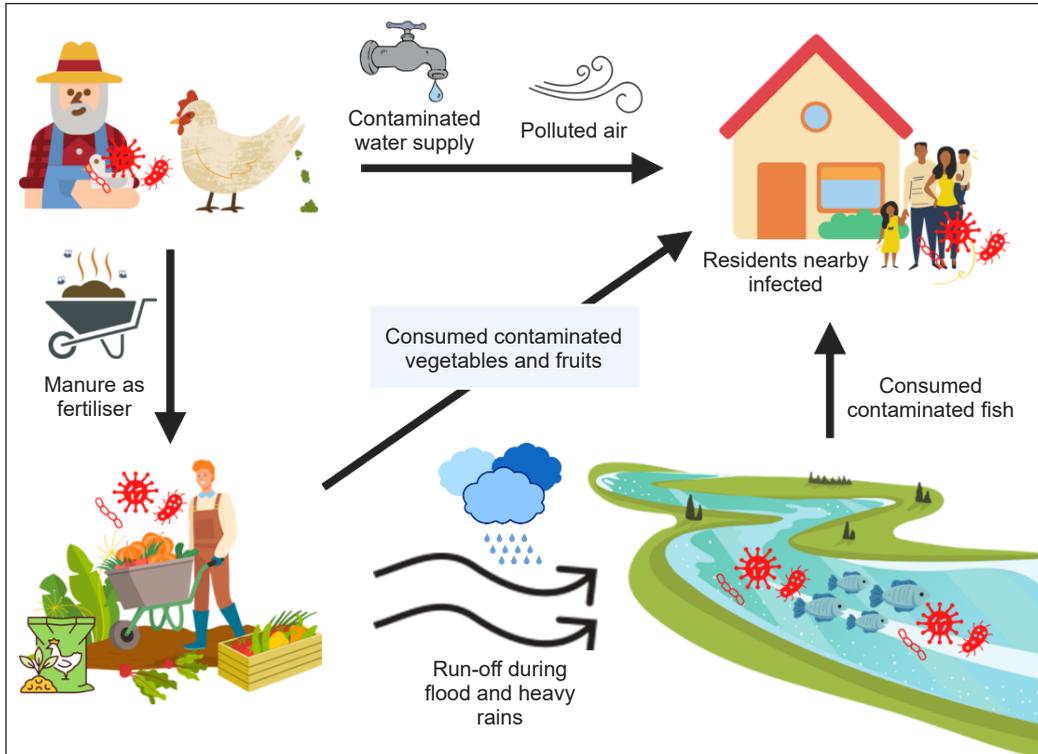


Figure 1. Possible pathogen transmission routes from poultry manure to humans. Improper waste management will spread pathogens to poultry farmers, adjacent inhabitants, and farmers who use contaminated manure as fertiliser via air pollution, water contamination, and the ingestion of contaminated vegetables and fruits. In addition, infections may spread from poultry wastes to water sources via run-off, which occurs during floods or heavy rains, resulting in humans consuming or ingesting water or marine-based food. Created with BioRender.com

Farmers are also typically exposed to the poultry manure-associated hazard, ranging from mild conditions, such as loss of olfactory recognition, to severe chronic pulmonary diseases, such as asthma and chronic obstructive pulmonary disease (COPD), that require special attention (Kitjakrancharoensin et al., 2020). For instance, the amounts of respirable dust and bioaerosol on exposed farmers were more significant than those measured with stationary indoor samplers. Although the respirable dust is still below the Occupational Safety and Health Administration's permissible exposure level, it surpasses the limit for animal buildings suggested by other studies (Jerez et al., 2014).

Some nearby inhabitants were also exposed to harmful odour compounds such as ammonium, dimethylamine, trimethylamine, butyric acid, phenol, and indole that may

irritate the human respiratory tract (Fan et al., 2020). Additionally, since poultry manures may also spread some bioaerosol-containing harmful pathogens, excessive and sustained intake of these pathogens might result in the fatal illnesses listed in Table 1. Meningitis and encephalitis are common disorders associated with pathogen infections caused by excessive inflammation. Chronic or sustained exposure to these inflammatory processes may also contribute to the advancement of cancer as inflammation and cancer cross-talked (Grivennikov et al., 2010).

Table 1
List of pathogens commonly found in poultry waste

Pathogen	Host	Route	Disease
<i>Listeria monocytogenes</i>	Cattle, sheep, pigs	Food, water	Listeriosis, febrile gastroenteritis, Perinatal infection
<i>Brucella</i> spp.	Cattle	Direct food, inhalation	Brucellosis
Enterohemorrhagic <i>E. coli</i>	Cattle, sheep, pigs	Food, water	Haemorrhagic colitis
<i>Campylobacter jejuni</i>	Poultry, pig, Cattle	Food, water, direct	A neurological disorder in very young, elderly or immunocompromised human patients. Guillain-Barre syndrome in human Campylobacteriosis
Hepatitis E virus	Pigs, poultry, rats	Faecal-oral, food, water	Hepatitis
<i>Yersinia enterocolitica</i>	Pigs	Food, direct water	Yersiniosis
<i>Mycobacterium bovis</i> & <i>M. tuberculosis</i>	Pigs, cattle	Inhalation	Tuberculosis
<i>Salmonella</i> spp.	Pigs, cattle	Faecal-oral, food, water, direct	Diarrhoea, nausea, chills, fever, headache, abdominal pain
<i>Escherichia coli</i>	Cattle, pigs and sheep	Food, water	Diarrhoea

Drainage and Surface Water System

Pathogen transport from poultry manure can also occur via tilled drained land or drainage and surface water systems such as spray irrigation for agricultural activities. The reused of agricultural wastewater, including manure and other wastes from farms, poultry houses and slaughterhouses, is common, especially in some European and Mediterranean countries that suffer from water scarcity (Al-Gheethi et al., 2018). Some Italian regions have been adversely affected by drought, and the lack of water resources has primarily hampered agricultural activity, which consumes more than half of the total available water. For these reasons, other water sources are required, and usually, the most readily available source of water to meet the rising need for crop irrigation is treated municipal wastewater. Besides, agriculture wastewater recycling has gained importance because it provides a significant

amount of irrigation water, helps conserve potable resources, and reduces the environmental impact of effluents discharged into water systems (Mokhtar et al., 2022). However, vigilance must be exercised while reusing these wastewaters to minimise the hazards to agricultural goods, soil, and groundwater from toxic and pathogenic pollutants, which pose possible health risks to consumers when they reach the food chain (Mokhtar et al., 2022).

IMPLICATIONS TO HUMANS: HEALTH-RELATED RISKS

Infection-Induced Inflammation

Although sewage sludge contains several nutrients and organic matter useful for improving soil structural, chemical and biological properties (Gubišová et al., 2020), it also contains several pathogens that may affect human health (Table 1). It is because of the favourable conditions of poultry manure, including high moisture, nutrients, and optimal pH and temperature, which are suitable for pathogens to thrive and grow in abundance (Black et al., 2021). As a result, pathogens have a high proclivity for spreading from poultry to humans via a variety of routes, such as via food, water, inhalation or direct contact. All these pathogens are the source of infection and may elicit an immune response, causing inflammation.

Listeria Infection. *Listeria* species are Gram-positive bacteria that belong to the *Listeriaceae* family. There are 17 *Listeria* species in the phylogeny, with 9 recently described in 2009 (Orsi & Wiedmann, 2016). It favours cool, damp environments and can be found throughout the environment (Zhu et al., 2017). Apart from their reputation as food-borne diseases, numerous *Listeria* species, the most common of which are *Listeria monocytogenes*, *L. innocua*, and *L. ivanovii*, have been found plentiful in poultry manure. Exposure to these bacteria can cause listeriosis in humans. Some species have also developed resistance to more than three types of antibiotics (multidrug resistance), including ciprofloxacin, penicillin, and fluoroquinolone (Cokal et al., 2022). Hence, to reduce cross-contamination and the zoonotic potential of listeriosis, food safety management systems and interventions were required at all phases of the broiler-rearing cycle (Zhu et al., 2017). It is due to its adaptability to hostile environments. For instance, *Listeria* was found to survive for three months in animal slurries and unclean water and one month in manure heaps with temperatures exceeding 55 °C. Even after manure was spread to agricultural land, *Listeria* survived for over a month in clay loam grassland soils up until 270 days (Chen & Jiang, 2014).

Furthermore, *Listeria* may persist in severe environments and build biofilms on a range of environmental surfaces (Beresford et al., 2001). Because of the possibility of contamination, this clearly poses a substantial risk to human safety and hence signifies the need to eradicate *Listeria*, such as through disinfection with disinfectants or antibiotics. Nevertheless, the persistence used of antibiotics in animals as a growth stimulant and

infection control measure may result in the evolution or development of antibiotic-resistant *Listeria* (Chattopadhyay, 2014), especially those resistant to chloramphenicol and ampicillin (Odjadjare et al., 2010). It could eventually become a global issue as present antibiotics may be insufficient in addressing its pathogenicity.

Listeria is primarily spread to people by consuming infected food or drink. Depending on the host's health, listeriosis infection causes various clinical symptoms ranging from invasive to non-invasive. During invasive manifestation, *L. monocytogenes* can infect its host's body by penetrating the blood-brain barrier or the placenta, resulting in a brain or foetal infection. In most cases, the invasive type of Listeriosis affects mainly high-risk people, such as immunocompromised people, the elderly, and newborns. This population typically gets meningitis and septicaemia at the start of listeriosis (Silk et al., 2012). Non-invasive Listerial gastroenteritis, also known as febrile Listerial gastroenteritis, is a milder infection commonly accompanied by fever, diarrhoea, headache, and muscle discomfort (Sim et al., 2002).

L. monocytogenes was found in 20 to 50 % of retail beef and poultry meat items sold in Malaysian wet markets and supermarkets. Despite this, no instances of food-borne listeriosis have been documented, which could be attributable to a lack of recognition of the disease or a lack of a national registry (Goh et al., 2012). The presence of *L. monocytogenes* in raw chicken meat is undesirable yet unavoidable. As a result, additional research on the processing procedure to minimise and eliminate this type of bacteria in chicken meat before eating is required.

Salmonella Infection. *Salmonella* is the next most frequently encountered pathogen in poultry waste. It is abundant and is thought to be associated with reptiles, rodents, and mammals' intestinal tracts. *Salmonella* is a motile bacterium that is a member of the Enterobacteriaceae family. According to Voetsch et al. (2004), *Salmonella* causes 1.4 million cases yearly, with 15,000 requiring hospitalisation and 400 resulting in death. Additionally, it is widely accepted that humans' primary Salmonellosis sources are poultry and poultry products (Moultotou et al., 2017). According to Djefal et al. (2018), approximately 34.37% of poultry farms were found to be contaminated with *Salmonella*. *Salmonella* is classified into two distinct species: *S. enterica* and *S. bongori*, and six distinct subspecies: *enterica*, *houtenae*, *arizonae*, *diarizonae*, *salamae*, and *indica* (Lamas et al., 2018). Only *S. enterica* serovar Gallinarum and *S. enterica* serovar Pullorum, however, are primarily associated with poultry (Xiong et al., 2018), whereas *S. enterica* serovar Typhi is primarily associated with humans (Garai et al., 2012).

Humans may become infected with *Salmonella* because of improper poultry farming management (Moultotou et al., 2017). Besides, since it can survive months in soil (Jechalke et al., 2019), the risk of human infection, particularly among poultry farmers, is high. You

et al. (2006) discovered that *S. enterica* serovar Newport can survive for 184, 332, and 405 days in manure, manure-amended unsterilised soil, and manure-amended sterilised soil, respectively (You et al., 2006). Additionally, *S. enterica* serovar Enteritidis persisted for approximately a year in the dust of an empty broiler breeder, despite disinfection and cleaning (van Immerseel et al., 2009). Therefore, it is vital to explore viable methods for reducing the risk of Salmonellosis, such as employing composting techniques that have effectively prevented pathogen growth (Chen & Jiang, 2014). Although high-temperature composting helps reduce *Salmonella*, the pathogen persists in manure and litter by adapting to thrive in dry environments (Avidov et al., 2021), contributing to *Salmonella*'s dispersion throughout the food chain (Waldner et al., 2012).

***Campylobacter* Infection.** *Campylobacter* is also thought to be a source of human infections from poultry waste. While it colonises the intestines of poultry without generating symptoms, it is known to induce food-borne enteritis in humans (Facciola et al., 2017). *Campylobacter jejuni* is the most common *Campylobacter* species linked with poultry and the most common *Campylobacter* species involved with human disease (Sibanda et al., 2018). Infected laying hens regularly excrete large amounts of *C. jejuni* with their faeces, representing a reservoir of infection within the flock and animals in the region. Culturable *C. jejuni* can survive up to 96 hours in artificially infected faeces and 120 to 144 hours in spontaneously colonised flocks to make matters worse (Ahmed et al., 2013), making it highly transmissible to humans.

Pigeon manure piles may also contribute to *Campylobacter* infection in humans via vectors like flies (Nichols, 2005). The flies will then contaminate human food with *Campylobacter*, resulting in food poisoning. Arsenault et al. (2007) consistently discovered that when manure is located approximately 200 meters from a poultry farm, the prevalence of *Campylobacter* in poultry is 5.2 times higher.

Although the number of infection cases in Malaysia is not documented, there is an increased number of Listeriosis, Salmonellosis and Campylobacteriosis cases in Australia from 67, 6151 and 13595 cases in 2000 (Lin et al., 2010) to 84, 18088 and 24164 cases in 2016 (Hood, 2021), respectively. A similar pattern has been observed for Campylobacteriosis in England and Wales, between 2013 and 2020, with 3099 cases in 2013 (Public Health England, 2013) and 3378 cases in 2020 (UK Health Security Agency, 2020). It proves that the infection can occur in any nation but critically depend on the farmers' existing practices. Nevertheless, although significant measures and awareness have been taken, the number of cases continues to rise, highlighting the need for a more robust global response.

Numerous studies have also demonstrated that persistent infections may promote inflammation and that chronic or protracted inflammation may lead to cancer development.

It is because aberrant inflammatory responses have a role in numerous phases of tumour growth, including initiation, promotion, malignant conversion, invasion, and metastasis (Grivennikov et al., 2010). Germline mutations cause only 10% of all malignancies, while somatic mutations and environmental factors cause most (90%). According to Aggarwal et al. (2009), these environmental factors are highly related to bacterial or viral infections that induce chronic inflammation.

Cancer

Viral Infection-induced Cancer. Exposure to poultry manure is also linked to cancer development in humans, particularly among poultry workers. It could be due to recurrent or extended contact with oncogenic viruses in poultry faeces. According to Johnson et al. (2010), workers are more prone to get these oncogenic viruses due to daily contact with a high number of fowl and wound or skin injury that often occurs among workers. Oncogenic viruses discovered in poultry manure include reticuloendotheliosis virus (REV), avian leucosis sarcoma viruses (ALSV), papillomaviruses, and Marek's disease virus (MDV), all of which have been linked to haematological and lymphatic malignancies in both poultry and humans (Gopal et al., 2012).

Viral infection induces an inflammatory response necessary for virus elimination and tissue homeostasis, including tissue repair, regeneration, and remodelling (Medzhitov, 2008). Nonetheless, mounting evidence shows that tumour-associated viruses might avoid host protection, boosting cancer growth. It is owing to similarities between the innate immune system and tumour suppressor signalling, as both processes initiate cell cycle arrest and trigger apoptotic pathways. For instance, the main players of these signalling networks, p21 cyclin-dependent kinase inhibitor and p53, are present in both tumour suppressor and innate immune surveillance signalling networks. It suggests that the virus's capacity to target tumour suppressor pathways may be an immune evasion response that inhibits antiviral pathways and promotes the malignant transformation of the infected cell (Moore & Chang, 2010).

Interestingly, almost 20% of cancer cases begin with infection and chronic inflammation at the same site of inflammation (Grivennikov et al., 2010). Usually, chronic inflammation caused by infections may promote oncogenic mutations, early tumour promotion, genomic instability, and angiogenesis (Grivennikov et al., 2010). Nonetheless, tumour-associated inflammation often co-occurs with tumour formation, with upregulation of responses to tumour development, inflammation, neoangiogenesis, metastatic dissemination, tumour progression, local immunosuppression, and genomic instability (Grivennikov et al., 2010).

Aside from cancer, viral infection can cause various illnesses ranging from mild upper respiratory tract infection to severe pneumonia, acute respiratory distress syndrome, and even death. The fact that most human cases of influenza A (H5N1) and A (H7N9) virus

infection have been attributed to direct or indirect contact with infected live or dead poultry poses a public health risk. Hence, to reduce the risk to humans, it is necessary to establish an effective and safer poultry waste disposal system for all poultry, regardless of their health status. It is because the infection can only be discovered after it has affected individuals, making the treatments more challenging (Christin et al., 2016).

Heavy Metals-induced Cancer. Furthermore, it was revealed that poultry manure has a high concentration of heavy metals such as Cu, Mn, Zn, Fe, Mo, cobalt (Co), nickel (Ni), and selenium (Se), which are all beneficial to plant growth and development (Singh et al., 2018). Poultry manure also contains arsenic (As) and chromium (Cr) (Wang et al., 2021), both of which are known to generate epigenetic alterations and genetic defects when exposed to them for an extended period (Abdul et al., 2015).

Heavy metal poisoning may accelerate cancer growth by creating reactive oxygen and nitrogen species, which may result in oxidative stress and DNA damage. Consequently, this genetic instability will result in protein misfolding and the inactivation of enzymes essential for cells' proper functioning. Lead (Pb), nickel (Ni), and arsenic (As) are heavy metals that have been linked to an increased risk of cancer, with excessive exposure or ingestion promoting the growth of skin, bladder, lung, liver, colon, and kidney cancers (Mokhtar et al., 2022) (Figure 2).

Despite these risks, heavy metals such as As, Cu, Co, Fe, Se, Mn, and Zn are continuously added to poultry feed at levels greater than those permitted by regulatory authorities such as the National Research Council (NRC) and the European Union (EU), primarily for disease prevention and to increase weight gain and egg production in poultry (Adekanmi, 2021). According to Bolan et al. (2010), approximately

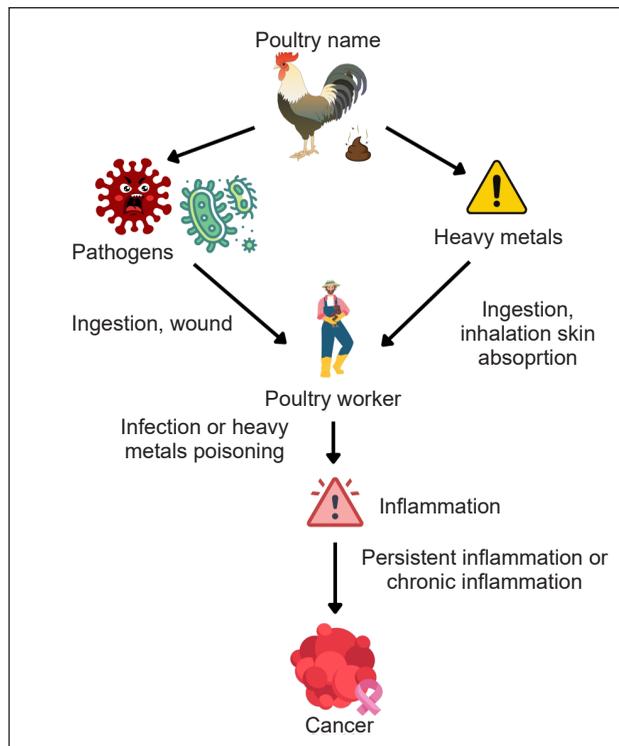


Figure 2. Human health-related risks associated with exposure to poultry manure. Poultry manure is known to contain pathogens and heavy metals. Exposure to these contaminants through ingestion, inhalation, wound or skin absorption may promote inflammation in humans, especially among poultry workers. Persistence or chronic inflammation will later promote cancer progression. Created with Canva.com

5 to 15% of heavy metals are absorbed, while the rest are excreted in faeces and urine into the poultry litter, which is then used as manure (Bolan et al., 2010). As a result, safe levels of heavy metals in poultry manure must be established for land application to avoid these negative consequences. Besides, using these supplements raises the daily discharge of anthropogenic wastes into the environment, particularly the aquatic environment, posing a severe health danger to humans and marine life (Adekanmi, 2021).

With these risks and implications, there is a need for suggestions to ease this issue and to ensure that the use of poultry manure is beneficial rather than detrimental. As mentioned previously, poultry manure is an excellent fertiliser due to its high concentration of nutrients necessary for plant growth and development, but it can also generate electricity via microbial fuel cell (MFC) technology due to high carbon sources, which could eventually serve as another source of renewable energy (Oyiwona et al., 2018).

SUGGESTIONS TO ALLEVIATE THE HEALTH-RELATED RISKS

Intense farming, livestock and poultry can excrete bacteria and viruses, including opportunistic pathogens, through their faeces, which may harm humans and the environment (Jiang et al., 2018). Treatment practices that aid in pathogen reduction in poultry waste are necessary to prevent the spread of these pathogenic microorganisms to humans. However, it is also critical to consider their implications in agricultural settings to ensure that agricultural production is not affected and that agricultural products are safe for consumption (Manyi-Loh et al., 2018).

Disinfection

Disinfection of poultry houses is a crucial step in preventing the transmission of pathogenic germs between batches in large-scale poultry farms. Infectious diseases can be prevented in poultry houses by selecting the appropriate disinfectants, disinfection procedures, and technologies. These techniques consist primarily of washing, soaking, fumigating, spraying, and UV irradiation (Jiang et al., 2018). Furthermore, aerosolised disinfectants have been utilised for more than half a century, as it is known to preserve resources while providing a disinfecting aerosol-vapour gas system. Besides, aerosolised disinfectant also improves the disinfectant's ability to penetrate the bacterial cell wall, increases the disinfection impact, and shortens the disinfection time (Jiang et al., 2018).

Composting

Composting, where poultry wastes are processed to be utilised as organic fertiliser, is one of the most used treatment procedures (Glatz et al., 2011). It is a microbe-driven process that is beneficial for eradicating pathogens such as *Campylobacter* and *Listeria*. *Bacillus* and *Lentibacillus* are two effective microorganisms (EMs) commonly used in composting

due to their high amino acid metabolism. These EMs secrete diverse proteases and can stimulate the dominant microbiota in poultry manure's carbohydrate metabolism (Zhang et al., 2018). Several co-composting options combine various kinds of waste to obtain 'tailored' products with designed properties (Giagnoni et al., 2020).

Although composting has been used for an extended period, the accumulation of waste at the producer level underscored the importance of proposing an environmentally safe composting system. According to Lemunier et al. (2005), *L. monocytogenes* was detected in 4-week-old seeded in-vessel biowaste composts, showing the need for a more thorough and prolonged composting process that can inhibit the pathogen's survival. Thus, by extending the composting process, it is possible to reduce the pathogens' survivability and thus prevent their spread and manifestations in humans. However, composting does not guarantee that the composted product is pathogen free, as some pathogens, such as thermolabile *Salmonella*, are heat resistant. In addition, some cells may become stress-adapted throughout the build-up or composting process, which protects them from future treatments (Lemunier et al., 2005).

Deep Stacking

The storage of poultry litter serves two primary functions: (1) it serves as a holding area between cleaning and feeding, and (2) it serves to eradicate any pathogens found in the litter (Waziri, 2017). Deep stacking is the most widely used and cost-effective storage method for four to six weeks. The litter is said to undergo a combined composting-ensiling process, where EMs are used as an initiator due to their metabolic processes, which heat the litter stacks from 140 °F to 160 °F. With this elevated temperature, any pathogens found in raw litter, such as *Salmonella*, can be eradicated (Bush et al., 2007; Wilkinson et al., 2011). However, caution should avoid overheating the litter, which can deplete the nutrients.

The litter should contain between 20%–30% moisture and be stacked at approximately 6–8 feet to ensure proper heating during deep stacking. It is because humidity below this point can obstruct heating to the 130-degree threshold, interfering with the margin of safety against pathogens. Additionally, it has been discovered that deeper stacking promotes better heating due to its critical mass and can inhibit mould growth. Before use, it is recommended that the litter be deep stacked for four to six weeks to allow for sufficient heat generation to kill pathogens, including some thermolabile pathogens such as *Salmonella* (Bush et al., 2007).

Microbial Fuel Cell (MFC) Technology

Interestingly, due to the large number of carbon sources in poultry waste, it has also been used as a substrate for producing renewable energy. It is accomplished through a process known as microbial fuel cell (MFC) technology, which utilises electrogenic bacteria (EB)

such as *Bacillus subtilis* as a catalyst to oxidise the organic and inorganic matter in poultry waste to generate electricity (Muaz et al., 2019) (Figure 3). Not only can this technology be used to generate electricity, but it can also initiate and promote the biodegradation of organic wastes (Muaz et al., 2019).

Although no study has been conducted to date on the benefits of MFC in reducing health-related risks, it may aid in the removal of harmful substances found in poultry manure (Mokhtar et al., 2022). It is because MFC utilised some EB that may secrete metabolites, bacteriocin or macromolecules with anti-inflammatory or anti-cancer properties. Interestingly, *Bacillus subtilis* has been shown to possess an anti-inflammatory property due to its ability to secrete Exopolysaccharide (EPS), which promotes the development of M2 macrophages, inhibiting T cell activation (Paynich et al., 2017). Additionally, bioflocculant, a metabolite composed of polysaccharides, proteins, glycoproteins, and proteoglycans from *Bacillus subtilis* F9, was shown to have a high capacity for scavenging DPPH, hydroxyl, and superoxide radicals, making it a promising antioxidant or anti-cancer agent (Giri et al., 2019). The MFC also produces carbon dioxide and water, which are essential vegetation components, demonstrating the MFC's utility in an agricultural setting.

Aside from that, several studies have discovered the benefits of MFC technology in promoting bacteria found in WWTPs to be susceptible to antibiotics. It is due to MFC's ability to break down antibiotics and Antibiotic resistance genes (ARGs), which is a major contributor to AMR development, increasing the likelihood that it will help prevent AMR transmission in the environment. It is proven by Ondon et al. (2020) and Xue et al. (2019), who found MFC technology to be able to remove 85.1% and 65.5% of sulfamethoxazole (SMX) and norfloxacin (NFLX), respectively (Ondon et al., 2020; Xue et al., 2019).

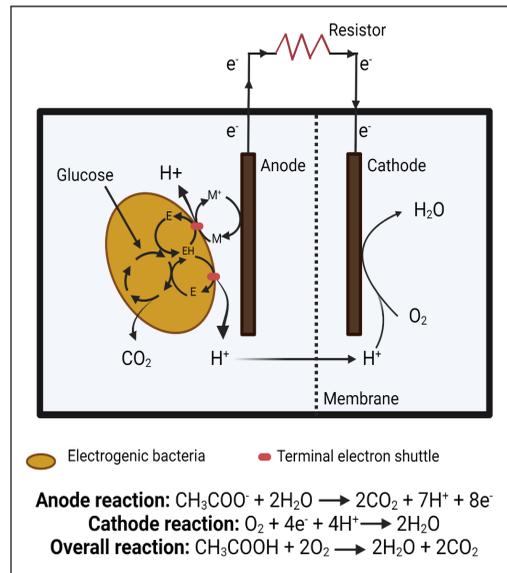


Figure 3. The principal operation of the microbial Fuel cell. Biodegradable substrates varying from pure chemicals to complex mixtures of organic compounds are metabolised by electrogenic bacteria (EB). EB near the anode would decompose the organic materials, transporting the electrons directly through cell components such as proteases or nanowires on the membrane surface or indirectly via the electron shuttle. The cathode accepts electrons and protons from the anode and initiates a reduction process. The MFC, also known as mediator-less MFC, should no mediators be added or utilised. M: redox mediator; E and EH represent the enzyme in reduced and oxidised form, respectively. Adapted from (Zhu et al., 2019). Created with BioRender.com

Additionally, the number of ARGs and integrons after MFC treatment was significantly less than that discovered in WWTPs. For example, the relative abundance of the *int11* is between 63.11 and 652.00 copies/mL(g) in the MFC product compared to 109 to 1011 copies/mL in WWTPs (Chen et al., 2021).

Nevertheless, it is critical to remember that each treatment process must be appropriately managed. Even composting, which is exceptionally effective at pathogen reduction, may cause *Salmonella* regrowth if the composting process and composed litter are adequately handled (Sidhu, 2001). The most effective way to prevent disease outbreaks among poultry farmers is to dress appropriately and avoid confined or poorly ventilated areas, which is more practical and applicable to everyone. Additionally, the awareness of farmers and authorities needs to be raised regarding poultry manure management. There should be stricter enforcement of existing environmental regulations and the enactment of new legislation to minimise the threats that the farmers' current practices pose to their health and the environment.

CONCLUSION AND FUTURE DIRECTIONS

Even though poultry manure has been routinely applied to land as organic fertiliser or soil improvement, it will surely influence the survival and spread of pathogens such as *Listeria*, *Salmonella*, and *Campylobacter* to the environment. Improper handling and treatment of poultry manure contribute to spreading these pathogens to the environment and humans, promoting inflammation and cancer progression in the long run. Thus, before land application, it is vital to improve current approaches for preventing these pathogens from colonising. Nonetheless, current therapies are ineffective and require additional refinements, such as developing new technologies or procedures capable of fully utilising poultry manure while eradicating pathogenic microflora and pathogens. Furthermore, it would be advantageous to implement new technologies or techniques that expedite manure processing while minimising capital expenditures.

Physical, chemical, and biological treatments are all viable options for eliminating and inactivating heavy metals and quantifying reductions in various bacterial pathogens and indigenous microorganisms in poultry manure. However, these treatments may not eradicate heavy metals or food-borne microorganisms permanently. It is due to the possibility of pathogens, such as faecal coliforms, which are resistant to treatment and undiscovered by existing laboratory detection methods. However, not all faecal coliforms or detected pathogens originate from animal faeces, making it more challenging to study the fate of pathogens in animal wastes after various treatments. Nevertheless, the priority should be inactivating the most resistant and tenacious varieties of infections one could encounter. Therefore, future research should focus on analysing the survivability of selected pathogens in response to various treatments under specific conditions often encountered

when treating poultry manure. It will enable the identification of a comprehensive profile of the various types and concentrations of each pathogen following various treatment approaches, facilitating an accurate evaluation of their risk to humans. These data would aid the poultry business, the healthcare sector, and allied agricultural industries, allowing them to manage waste effectively and reap its benefits without endangering human life.

In addition, each type of treatment can be employed in conjunction with other disinfection or treatment procedures to increase pathogen lethality. This approach may completely eradicate pathogens from poultry manure if the appropriate control mechanisms are implemented. However, owing to the many treatments involved, it will undoubtedly increase the capital costs associated with poultry management.

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