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Invited Review Article

Unusual stories of transmission of diseases from plants to animal kingdom: Tale of phytonoses scripted

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Abstract

'Phytonosis' (plural phytonoses), the terminology coined by van der Riet in 1997, is any infectious disease that can be transmitted from plants to humans or vice versa. Although the concept of transmission of diseases between plants and human has long been neglected or considered of minor importance, recent emergence of several human disease outbreaks from plant sources makes this topic very relevant and important. A paradigm-shift in the way we think about communicable diseases happened with the first reported outbreak of hemolytic uremic syndrome in Germany and France in 2011 caused by a human pathogenic bacterium that was adapted to the plant environment for a long time. The major mechanism of adaptation of human pathogens to plant sources is horizontal gene transfer among microorganisms residing in soil, human digestive tract (manure), water and plants. In the impending climate change scenario, phytonoses may have critical impacts on human and animal health and safety, and should be given high importance in line with 'One health approach'. This review deals with the concept of phytonosis, molecular mechanisms of microorganisms for cross-kingdom jumping, some reports of bacterial, fungal and viral pathogens with cross-kingdom jumping potential and safety measures to be taken for control of phytonosis.

Keywords: Human, One health, Phytonosis, Plants, Transmissible diseases

Highlights

- Phytonoses are diseases that can be transmitted from plants to humans or vice versa.
- Recent emergence of several devastating human disease outbreaks from plant sources has been recorded.
- Horizontal gene transfer is considered as the major mechanism of cross-kingdom host jump.
- Recent impending climate change scenario may create a favourable environment for cross-kingdom infection.
- Proper care and precautions should be taken in handling plant pathogens and plant-associated microorganisms.

INTRODUCTION

Recently "One health approach' has gained momentum not only to prevent zoonotic disease outbreaks but also to address other emerging environmental issues like antimicrobial and anthelmintic resistance, food safety and to attain better public health outcomes (Essack, 2018; Aggarwal and Ramachandran, 2020). It is a holistic integrated approach to optimize the health of humans, animals, and surrounding ecosystems (Prata *et al*., 2022).We always speak about transmission of infectious agents from animals to human or vice-versa. But besides the kingdom of animals (both terrestrial and aquatic), another kingdom co-exists which we call as plant kingdom. When we call the experts of zoonotic diseases, we fill up the forum with medicos, public health experts, veterinarians, wildlife experts and the professionals dealing with fish diseases. But one health approach to control diseases to *Homo sapiens* transmitted from animals and as well as from plants should be taken care of, then the forum of experts become saturated.

The hypothesis of transmission of diseases between plants and human was proposed by van der Riet in 1997 (van der Riet, 1997; van der Riet, 2000). This hypothesis was based on the findings that the genome of human uveitis mycoplasma-like organisms (MLO) shared a high degree of similarity to plant MLO, which prompted him to hypothesize that human and plant MLO descended from a common ancestor or this might be due to the convergent evolution of the organism infecting plants and human (van der Riet, 1997). He coined the term 'phytonosis' (plural phytonoses) to depict any infectious diseases transmissible between plants and human (van der Riet, 1997) keeping similarity with the term 'zoonosis'(Andrews and Walton, 1977). In another words, phytonoses are those diseases which undergo inter/cross

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kingdom transfer, i.e., transfer of diseases from plants to animals, and the organisms may be animal/human pathogens living around the created microenvironment by plants or those organisms may be related to plant kingdom either in mutualistic or commensal forms or may be a virulent plant pathogen (Kim *et al*., 2020).

Pathogenic microorganisms that infect both plants and humans did not get much attention until recently (Kirzinger *et al.*, 2011; Vidaver *et al.*, 2017). Hubálek (2003) classified emerging human diseases into three categories; (i) anthroponoses: diseases transmissible between humans, (ii) zoonoses: diseases transmissible from animals to humans or vice versa and (iii) sapronoses: diseases transmissible from environment to humans. In this classification of emerging diseases, 'phytonoses' was not mentioned. Species under Pantoea, Burkholderia, Rhizobium and Pseudomonas are primarily plant pathogens but can cause human or animal diseases. On the other hand, some species of *Salmonella* (Schikora *et al.*, 2008; Barak *et al.*, 2011), Enterobacter (Nishijima *et al.*, 2007), Shigella (Jo *et al.*, 2019) and Enterococcus (Jha *et al.*, 2005) can infect plants despite being considered as animal pathogens. It is relevant to mention that large disease outbreaks with human pathogenic bacteria especially *Escherichia coli* and *Salmonella enterica* resulting from contamination of vegetables and sprouts are not very rare (Lim *et al*., 2014; Callejón *et al*., 2015). First recognized community outbreak of haemorrhagic colitis due to verotoxin-producing *Escherichia coli* O 157:H7 was recorded in the UK (Morgan *et al*., 1988). Thereafter, from time-to-time disease outbreaks from vegetables and fruits have been recorded (Table 1). In India, a total of 172 outbreaks from grains and beans and 94 outbreaks from fruits and vegetables have been reported from 2009–2018 (Bisht *et al*., 2021).

The first outbreak incidence caused by a human pathogenic bacterium that was adapted to the plant environment was reported in Germany and France in 2011, and this incidence created a paradigm shift in the way we think about communicable diseases. The outbreak was due to *Escherichia coli* O104:H4, and more than 4000 persons were infected including 54 casualties and more than 900 cases of hemolytic uremic syndrome (HUS) (Karch *et al.*, 2011; Beutin and Martin, 2012). Epidemiological investigations indicated that the pathogens were transmitted to human from infected fenugreek seeds that were transported to the Netherlands from Egypt approximately 17 months before appearance of the first disease incidence(Karch *et al.*, 2011). This was remarkable because a human pathogen can survive in an uncommon environment for such a long time, and

Table 1. Some examples of community disease outbreaks resulting from contamination of vegetables and sprouts with human pathogenic bacteria

Location	Pathogen	Food source	References
East Anglia (UK)	*E. coli* O157:H7	Potato tubers	Morgan *et al.*(1988)
Osaka (Japan)	*E. coli* O157:H7	Radish sprouts	Michino *et al.* (1999)
Connecticut (USA)	*E. coli* O157:H7	Mesclun lettuce	Hilborn *et al.* (1999)
Western USA, British Columbia (Canada)	*E. coli* O157:H7	Unpasteurized apple juice	Cody *et al.* (1999)
California (USA)	*E. coli* O157:H7, *S. enterica*	Alfalfa and clover sprouts	Mohle-Boetani *et al.* (2001)
Michigan (USA)	*E. coli* O157:H7	Alfalfa sprouts	Breuer *et al.* (2001)
Multistate outbreak (USA)	*E. coli* O157:H7	Packaged spinach	Wendel *et al.* (2009)
Hamburg (Germany)	*E. coli* O104:H4	Fenugreek sprouts	Bielaszewska *et al.* (2011)
USA	*E. coli* O121	Raw clover sprouts	CDC, 2014
USA	*E. coli* O157:H7	Romaine lettuce	CDC, 2012
USA	*E. coli* O104:H4	Sprouts	CDC, 2011
German	*E. coli* O104:H4	Sprouts	Buchholz *et al.* (2011); Frank *et al.* (2011)
France	*E. coli* O104:H4	Fenugreek seeds	King *et al.* (2012)
England, Wales and Scotland	*E. coli* O157 PT8	Raw leeks and potatoes	Launders *et al.* (2016)
Brazil	*Salmonella*	Fruits and vegetable	Elias *et al.*(2018)

maintain pathogenicity was never thought of (van Overbeek *et al.*, 2014). Moreover, it is important to note that *E. coli* strain O104:H4 is not generally associated with disease incidences in humans, whereas *E. coli* strain O157:H7 and *Salmonella enterica* are generally associated. It was highly reasonable to hypothesize that *E. coli* O104:H4 which was responsible for outbreak in Germany and France must have acquired virulence through horizontal gene transfer (Mellmann *et al.*, 2011; Muniesa *et al.*, 2012).

Cross road of different ecosystems: A vulnerable factor for emergence of pathogens with cross-kingdom jumping potential

To understand plant associated microbial communities, two terminologies are very relevant, one is Rhizosphere and another is Phyllosphere. The rhizosphere also known as the root microbiome, is the microbial communities associated with the soil and root system that is directly influenced by root secretions and associated soil compositions, whereas the Phyllosphere is defined as the aerial part of the plant or the parts of a plant above the ground, usually the surface of leaves, and is considered to be a habitat for microorganisms (Turner *et al.*, 2013). Agricultural plant ecosystem is considered as the cross road where microbial communities from four to five different environments (soil, plants, animal derived manure, water) intermix with each other (Enagbonma *et al.*, 2023). The flow or intermixing of the microorganisms in plant ecosystem is presented in Fig. 1.

Movement of microorganisms residing in animal guts

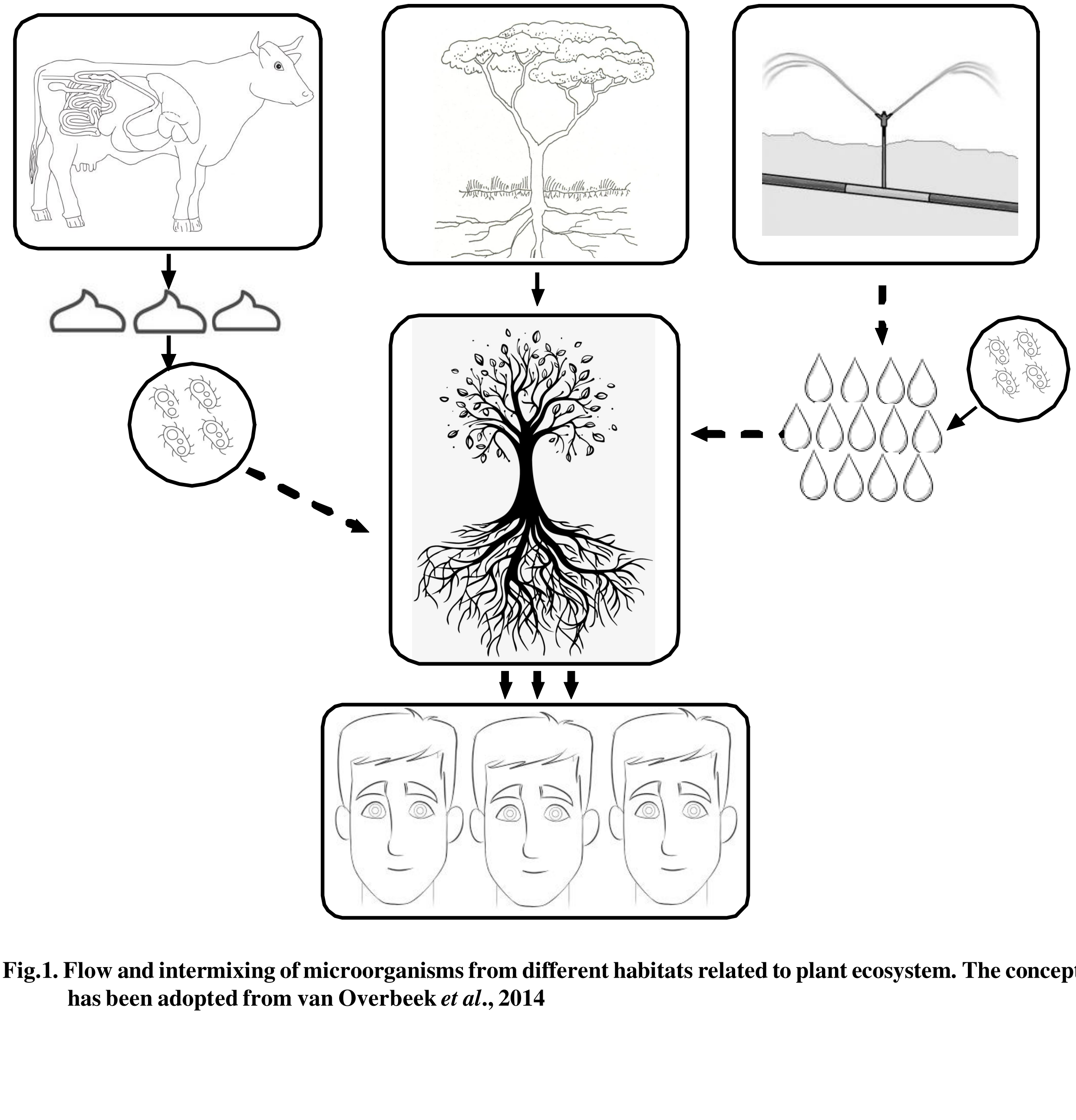

Fig.1. Flow and intermixing of microorganisms from different habitats related to plant ecosystem. The concept has been adopted from van Overbeek *et al.*, 2014

into plant ecosystems may occur through manure applied to agricultural land. Irrigation of agricultural land with contaminated water may lead to infection of soil or plant surface. Interchange of microbial communities between animals and plants happen through direct contact or may be facilitated by insects. Microbial community structure of these ecosystem varies considerably from each other but plant ecosystem is the place where different microbial communities get a chance to intermix with each other or into physical contact with each other which induces genetic exchanges via horizontal transfer (Aminov, 2011). Horizontal gene transfer mediated evolution of the microorganisms is considered as the driving force for the microorganisms to adapt to uncommon environment or host (Emamalipour *et al.*, 2020). Human pathogens may obtain genetic fragments from plant-associated bacteria, making them fit for survival in the plant environment and vice versa (Szmolka and Nagy, 2013).

Plant Rhizosphere and Phyllosphere are two important storehouses of microbial communities. These microorganisms may be human/animal pathogens and plant associated bacteria (mutualistic/commensal/ pathogenic to plants). Animal/human pathogens may obtain genetic material from bacteria associated with plants, which could result in new phenotypes with traits including improved persistence in plants or their propagation materials, greater stress resistance, or a wider range in the acquisition or utilization of available nutrients (van Overbeek *et al.*, 2014). Thus, the pathogens will be better able to survive in a plant environment because of these characteristics. On the contrary, plant associated bacteria may obtain virulence genes from animal/human pathogens, and new pathogen evolves which could infect the members of animal kingdom (Kirzinger *et al.*, 2011). As for example, opportunistic human pathogens like *E.coli* and *Salmonella* are very common on plant surfaces, and there is a high chance of gene transfer with typical plant-associated bacteria like*Enterobacter*, *Serratia, Klebsiella*, *Erwinia*, *Pantoea* and *Pectobacterium* (van Overbeek *et al.*, 2014). Similarly, commensal organisms living on plant surfaces may acquire genetic elements from plant-invasive human pathogens and transform into human pathogenic organisms (Szmolka and Nagy, 2013). Phytonoses start either with the better adoptable human/animal pathogen in plant environment or with the emerging recombinant plant associated bacteria infective to human/animal (Wilkinson *et al.*, 2011).

Mechanism of microbial infection

In general, pathogenic organisms have a specific host range which is known as 'host specificity' (Kirzinger *et al.*, 2012). Pathogenic organisms exhibit various levels of host specificity; some organisms are highly adapted to a particular single-host species, whereas some pathogenic organisms have the ability to infect a wide variety of organisms and in some cases, organisms belonging to different biological kingdoms. One good example of microbial organism with cross-kingdom jumping potential is *Agrobacterium tumefaciens*, an alphabacterium found in soil. It infects rosacoons plants and causes tumor formation in susceptible plants (Hayward and Waterston, 1965). Later, it was found that the organism has the potential to infect humans also (Paphitou and Rolston, 2003; Lacroix *et al.*, 2006). It will be interesting to understand how a pathogenic organism which is adapted to a particular host belonging to a kingdom can infect other hosts of a different kingdom.

Pathogenic microorganisms can be divided into three major categories (i) obligate (ii) facultative and (iii) opportunistic pathogens. The host range of obligate pathogens are generally very narrow as they are dependent on the living host for replication and survival. Facultative pathogens also have a narrow host range, but they have the ability to survive outside the host species (inanimate environment). Opportunistic pathogens show a wide-array of host range as they can survive on a wide range of organic substrates. Generally, they have low virulence, but can become aggressive when the host species become weak with compromised immune system.

The well-accepted seven kingdoms of life are:

(i) Eubacteria (Woese and Fox, 1977)
(ii) Archaea (Woese and Fox, 1977; Woese *et al.*, 1990)
(iii) Protista (Whittaker, 1959)
(iv) Chromista (Cavalier-Smith, 1981)
(v) Fungi (Whittaker, 1959)
(vi) Plantae (Whittaker, 1959)
(vii) Animalia (Whittaker, 1959)

Establishment of infection by pathogenic microorganisms

Although the mechanism of establishment of infection varies among microorganisms, the basic steps remain the same (Fig. 2). To establish infection, any pathogen must be able to invade and colonize the host, escape the host immune system, replicate themselves with the resources of the host and spread to another host (Alberts *et al.*, 2002).

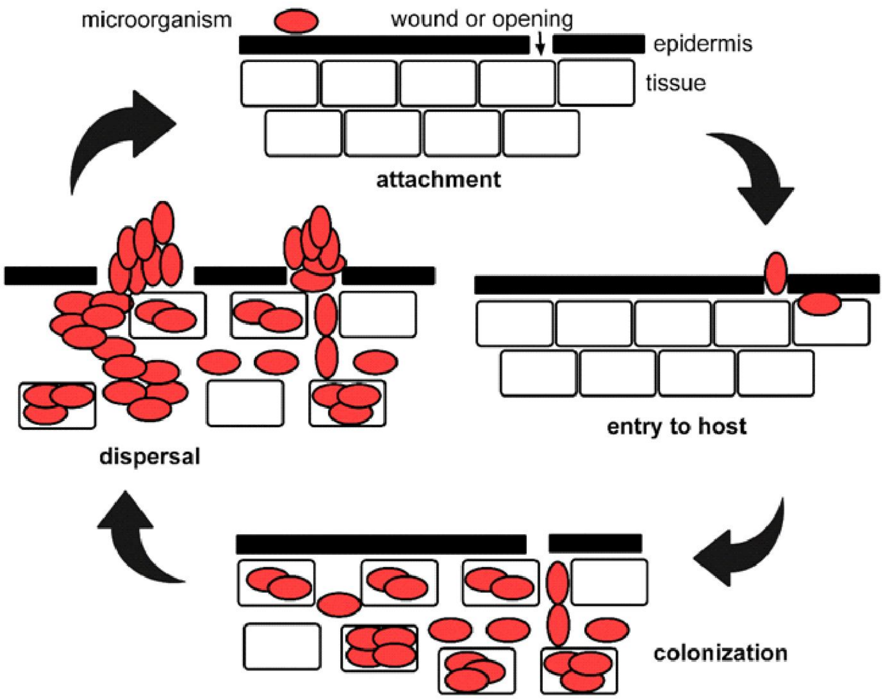

Fig. 2. General mechanism of a microbial infection. The concept has been adopted from van Baarlen *et al.*, 2007

Attachment of the microorganisms to the host tissue or cells: Pathogenic organisms use specific surface-associated adherence factors (Hahn, 1997) or Microbial Surface Components Recognizing Adhesive Matrix Molecules (MSCRAMMs) for attachment (Kreikemeyer *et al.*, 2004; Rivas *et al.*, 2004)

Entry of the microorganisms to the host: Microorganisms may enter the host cell (intracellular) or may remain in the intercellular spaces between host cells (extracellular). Intracellular microorganisms enter cells with the help of surface-exposed proteins (Isberg *et al.*, 1987) or by secreting toxins that induce cytoskeleton remodelling (Takenouchi *et al.*, 2004). Extracellular microorganisms enter cells through wounds or natural openings.

Colonization of the microorganisms in the host: The microorganisms colonize in the host in order to survive and replicate. Plant-specific microorganisms are classified into two major groups; biotrophs and necrotrophs (Thomma *et al.*, 2001). Biotrophs suppress host defence system and feed on living plant cells (Vogele and Mendgen, 2003), whereas necrotrophs secrete toxins or lytic enzymes and get nutrients from necrotic tissues. In case of humans or animals, the infection may be acute when the pathogen spreads quickly or chronic when it causes long term infection.

Disposal: In this stage, the organism is released from the host and infects a new host.

Molecular mechanism of cross-kingdom host jumps

To infect a host, the microorganism must be compatible with the host (Casadevall and Pirofski, 2000). Genetic constitution of the microbial pathogen and the target host determines the compatibility. Moreover, environmental conditions also play a role. The important requirements for establishing a pathogenic relationship are as follows.

- Proximity and physical contact between the pathogen and the target host
- For establishment of pathogenicity, the host should be able to meet all required conditions for the microorganisms to complete its life cycle. The host should be able to provide essential cellular and nutrient requirements such as water, amino acids, micronutrients and energy.
- The microorganism should be able to suppress or avoid the immune system of the host.

The major mechanism of adaptation of human pathogens to plant sources is horizontal gene transfer

(Aminov, 2011) among microorganisms residing in soil, human digestive tract (manure), water and plants. Gene transfer among microorganisms occurs when they physically interact with each other in the same habitat (Toth *et al.*, 2006). This transfer happens mainly through plasmids, (pro) phages and conjugative transposons (Juhas *et al.*, 2009). There are three mechanisms of horizontal gene transfer (Fig. 3); transformation, transduction and conjugation. In transformation, following the death of a microorganism, the genetic material leaks out, which is absorbed by another microorganism and incorporated into its genome. Transduction happens through bacteriophage. If a bacteriophage infects a bacterium, the bacteria is forced to produce more phages, and some phages may contain some part of bacterial genome. When these phages infect another bacterium, the bacterial genome is transferred to the other bacteria. Conjugation happens through transfer of plasmids, which are transferred from one microorganism to another through sex pilus. Rhizosphere and Phyllosphere are two such environments where such gene transfer occurs.

After transfer of a microorganism to unnatural host, survival of the organism depends on its adaptation to

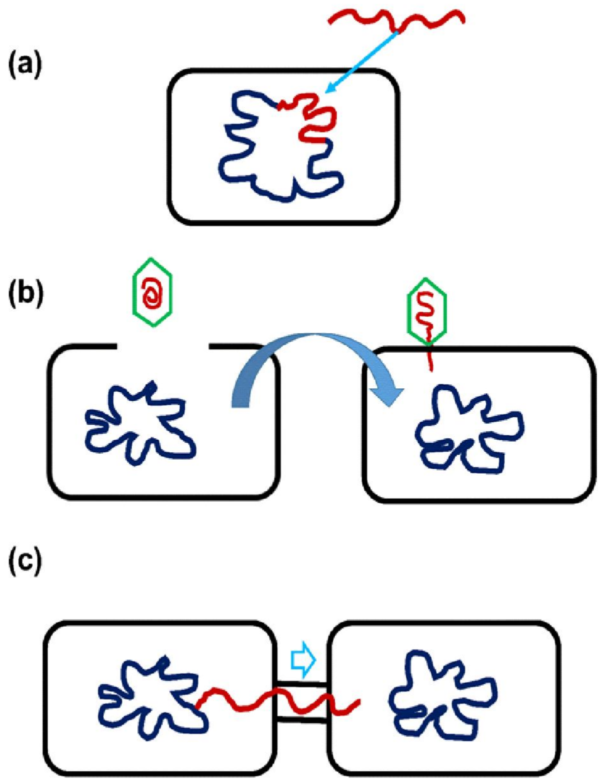

Fig. 3. Horizontal gene transfer, (a) transformation, (b) transduction and (c) conjugation

host environment. Pathogenicity of the microorganism may be altered based on modifications at the transcriptional level (Berg *et al.*, 2005). For establishing pathogenicity, the microorganism must suppress or avoid immune responses of the host. There is a drastic variation in immune system of animals and plants. Self-defence of invertebrate animals and plants depend completely on innate immunity (van Baarlen *et al.*, 2007), whereas vertebrate animals have a complex immune system including innate immunity and adaptive immune system (Litman *et al.*, 2010). Despite differences, some features like molecular structures involved in microbial recognition, the defensive use of reactive oxygen species and antimicrobial peptides and proteins are very much common among immune systems of different higher eukaryotic kingdoms (van Baarlen *et al.*, 2007). Moreover, host defence mechanism at molecular level shares high degree of similarity among different kingdoms (van Baarlen *et al.*, 2007) and the ability of a microorganism to overcome immune system of one host is linked to its ability to overcome immune system in other hosts through similarities in their defence methodologies (van Baarlen *et al.*, 2007).

Examples of plant and human cross-kingdom pathogens

Although the diseases transmitted from plants to humans and vice-versa were neglected for a long time, in recent years, much emphasis has been given to the topic, and increasing numbers of plant-pathogenic microbial organisms associated with human diseases have been reported (van Baarlen *et al.*, 2007; Kirzinger *et al.*, 2011). In case of bacterial pathogens, around 5% of 500 pathogenic bacteria species associated with human infections are plant pathogens (Taylor *et al.*, 2001). Few important examples of plants associated bacterial pathogens involved in reported human infections are presented in Table 2.

In the context of fungal infections in human, more than 300 pathogenic fungi have been isolated from human, of which at least 54 are known plant pathogens (Taylor *et al.*, 2001; Pfaller and Diekema, 2010). Some important examples of plants associated fungal pathogens involved in reported human infections are presented in Table 3.

The plant viruses that are very much stable in soil, water and non-living environment are most potent to infect humans (Mandal and Jain, 2010; Baènik *et al.*, 2020). As for example, tobacco mosaic virus (TMV) was reported to be associated with pulmonary disease in smokers in 1967 (LeClair, 1967). Some important examples of plants associated viral pathogens involved in reported human infections are presented in Table 4.

Table 2. Some important examples of plant-associated bacterial pathogens involved in human diseases

Pathogen name	Plant disease	Human disease	References
Bacillus megaterium	White blotch of wheat	Oral mucosal inflammation	Murdoch and Campana,1983; Rubinstein and Pedersen, 2002
Bacillus circulans	Date palm disease	Peritonitis, diarrhoea	Berry *et al.*, 2004; Rowan *et al.*, 2003; Deva and Narayan,1989
Bacillus pumilus	Bacterial blotch of immature Balady peach, root disease in soybean	Oral mucosal inflammation	Saleh *et al.*, 1997; Suominen *et al.*, 1999; Rubinstein and Pedersen, 2002
Burkholderia cepacia	Sour skin of onion	Cardiac cirrhosis and endophthalmitis	Burkholder, 1950; Yohalem and Lorbeer, 1997; Lau *et al.*, 1999; Pathengay *et al.*, 2005
Burkholderia cenocepacia	Fruit rot	Septicemia	Lee and Chan, 2007; Kirzinger *et al.*, 2011
Burkholderia glumae	Rice rot	Chronic granulomatous disease	Maeda *et al.*, 2006; Kirzinger *et al.*, 2011
Burkholderia plantarii	Seedling blight of rice	Melioidosis	Maeda *et al.*, 2006; Kirzinger *et al.*, 2011
Burkholderia pseudomallei	Tomato rot	Meliodosis, glanders	Lee *et al.*, 2010; Kirzinger *et al.*, 2011
*Curtobacterium flaccumfacien s*pv. *flaccumfaciens*	Bean wilt and blight	Septic arthritis	Collins and Jones,1983; Francis *et al.*, 2011
Erwinia persicina	Necrosis in fruits, vegetables	Urinary tract infection	Hao *et al.*,1990; O'Hara *et al.*,1998
Stenotrophomonas maltophilia	Plant pathogen	Respiratory tract infections	Denton and Kerr, 1998; Suckstorff and Berg, 2003; Goss *et al.*, 2004
Pseudomonas aeruginosa	Onion rot	Meningitis, bacteremia, and sepsis	Cother *et al.*, 1976; Torii *et al.*, 2003
Serratia marcescens	Alfalfa crown and root rot, cucurbit yellow vine disease, and endophytic colonization of rice	Respiratory tract infections, urinary tract infections, and bacteremia	Lukezic *et al.*, 1982; Gyaneshwar *et al.*, 2001; Ostrowsky *et al.*, 2002; Bruton *et al.*, 2003

Safety measures in dealing with plant pathogens

As the transmission of diseases from plants to humans is generally neglected, any specific standard operating procedure or cautionary statement with respect to potential human health risks is not clearly mentioned in laboratory manuals that deal with methods of handling plant pathogens (Vidaver *et al.*, 2017). Moreover, safety measurements relating to handling of plant pathogens or plant-associated organisms during occupational exposure are not properly depicted in any written document (Vidaver *et al.*, 2017). Almost all plant-associated microorganisms have been grouped under NIH risk group 1 (NIH, 2002). For handling of pathogens under NIH risk group 1, which are considered safe for humans, biosafety level 1 (BSL1) is usually recommended. As the recent concept of phytonoses emerges, plant pathogens may infect human beings and sometimes may cause life-threatening diseases; certain safety measures should be taken in healing with plant-associated microorganisms. Humans may get infection

Table 3. Some important examples of plant-associated fungal pathogens involved in human diseases

Pathogen name	Plant disease	Human disease	References
Alternaria alternata	Leaf spots, blights, damping off, and stem and fruit rots in a wide variety of plants and vegetables	Phaeohyphomycosis, palatal ulcers	Duffill and Coley, 1993; Westcott, 2001; Revankar and Sutton, 2010
Alternaria tenuissima	Strawberry fruit rot, leaf spot of high bush blueberry	Phaeohyphomycosis	Howard and Albregts, 1973; Milholland, 1995; Romano *et al.*, 1996; Romano *et al.*, 1997
Aspergillus flavus	Kernel rot of maize, yellow mold of peanut, and boll rot on cotton	Systemic aspergillosis, endocarditis and keratitis	Smart *et al.*, 1990; Pitt *et al.*, 1991; Brown *et al.*, 1992; Yamada *et al.*, 1998; Rao and Saha, 2000; St Leger *et al.*, 2000; Thomas and Kaliamurthy, 2013
Aspergillus niger	Black mold of peanut and onion and maize ear rot	Pulmonary aspergillosis	Tanakaand Nonaka, 1977; Nyvall, 1979; Yamaguchi *et al.*, 1992
Aureobasidium pullulans	Russet of apple fruit	Pulmonary mycoses, scleritis and phaeohyphomycosis	Kaczmarski *et al.*, 1986; Heidenreich *et al.*, 1997; Gupta *et al.*, 2001
Bipolaris spicifera	Leaf spot of cotton	Meningitis and peritonitis	Latham, 2000; Bava *et al.,* 2003
Colletotrichum coccodes	Black dot of tomato and potato	Phaeohyphomycosis	Dillard and Cobb,1997; Andrivon *et al.*, 1998; O'Quinn *et al.*, 2001
Colletotrichum dematium	Anthracnose of grains	Keratitis	Serfling *et al.*, 2007
Curvularia bracyspora	Leaf spot disease of *Rosa* spp.	Mycotic keratitis	Kore and Bhide, 1976; Marcus *et al.*, 1992
Curvularia geniculata	Banana leaf spot	Mycotic keratitis	Meredith, 1963; Georg, 1964
Curvularia pallescens	Leaf spot of sugarcane, leaf spot and ear rot of maize	Phaeohyphomycosis	Rao *et al.*, 1992; Lal and Tripathi, 1977; Agrawal and Singh, 1995
Fusarium fujikuroi	Bakanae disease (Foolish seedling disease in rice)	Keratitis	Chang *et al.*, 2006; Hwang *et al.*, 2013
Lecythophora hoffmannii	Soft rots of timber	Chronic sinusitis	Bugos *et al.*,1988; Marriott *et al.*, 1997
Phaeoacremonium rubrigenum	Woody plants, wilt and decline	Phaeohyphomycosis	Mostert *et al.*, 2005
Mucor circinelloides	Mucor rot of mango	Gangrenous mucormycosis	Boyd *et al.*, 2003

from infected plant materials like infested seeds, contaminated farm machinery and containers, irrigation water, and during post harvest handling. People working on pathogen isolation and culture or conducting experiments with plant diseases are more vulnerable to get infection. Therefore, it is always prudent to use some

Table 4. Some important examples of plant-associated viral pathogens involved in humandiseases

Pathogen name	Plant disease	Human disease	References
Tobacco mosaic virus (TMV)	Mosaic disease of tobacco, tomato, Pepper and other hosts	Pulmonary diseases	Harrison and Wilson, 1999; Lipkin and Anthony, 2015
Pepper mild mottlevirus	Mottling of pepper leaves and severe distortion of fruits	Abdominal pains and pruritus immune responses	Alonso *et al.*, 1989; Zhang *et al.*, 2006; Jarret *et al.*, 2008; Nakamura *et al.*, 2009
Acanthocystis turfacea chlorella Virus1 (ATCV-1)	Infects *Chlorella heliozoae*	Impaired cognitive functions	Nault, 1997; Van Etten *et al.*, 2012
Phaeodactylum tricornutum virus (PtV)	Infects *P. tricornutum*	Uterus fibroids and uterine cervix erosion	Stepanova *et al.*, 2011

precautionary steps during handling of plant-associated microorganisms or diseased plant specimens to minimize the chance of infection to humans.

- Immunocompromised persons are more vulnerable to get infection from plant-associated microorganisms. Therefore, they should take special care in handling plant microorganisms. During handling direct contact with skin should be avoided.
- Laboratory persons handling with plant pathogens should be always equipped with Personal Protective Equipment (PPE).
- It is always advisable to use disposable gloves and alcohol-based hand sanitizers in handling plant-associated microorganisms or diseased plant specimens.
- BL1-P or BL2-P plant containment conditions should be followed while working in the greenhouse.
- Guidelines and safety measures during handling plant microorganisms at field or natural ecosystem have been mentioned by the U.S. Department of Agriculture (USDA, 1992). During handling of plant-associated microorganisms like isolation, culture or related experiments, protocols and safety measures mentioned should be strictly followed.
- Standard procedure should be followed for the disposal of infected materials in laboratory and greenhouse. Cultures and pathogen-infected materials need to be autoclaved to make them biologically inactive.
- In gardens, experimental fields and open environment, standard chemical treatments or biological control agents should be used to control plant diseases. Other standard management practices like crop rotation, planting of resistant varieties etc. should be adopted.
- Visit of outbreak of agricultural field with proper protection and handling of raw vegetables wearing disposable gloves.

Conclusion

It is highly likely that over the years more information will be available on cross-kingdom microorganisms, and a greater number of such microorganisms will be identified due to greater exposure of humans to such potential pathogens. In addition, impending climate change may create a favourable environment for cross-kingdom infection. Therefore, care and precautions should be taken in handling plant pathogens and plant-associated microorganisms. This is more applicable for immunocompromised persons or persons with open wounds as they are more vulnerable to get infection from plants.

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Author's contributions: AKD, DB: Conceptualization; AKD, SG, PP, DB: Review of literature; AKD: Writing and original draft preparation; DB: Writing, review and editing. All authors have read and agreed to the current version of the manuscript.

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