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Editorial

The editorial team of *J. Microbiol. & Health Educ.* Vol. 4 (num. 1): 2022, wants to express its gratitude to the CONACYT Scientific and Technological Research Fund for the support granted.

We welcome new members of the Editorial Committee and invited reviewers.

We thank readers for their interest in our magazine. We have observed a significant increase in the number of referrals and potential evaluators. Our index and databases that index our articles have also been increased, such as Google scholar, Google Books, DOAJ-Directory of Open Access Journals and ROAD-Directory of Open Access scholarly Resources.

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Elvira D. Jacobi Salazar, Ph.D.
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- Food safety and food toxicology, science and technology

- Education for health; safety, infection prevention, therapy and pharmacotherapeutic monitoring of infections, epidemiology of infections, health education (personal hygiene and health care), healthy eating, drug use and prevention of multi-drug microbial resistance, risk analysis and risk factors that favor the infection.

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DISSERTATION / DISERTACIÓN

Underreporting: the situation of gastrointestinal and parasitic diseases in Mexico

Subnotificación: la situación de las enfermedades gastrointestinales y parasitarias en México

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Gastrointestinal diseases refer to disorders that affect the digestive system, including the esophagus, stomach, intestines, liver, gallbladder, and pancreas. Some common gastrointestinal diseases include gastritis, gastroenteritis, viral, bacterial or parasitic infections, peptic ulcers, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and liver diseases such as hepatitis.

It is difficult to assess the exact situation of gastrointestinal diseases in Mexico due:

a) potential underreporting and variations in healthcare access and
b) deficient reporting systems.

Underreporting can occur for various reasons, including:

a) limited access to healthcare,
b) lack of awareness or education about gastrointestinal diseases,
c) cultural factors, and
d) inadequate surveillance systems.

However, some studies and reports have highlighted specific gastrointestinal diseases in Mexico. For example, a study published in 2018 reported a high prevalence of irritable bowel syndrome (IBS) in Mexico, with an estimated prevalence rate of 16.7%. Another study published in 2017 found that the prevalence of peptic ulcers in Mexico was around 6.5%.

In terms of infectious gastrointestinal diseases, such as gastroenteritis, Mexico has faced challenges in the past. Outbreaks of diseases like cholera, salmonellosis, and norovirus infections have been reported, particularly in areas with inadequate sanitation and water supply.

Parasitic gastrointestinal diseases are a significant public health concern in Mexico, with several common parasitic infections affecting the population. These infections can be caused by various parasites, including protozoa and helminths.

Here are some examples of parasitic gastrointestinal diseases in Mexico:

Amebiasis: Amebiasis is caused by the protozoan parasite *Entamoeba histolytica*. It can lead to diarrhea, abdominal pain, and in severe cases, liver abscesses. Mexico has reported cases of amebiasis, particularly in areas with poor sanitation and limited access to clean water.

Giardiasis: Giardiasis is caused by the protozoan parasite *Giardia lamblia*. It can cause diarrhea, abdominal cramps, bloating, and weight loss.

Mexico has reported cases of giardiasis, especially in rural areas with inadequate sanitation and hygiene practices.

Cryptosporidiosis: Cryptosporidiosis is caused by the protozoan parasite *Cryptosporidium* spp. It can result in severe diarrhea, abdominal pain, nausea, and vomiting. Mexico has reported cases of cryptosporidiosis, often associated with contaminated water sources and poor hygiene practices.

Ascariasis: Ascariasis is caused by the roundworm *Ascaris lumbricoides*. It can lead to intestinal obstruction, abdominal pain, and nutrient deficiencies. Mexico has reported cases of ascariasis, particularly in rural and impoverished areas with limited access to proper sanitation and hygiene facilities.

Trichuriasis: Trichuriasis is caused by the whipworm *Trichuris trichiura*. It can cause chronic diarrhea, abdominal pain, and anemia. Mexico has reported cases of trichuriasis, especially in areas with poor sanitation and hygiene practices.

Taeniasis/Cysticercosis: Taeniasis is caused by the tapeworm *Taenia solium*, while cysticercosis is the result of the larval form of the same parasite. Taeniasis can cause gastrointestinal symptoms, while cysticercosis can lead to neurologic manifestations. Mexico has reported cases of both taeniasis and cysticercosis, particularly in regions where pork consumption and inadequate food preparation practices are prevalent.

It is important to note that efforts is a made in Mexico to improve surveillance, prevention, and treatment of parasitic gastrointestinal diseases. These include public health campaigns promoting hygiene practices, access to clean water, proper sanitation facilities, and deworming programs to reduce the burden of these infections.

For the most up-to-date and detailed information on the prevalence and specific measures taken to address parasitic gastrointestinal diseases in Mexico, I recommend consulting reports and studies from reputable health organizations such as the Secretaría de Salud (Ministry of Health) of Mexico or the National Institute of Public Health (Instituto Nacional de Salud Pública).

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DISERTACIÓN/DISSERTATION

El consumidor y los productos cárnicos deteriorados

The consumer and spoiled meat products

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El consumo y conservación de la carne ha sido una actividad prioritaria desde tiempos remotos. Actualmente, aun cuando existen tendencias de alimentación que excluyen a la carne, en muchos hogares este elemento ya sea crudo, mínimamente procesado o procesado, sigue siendo un componente importante y muy presente en el día a día. Esto conlleva a tener la misma importancia en el mercado de la industria alimentaria, por esta razón la calidad e inocuidad de la carne y sus productos cobra relevancia.

Es bien conocido que la carne cruda puede poseer contaminación de origen tanto por microorganismos patógenos (*Escherichia coli*, *Salmonella* y *Campylobacter*), como deterioradores (*Pseudomonas*, bacilos y bacterias ácido lácticas). Estos microorganismos suelen estar presentes en el animal desde la crianza y por ende en el posterior faenado, esto debido a la falta de buenas prácticas de higiene en el proceso de la matanza y acondicionamiento de la canal. Sí bien, la presencia de microorganismos patógenos y deterioradores en la carne mínimamente procesada no condena al producto a su deterioro o a la enfermedad del consumidor, sí está presente el potencial peligro, por lo que si se favorecen las condiciones para que el desarrollo microbiano alcance un número suficiente para detonar el deterioro o alcanzar la dosis infectiva, se magnífica el riesgo de que esto ocurra.

Cabe mencionar que la mayoría de los microorganismos patógenos no deterioran al alimento, por lo que su presencia puede pasar desapercibida para el consumidor, asimismo la mayoría de los microorganismos deterioradores no suelen comportarse como microorganismos patógenos, sin embargo, las condiciones bioquímicas y toxicológicas generadas tras su desarrollo en un alimento pudieran generar una enfermedad de origen alimentaria (no necesariamente una infección). Por lo que esto sugiere qué un alimento deteriorado no es apto para su consumo.

Actualmente, la mayoría de los consumidores están sensibilizados del peligro de consumir alimentos contaminados o deteriorados, sin embargo, muy pocos consumidores conocen las características propias del deterioro de cada alimento; fecha de vida útil, fecha de consumo preferente bajo alguna condición de almacenamiento o conservación.

La premisa es que los alimentos se deterioran porque no son consumidos antes de que esto ocurra, sin embargo, el tiempo de aparición de los signos de deterioro puede verse acelerado y ocurrir antes de la fecha estimada si se descuidan las condiciones apropiadas para su almacenamiento y conservación.

En los productos cárnicos procesados, ya sean horneados, ahumados y/o empacados al vacío, el

deterioro suele presentarse con la aparición de limo lechoso y viscoso, colonias microbianas blanquecinas en la superficie del alimento y la aparición de gas en el empaque, también pueden presentar una despigmentación del tejido o cambio de color a una pigmentación verdosa, además de olor fétido característico de las aminas biógenas. Estos signos de deterioro de la carne suelen presentarse en piezas crudas o productos procesados que fueron expuestos a condiciones fuera de las recomendadas para su almacenamiento y conservación.

Se han documentado numerosas faltas a las buenas prácticas de conservación de los alimentos cárnicos crudos y procesados, principalmente en puntos de comercialización mayorista y expendios minoristas. Estas faltas favorecen el deterioro de los productos cárnicos incuso antes de que el consumidor los adquiera. Sin embargo, los consumidores también juegan un papel importante en el correcto manejo y almacenamiento del alimento en el hogar, ya que el manejo que se le dé al alimento favorecerá o no, el desarrollo microbiano en el producto.

El consumidor común, usualmente no está consciente y no da prioridad a las condiciones óptimas de transporte de estos alimentos (cárnicos) desde el expendio hasta su hogar, por lo que es frecuente que estos productos se mantengan en condiciones de refrigeración desfavorables, es decir a temperaturas por arriba de los 8 grados centígrados (46 °F) por largos periodos de tiempo, lo que eventualmente permitirá el crecimiento de microorganismos psicrótrofos y mesófilos deterioradores y patógenos presentes.

Por último, para guiar al consumidor, es necesario que conozca que existen dos estrategias importantes para un mejor manejo de los productos cárnicos y por ende, reducir los riesgos tanto de infección, como de deterioro prematuro del producto:

Iniciando en el expendio,

a) El consumidor debe elegir correctamente el producto (sin deterioro evidente y en aparente buena higiene),
b) Asegurarse que éste se encuentre en buenas condiciones de refrigeración o congelación (2 a 8 °C, 28-46 °F),
c) Revisar las fechas de consumo preferente (con un margen de por lo menos 5 días posteriores), y
d) Debe elegir los productos refrigerados al final de la compra (de esta manera, asegurar que permanezcan el menor tiempo posible fuera de la temperatura adecuada de refrigeración de camino al hogar, que se recomienda sea menor a 2 horas).

Posteriormente en su hogar,

a) Seguir las recomendaciones de almacenamiento y conservación propias del alimento (usualmente se encuentran declaradas en el empaque), haciendo uso de congeladores y/o refrigeradores exclusivos para alimentos congelados y refrigerados,
b) Consumir primero los alimentos cárnicos con la fecha de consumo preferente más próxima.
c) Congelar en porciones individuales la carne cruda y descongelarla en refrigeración 24 horas antes de su preparación,
d) Evitar que se derramen sobre otros alimentos, los lixiviados de los productos cárnicos en el proceso de descongelación,
e) Evitar en medida de lo posible congelar por más de un mes los productos cárnicos,
f) Monitorear constantemente los signos evidentes de deterioro en los alimentos almacenados en congelación y/o refrigerados, ya que es la mejor estrategia para evitar el rezago de alimentos.
g) Es relevante la importancia que tiene el consumidor en la prevención del deterioro de los productos cárnicos y la disminución del potencial riesgo de contraer una enfermedad infecciosa al realizar un buen manejo y almacenamiento del alimento en el hogar.

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DISSERTATION / DISERTACIÓN

Biological risks in the workplace

Riesgos biológicos en el lugar de trabajo

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Biological risks in the workplace refer to potential hazards posed by biological agents that can cause harm to workers' health. These risks can arise from exposure to various biological substances, such as bacteria, viruses, fungi, parasites, and toxins. Here are some common examples of biological risks in the workplace:

a) Infectious diseases: Workers in healthcare settings, laboratories, or industries that involve close contact with people or animals may be at risk of contracting infectious diseases. This includes healthcare workers handling patients with contagious illnesses, laboratory personnel handling infectious specimens, or animal handlers exposed to zoonotic diseases.
b) Bloodborne pathogens: Workers who come into contact with blood or other potentially infectious materials, such as healthcare professionals, laboratory technicians, or waste management personnel, are at risk of exposure to bloodborne pathogens like HIV, hepatitis B, and hepatitis C.
c) Respiratory hazards: Workers exposed to airborne biological agents, such as bacteria, viruses, or fungi, can be at risk of respiratory infections. This may occur in industries such as healthcare, agriculture, animal farming, or waste management.
d) Allergens: Some workers may develop allergies or sensitivities to biological substances present in their work environment, such as dust mites, mold spores, animal dander, or pollen. These allergens can lead to respiratory symptoms or skin reactions.
e) Vector-borne diseases: Workers in outdoor occupations, such as forestry, agriculture, or landscaping, may face risks associated with vector-borne diseases transmitted by insects or ticks, such as Lyme disease, dengue fever, or West Nile virus.
f) Hazardous biological materials: Workers handling hazardous biological materials, such as certain bacteria, viruses, or genetically modified organisms (GMOs), may face risks associated with accidental exposure or contamination.

To address these biological risks, employers and workers can take various preventive measures, including:

a) Implementing appropriate personal protective equipment (PPE) such as gloves, masks, and protective clothing.
b) Providing training and education on the proper handling, storage, and disposal of biological materials.
c) Establishing protocols for infection control, including hand hygiene practices and disinfection procedures.

d) Conducting risk assessments to identify potential biological hazards in the workplace and implementing control measures to minimize exposure.
e) Regularly monitoring and evaluating the effectiveness of control measures.
f) Complying with relevant regulations and guidelines regarding biological hazards in the workplace.

It's important for employers to have occupational health and safety programs in place to mitigate the biological risks and ensure the well-being of their workers. Additionally, workers should be aware of the potential biological hazards in their work environment and follow the recommended safety practices and protocols. Here are some common practices and protocols that can help reduce biological risks:

a) Risk assessment: Conduct a thorough risk assessment to identify potential biological hazards in the workplace. This includes assessing tasks, processes, and materials that may pose risks to workers' health.
b) Engineering controls: Implement engineering controls to minimize or eliminate exposure to biological hazards. This may involve using ventilation systems, containment devices, or physical barriers to prevent the spread of airborne pathogens or other biological agents.
c) Administrative controls: Establish administrative controls to manage and reduce biological risks. This includes implementing policies, procedures, and work practices that minimize exposure, such as proper handling and disposal of biological materials, safe work procedures, and hygiene practices.
d) Personal protective equipment (PPE): Provide appropriate personal protective equipment to workers based on the identified biological risks. This may include gloves, masks, protective clothing, goggles, or face shields. Ensure proper training on the correct use, maintenance, and disposal of PPE.
e) Hygiene practices: Promote good hygiene practices among workers to minimize the spread of biological agents. This includes regular handwashing with soap and water, using hand sanitizers, avoiding touching the face, and practicing respiratory hygiene (covering mouth and nose when coughing or sneezing).
f) Training and education: Provide comprehensive training and education to workers about the potential biological risks in their workplace and the necessary precautions to prevent exposure. This should include information about the proper use of PPE, hygiene practices, and reporting procedures for incidents or concerns.
g) Vaccinations: Encourage or require appropriate vaccinations for workers, especially in industries with a higher risk of exposure to specific infectious diseases. This may include vaccinations for diseases like hepatitis B or influenza.
h) Cleaning and disinfection: Implement regular cleaning and disinfection protocols in the workplace, particularly in areas where biological agents may be present. Use appropriate disinfectants and cleaning methods to eliminate or reduce the risk of contamination.
i) Monitoring and evaluation: Regularly monitor and evaluate the effectiveness of the implemented practices and protocols. This may involve conducting inspections, audits, or health surveillance to ensure compliance and identify areas for improvement.
j) Compliance with regulations and guidelines: Stay up to date with relevant regulations, guidelines, and standards related to biological risks in the workplace. Comply with local, national, and international requirements to ensure a safe and healthy working environment.

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DISERTACIÓN / DISSERTATION

Control de patógenos y sustancias indeseables en alimentos para mascotas

Control of pathogens and undesirable substances in pet food

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Los patógenos en los alimentos para mascotas son microorganismos que pueden causar enfermedades en los animales que los consumen. Algunos de los patógenos comunes que pueden estar presentes en los alimentos para mascotas incluyen:

a) *Salmonella*: Esta bacteria puede causar enfermedades gastrointestinales graves en animales. Puede encontrarse en alimentos crudos o mal cocidos, así como en ingredientes de baja calidad.
b) *Escherichia coli*: Algunas cepas como la O157:H7, pueden ser perjudiciales para las mascotas y causar enfermedades gastrointestinales. La contaminación puede ocurrir a través de ingredientes crudos o contaminación cruzada durante la producción de alimentos.
c) *Listeria monocytogenes*: Esta bacteria puede causar infecciones graves en animales. Puede encontrarse en alimentos refrigerados y puede ser resistente a condiciones adversas, lo que la hace peligrosa incluso en bajas concentraciones.
d) *Campylobacter*: Esta bacteria es una causa común de enfermedades gastrointestinales en animales. Puede transmitirse a través de alimentos crudos o contaminados, como carne de ave cruda.
e) *Clostridium perfringens*: Esta bacteria es responsable de la intoxicación alimentaria en animales y puede encontrarse en alimentos mal almacenados o que no se han calentado adecuadamente.
f) Hongos toxigénicos

Es importante tener en cuenta que los alimentos para mascotas adecuadamente formulados y procesados generalmente están diseñados para eliminar o minimizar la presencia de patógenos. Además, se recomienda a los dueños de mascotas que manejen y almacenen los alimentos correctamente, siguiendo las instrucciones del fabricante, para evitar la proliferación de patógenos, promover la generación de micotoxinas en el alimento y proteger la salud de sus mascotas.

En este contexto, las micotoxinas son sustancias tóxicas producidas por hongos que pueden contaminar los alimentos para mascotas. Estas toxinas pueden encontrarse en ingredientes como granos, semillas y otros productos agrícolas que se utilizan en la fabricación de alimentos para mascotas. Algunas de las micotoxinas más comunes incluyen:

a) Aflatoxinas: Son producidas principalmente por los hongos del género *Aspergillus*. Las aflatoxinas pueden encontrarse en ingredientes como el maíz, maní, nueces y semillas. Son especialmente peligrosas para los perros y pueden causar problemas hepáticos graves.

b) Deoxinivalenol (DON): También conocido como toxina vomitoxina, es producido por el hongo Fusarium. Puede encontrarse en cereales como el trigo, cebada y avena. El consumo de alimentos contaminados con DON puede provocar problemas gastrointestinales y afectar la salud de las mascotas.
c) Zearalenona: Es otra micotoxina producida por el hongo *Fusarium*. Puede encontrarse en granos como el maíz, trigo y cebada. La exposición a zearalenona puede causar trastornos reproductivos y hormonales en las mascotas.
d) Ocratoxina A: Es producida por los hongos del género *Aspergillus* y *Penicillium*. Puede encontrarse en granos, café y frutas secas. La ocratoxina A puede tener efectos tóxicos en los riñones y el sistema inmunológico de las mascotas.

El control de las micotoxinas en los alimentos para mascotas es fundamental para garantizar la seguridad de los animales. Los fabricantes de alimentos para mascotas implementan diversas medidas para prevenir la presencia de micotoxinas, como:

a) Selección y evaluación de proveedores de ingredientes para asegurar la calidad y minimizar la contaminación por micotoxinas.
b) Análisis y pruebas de los ingredientes y productos terminados para detectar la presencia de micotoxinas.
c) Uso de técnicas de procesamiento adecuadas, como el secado y almacenamiento adecuado de los ingredientes, para prevenir el crecimiento de hongos y la producción de micotoxinas.
d) Cumplimiento de regulaciones y estándares de seguridad alimentaria establecidos por las autoridades competentes.

El control de patógenos y sustancias indeseables en alimentos para mascotas es crucial para garantizar la seguridad y la calidad de los productos. Aquí tienes algunas medidas y prácticas clave que se emplean comúnmente en la industria de alimentos para mascotas para controlar patógenos y sustancias indeseables:

a) Buenas Prácticas de Manufactura (BPM): Los fabricantes de alimentos para mascotas siguen las BPM para garantizar una higiene, saneamiento y manejo adecuados de ingredientes y productos terminados. Esto incluye mantener instalaciones limpias, un almacenamiento adecuado de ingredientes y seguir procedimientos operativos estandarizados.
b) Análisis de Peligros y Puntos Críticos de Control (HACCP): El HACCP es un enfoque sistemático utilizado para identificar y controlar riesgos en el proceso de producción. Los fabricantes de alimentos para mascotas implementan los principios del HACCP para identificar posibles riesgos, establecer puntos críticos de control y establecer procedimientos de monitoreo para prevenir o eliminarlos.
c) Selección y prueba de ingredientes: Los fabricantes de alimentos para mascotas seleccionan y obtienen ingredientes de proveedores confiables. A menudo establecen especificaciones para los ingredientes y realizan pruebas para asegurarse de que cumplan con los estándares de seguridad y calidad. Esto incluye la detección de patógenos como Salmonella y E. coli, así como pruebas de otros contaminantes o sustancias indeseables.
d) Control de calidad y pruebas: Los fabricantes de alimentos para mascotas tienen medidas rigurosas de control de calidad. Realizan pruebas regulares de materias primas, muestras en proceso y productos terminados para verificar su seguridad y calidad. Esto incluye pruebas microbiológicas, análisis nutricionales y verificación de contaminantes como micotoxinas.
e) Procesamiento térmico: Se utilizan técnicas de procesamiento térmico, como la cocción, horneado o extrusión, en la fabricación de alimentos para mascotas. Estos procesos ayudan a destruir o inactivar patógenos y microorganismos que puedan estar presentes en los ingredientes crudos.
f) Etiquetado del producto y transparencia: Los fabricantes de alimentos para mascotas

proporcionan etiquetado preciso y transparente de sus productos. Esto incluye listar los ingredientes, información nutricional y cualquier alérgeno o contaminante potencial que pueda estar presente.

g) Auditorías y aseguramiento de calidad de proveedores: Los fabricantes de alimentos para mascotas suelen realizar auditorías y evaluaciones de sus proveedores de ingredientes para asegurarse de que cumplan con los estándares apropiados de calidad y seguridad. Esto incluye verificar sus prácticas de fabricación, procedimientos de control de calidad y protocolos de prueba.
h) Cumplimiento normativo: Los fabricantes de alimentos para mascotas se adhieren a los requisitos y pautas reglamentarias aplicables específicas para la producción de alimentos para mascotas. Estas regulaciones pueden variar según el país o la región y a menudo incluyen pautas específicas para la obtención de ingredientes, etiquetado y estándares de seguridad.
i) Procedimientos de retiro: En caso de problemas de seguridad o contaminación potencial, los fabricantes de alimentos para mascotas tienen procedimientos establecidos para retirar rápidamente los productos afectados del mercado e informar a los consumidores.
j) Mejora continua: Los fabricantes de alimentos para mascotas buscan una mejora continua al mantenerse actualizados sobre las últimas investigaciones, mejores prácticas de la industria y problemas emergentes relacionados con la seguridad de los alimentos para mascotas. Monitorizan activamente e incorporan nuevas tecnologías, procesos y conocimientos científicos para mejorar los controles de seguridad.
k) Al implementar estas medidas, los fabricantes de alimentos para mascotas buscan minimizar la presencia de patógenos y sustancias indeseables en sus productos, garantizando la seguridad y el bienestar de las mascotas que consumen sus alimentos.

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REVIEW ARTICLE /REVISIÓN

Opisthorchis viverrini infection

Infección por *Opisthorchis viverrini*

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A B S T R A C T

Opisthorchiasis, caused by consuming infected raw cyprinid freshwater fish or contaminated water with *Opisthorchis viverrini*, is one of the most important risk factors for cholangiocarcinoma in endemic countries, such as Thailand, Laos, and Cambodia.[1,14] It has been stimated that 67.3 million people are at risk of acquiring an *O. viverrini* infection, and 10 million people are infected.[14] Nowadays, the gold standard for the diagnosis of liver fluke is the demonstration of eggs in stool samples, nevertheless, there are more diagnosis methods such as immunochromatography, ELISA and PCR test.[13] The diagnosis of cholangiocarcinoma in most of the patients is in stages III or IV, because most of the patients are asymptomatic or the diagnosis is incidental in a routine health check, that's the reason why it has a poor prognosis at 5 years.[12] The standard treatment is the praziquantel. People who don't tolerate praziquantel could be treated with tribendimidine, with less adverse effects.[14]

Keywords: Liver fluke, Cholangiocarcinoma, Freshwater snail, Cyprinid fish, Praziquantel.

R E S U M E N

La opistorchiasis, infección causada por el consumo de perscado de agua dulce del género *Cyprinid* o por la ingesta de agua contaminada con *Opisthorchis viverrini,* es uno de los más importantes factores de riesgo para colangiocarcinoma en países endémicos, como Tailandia, Laos y Cambodia. [1,14] Se ha estimado que 67.3 millones de personas están en riesgo de adquirir la infección, y 10 millones de personas se encuentran infectadas. Actualmente, el método diagnóstico de elección para la infección es la demostración de huevos in muestras de heces, sin embargo, existen otros métodos diagnósticos de utilidad como la inmunocromatografía, el ELISA y la PCR. [13] En la mayoría de los pacientes al diagnóstico, el colangiocarcinoma se encuentra en estadios III o IV, debido a que la mayoría cursan de forma asintomática o el diagnóstico se realiza de forma incidental posterior a un chequeo médico de rutina, esta, es la razón por la que el pronóstico es malo a 5 años. [12] El tratamiento de elección es el praziquantel, y como tratamiento alternativo se encuentra la tribendimidina, con menores efectos adversos.[14]

Palabras clave: Trematodo hepático, Colangiocarcinoma, Caracol de agua dulce, Pez ciprínido, Praziquantel.

INTRODUCTION

Ophistorchis viverrini is the etiologic agent of the ophistorchiasis, and one of the potential risk factors to cholecystitis, cholangitis and the worst consequence, cholangiocarcinoma in endemic regions. It's a trematode (liver fluke) of the family *Opisthorchiidae*, and genera *Amphimerus*.[3]

It has a complex life cycle that includes two intermediate hosts such as freshwater snail and the cyprinid fish, and different definitive hosts such as the human, dogs, cats, foxes, and bears.[3]

Most of the patients are asymptomatic, and they are inly diagnosed when the cholangiocarcinoma is in stages III or IV, and it's unresectable, or like an incidental diagnosis in a healthcare checkup.

EPIDEMIOLOGY

The global estimate of the number of people infected with liver fluke is 10 million people. (8 million in Thailand). *Opisthorchis viverrini* is known from continental Southest Asia, particularly in Thailand, Lao PDR, Cambodia, Southern Vietnam, Malaysia, Siangapore and the Philippines. (**Table 1**)

Table 1. Risk factors for *Opisthorchis viverrini* infection.
Tabla 1. Factores de riesgo para infección por *Opisthorchis viverrini.*

Risk factors	
Demographic factors.	Male
	Age younger than 24 years or older than 55 years
	Low level of education
	Fisherman[17]
	Rice Farmer[17]
	People who migrate from the northeast of Thailand have a 2.28-2.42-fold higher risk of infection than nonmigrants[8]
Environmental and geographic factors	Households with dogs and cats
	Absence of sanitation
Health behavior factors	Persistent smoking
	Consumption of alcohol
	Consumption of raw freshwater fish
	Contaminated drinking water
	Unsafe disposal of food waste
	Lack of knowledge about praziquantel treatment[17]

LIFE CYCLE

1. The embryonated eggs of *O. viverrini* are ingested by freshwater snails (*Bithynia siamensis, B. gioniomphalos and B. s. simensis*) which are the first intermediate hosts and in which it goes through an asexual reproductive cycle.
2. In the digestive tract of the freshwater snail, the embryonated egg becomes a miracidia, the miracidia penetrates the snail tissue and transforms into a sporocyst, then into a rediae and finally into a free-swimming cercariae, the duration from ingestion of eggs until release of the cercariae takes about 2 months.
3. The cercariae swims to find their second intermediate host, the cryprinid fish, in which attach to the skin and transform into a metacercariae.
4. The metacercariae becomes infective in about 1 month.
5. The definitive hosts acquire the infection by eating fermented, raw, or undercooked freshwater cyprinid fish containing the infective metacercariae, in which digestive duct transforms into a larva. The larva migrates into the biliary system.[8] The entire life cycle requires 4-4.5 months and worms have a lifespan of about 10 years.
6. Finally, the embryonated eggs are excreted with the host's feces, the worms lay about 2,000-4,200 eggs daily. [8] (**Figure 1**)

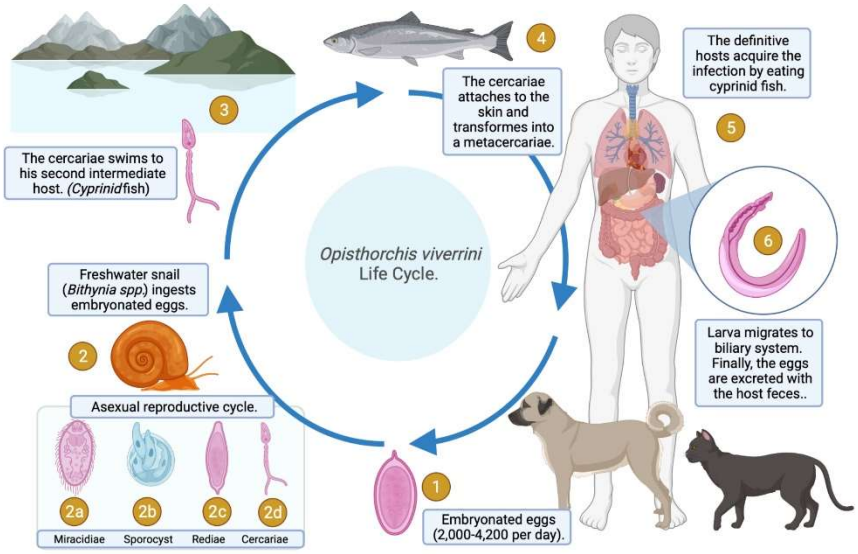

Figure 1. Life cycle of *O. viverrini*.
Figura 1. Ciclo de vida de *O. viverrini*.

PATHOGENESIS

O. viverrini is the most important risk factor to cholangiocarcinoma in endemic countries, nevertheless, the combination of exogenous carcinogens such as nitrosamines in fermented fish and pork magnify the risk of cholangiocarcinoma.[10]

The liver fluke suckers make a vicious cycle of ulceration (by clinging to the bile duct), inflammation and healing process those results in DNA damage and progression to cholangiocarcinoma.

O. viverrini causes an important immune response. One of the most important responses, is the interleukin-6 (IL-6), which is secreted in proinflammatory processes.

The IL-6 is associated with periductal fibrosis and promotes cell proliferation by activating progranulin expression.

The host defense system is activated by the O. viverrini's eggs antigens, which induce inflammatory cascade by upregulating TLR-4, activation of NFkB, inducible nitric oxide synthetase and cyclooxygenase-2; and expression and secretion of IL-6, IL-8, TNF-a, IL-B1 and oxidative stress reactants. [10] (**Figure 2**)

Macrophages activate by the egg's antigens generate an intense inflammatory cells infiltration and subsequently, granulomas around the eggs. [10]

One of the most interesting consequences of *the O. viverrini* infection is the different microbiome profile, *Helicobacter pylori* and *Opisthorchis viverrini* may potentially form an obligatory mutualism alliance. Both pathogens increase the degree of fibrosis, cholangitis, and duct hyperplasia.[10]

Cholangiocarcinoma is an aggressive cancer with high progression and metastasis, it's originated by chronic inflammation of the bile ducts in response to liver fluke infection.

The cholangiocarcinoma of the *O. viverrini* infection has different characteristic in contrast with primary sclerosing cholangitis and chronic inflammation's cholangiocarcinoma. [16]

In one study12, cancer cells characteristically present complex karyotypes with high aneuploidy, with different expression profiles and histological subtypes (adenocarcinoma, poorly differentiated (non-keratinized) and well-differentiated (keratinized) squamous cell carcinomas) of xenografted tumors.[16]

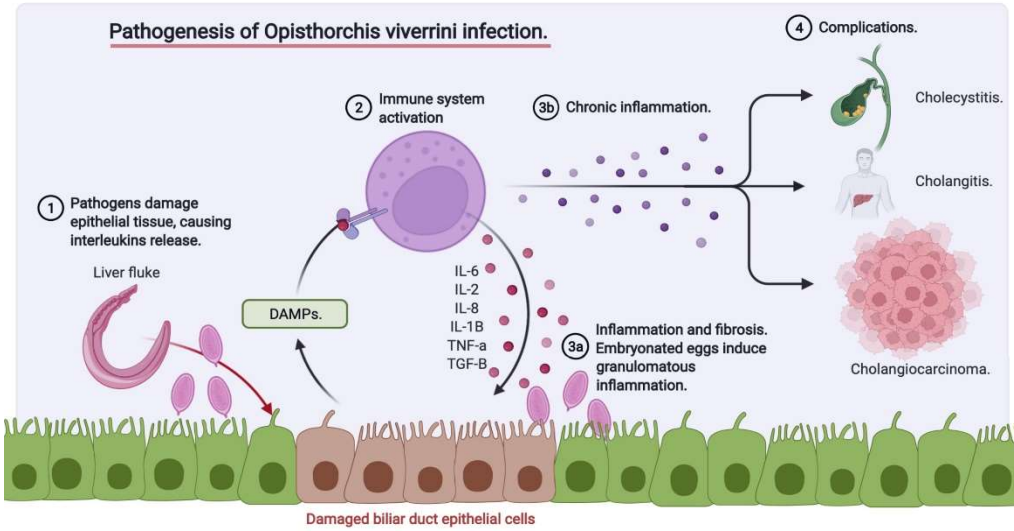

Figure 2. Pathogenesis of *Opisthorchis viverrini* infection. 1. The biliary ducts damaged release Damage-associated molecular patterns (DAMPs). 2. The DAMPs activate the immune system with the subsequent release of interleukins. 3. The chronic inflammation makes ulcers and fibrosis in the cubic epithelium. 4. The complications of *O. viverrini*'s infection are cholecystitis, cholangitis and cholangiocarcinoma.

Figura 2. Patogénesis de la infección por *Opisthorchis viverrini*. 1. El daño al epitelio cúbico de los conductos biliares ocasionan la liberación de patrones moleculares asociados a daño (DAMPs). 2. Los DAMPs ocasionan la liberación de interleucinas por activación del sistema inmune. 3. La inflamación crónica lleva a ulceración y fibrosis. 4. Las complicaciones asociadas a la infección por *O. viverrini* son la colecistitis, colangitis y el colangiocarcinoma.

CLINICAL MANIFESTATIONS

A major part of patients are asymptomatic or present unspecified manifestations before diagnosis, therefore, cholangiocarcinoma associated with this infection has a poor prognosis. Cholangiocarcinoma is the second most common primary liver cancer, after hepatocarcinoma, which derives from the epithelial cells of the bile ducts. Cholangiocarcinoma can be divided into 2 subtypes depending on the anatomical structure involved: extrahepatic (75%) and intrahepatic (25%), in turn, extrahepatic is subdivided into perihilar, middle and distal, depending on the location of the tumor. [10] (**Figure 3**)

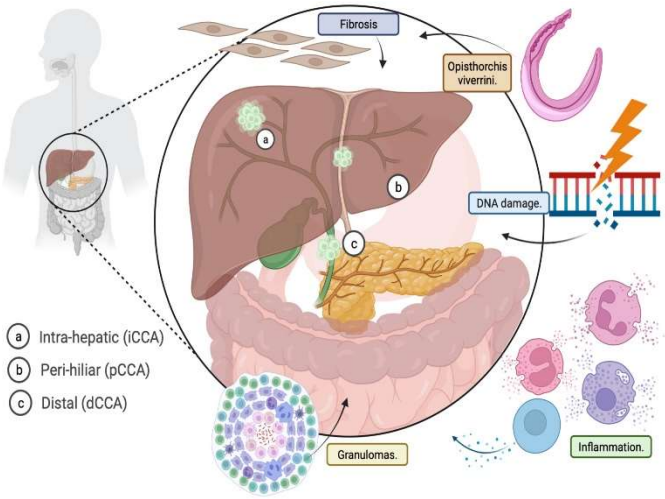

Figure 3. Cholangiocarcinogenesis. The *O. viverrini*'s infection produces chronic inflammation, biliary ducts granulomas, DNA damaged, and fibrosis, each of them, a necessary factor for cholangiocarcinoma. The cholangiocarcinoma is classified by its location, it could be intrahepatic (iCCA) or extrahepatic, which in turn is divided in perihiliar (pCCA) and distal (dCCA).

Figura 3. Colangiocarcinogénesis.

Extrahepatic cholangiocarcinoma can manifest with obstructive signs, such as pain in the right hypochondrium, pruritus, acholia, and coluria; and nonobstructive or systemic signs, such as fatigue, abdominal pain, weight loss, and liver mass on abdominal examination. [10]

Some patients are incidentally diagnosed on a medical check-up.

DIAGNOSIS

The diagnosis of *O. viverrini* infection is difficult, it needs a high grade of suspicious, because most of the patients are asymptomatic or it is diagnosed in a healthcare checkup. The gold standard continues to be the detection of eggs in feces, biliary fluid, or duodenal fluid, however, there are more diagnosis methods, with high sensitivity and specificity that can help us to diagnose the infection, such as immunochromatography, ELISA, etc. (**Table 2**)

Table 2. Diagnostic methods for *O. viverrini* infection and cholangiocarcinoma.
Tabla 2. Métodos diagnósticos para infección y colangiocarcinoma por *O. viverrini.*

Diagnostic method	Accuracy.				Characteristics
	Sensitivity.	Positive Predictive value	Specificity	Negative Predictive value	
Laboratory examination.	Direct simple smear: 12.4%. (7.5-18.9%)[1] Kato-Katz technique: 68.3%. (60-75.7%)[1] Detection by fecal parasite concentrator kit (FPCK): 32.4%. (24.9-40.7%)[1]			Direct simple smear: 68.5%. (63.7-73%)[1] Kato-Katz technique:85.7% (81.4-89.3%)[1] Detection by fecal parasite concentrator kit (FPCK): 73.8%. (69-78.2%)[1]	It's the gold standard for diagnosis of human live fluke infection, the sample could be feces, bile, or duodenal fluid.[10]
ELISA-based serodiagnosis.	100%.[13]	97.9%.[13]	98.3%.[13]	95.4%.[13]	Consists in the reaction of antibodies to an antigen of *Opisthorchis viverrini* in the sera of infectious patients.[13]
Immunochromatographic test (ICT) - based serodiagnosis.	94.6%.[13]	91.2%.[13]	89.7%.[13]	95.4%.[13]	It´s a speedy and simple technique by dropping the sample containing an analyte onto a test strip, that produces a result in 10 to 15 minutes.[13]
Stool-PCR amplification test of OvNad subunits.	OvNad1: 64%. OvNad2: 88%. OvNad4: 80%. OvNad5: 100%.[9]	OvNad1: 100%. OvNad2: 100%. OvNad4: 100%. OvNad5: 100%.[9]	OvNad1: 100%. OvNad2: 100%. OvNad4: 100%. OvNad5: 100%.[9]	OvNad1: 77.12%. OvNad2: 91%. OvNad4: 85.85%. OvNad5: 100%.[9]	NADH dehydrogenase subunits were designed from partial sequence of *Opisthorchis viverrini* mitochondrial DNA.[9]
Endoscopic Ultrasonography.	96%.[11]	60%.[11]	96%.[11]	60%.[11]	The endoscopic ultrasonography is a minimally invasive procedure that uses high-frequency sound waves to produce detailed images of hepatobiliary and pancreatic systems. [11]
Magnetic resonance cholangiopancreatography (MRCP).	95.35%.[11]	94.74%.[11]	93.18%.[8]	94.43%.[11]	The MRCP is a special type of magnetic resonance imaging exam that produces detailed images of the hepatobiliary and pancreatic systems, including liver, gallbladder, bile ducts, pancreas, and pancreatic duct. [11]
Endoscopic Retrograde Cholangiopancreatography (ERCP) with Histopathology.	Aspiration cytology: 42.1%. Brush cytology: 58.4%. Biopsy: 63.5%. Double-tissue sampling (DTS): 64.9%. Triple-tissue sampling (TTS): 85%.[4]	Aspiration cytology: 100%. Brush cytology: 100%. Biopsy: 100%. Double-tissue sampling (DTS): 100%. Triple-tissue sampling (TTS): 100%.[4]	Aspiration cytology: 100%. Brush cytology: 100%. Biopsy: 100%. Double-tissue sampling (DTS): 100%. Triple-tissue sampling (TTS): 100%.[4]	Aspiration cytology: 32.7%. Brush cytology: 50%. Biopsy: 54.8%. Double-tissue sampling (DTS): 62%. Triple-tissue sampling (TTS): 53.8%.[4]	The Endoscopic Retrograde Cholangiopancreatography (ERCP) is an endoscopic technique used to obtain tissue samples. This technique increments the sensitivity and specificity of the diagnostic method.[4]

TREATMENT

The treatment against the oncological liver fluke consists of two guidelines which are based on, a) the control of the transmission of cases with the eradication of this parasite and, b) the prevention of the progression of the pathology to reduce the number of cases of cholangiocarcinoma induced by infection caused by *Opisthorchis viverrini.*[2]

For a long time, praziquantel has been used as an antimalarial treatment in conjunction with health campaigns focused on promoting the consumption of properly cooked meat and fish as well as reducing the spread of fecal matter in the environment due to deposition at ground level, inadequate latrines, defective drainage, and irrigation of plantations with wastewater. All these measures showed a 57-64% decrease in cases, as well as a 3-5% decrease in prevalence. However, infection by *O. viverrini* does not provide protective immunity to a person, so they are still susceptible to reinfection.[7]

In endemic areas, both cases of reinfection and cholangiocarcinoma have been reported, which have been associated with the consumption of praziquantel. Due to its poor control, dependence on deworming, self-medication by the population, and easy availability of the antimalarial in pharmacies as it is an over-the-counter product.[2] Although the data suggest an increase in cases, there is a lack of evidence linking treatment with praziquantel and the appearance of cholangiocarcinoma. The available evidence in animal models suggests that the factors that increase the risk of cholangiocarcinoma a load of worms and substances secreted in the bile duct that cause liver damage as well as periductal fibrosis, while another model in hamsters with cholangiocarcinoma was treated with praziquantel presented a slow progression of this pathology. And those studies in humans infected with *O. viverrini* relate to alcoholism and the consumption of foods rich in nitrosamines as risk factors for the development of cholangiocarcinoma. [15,7]

Alternative treatment

In one study, (Sayasone S, Keiser J, Meister I, et. al.) The use of tribendimimidine (single dose 200 mg children and 400 mg adults) was shown to be inferior compared to praziquantel (50 mg/kg of weight and 25 mg/kg of weight, two doses) against infection by O. *viverrini (All children included in the study were* cured).[14]

Nowadays, tribendimidine could be used to treat *O. viverrini* infection in people who don't tolerate praziquantel.[6,14]

Despite other pharmacological alternatives, praziquantel is the first-line medication, as it is a drug with a short half-life, which is safe and effective against the parasite and other trematodes.[15]

The WHO recommends annual deworming in endemic regions with a prevalence greater than 20% and every two years in populations with a risk of less than 20%. Thanks to the use of this sanitary measure, a decrease in cholangiocarcinoma morbidity was found when praziquantel was used as the first choice for infection caused by *Opisthorchis viverrini*.[2]

PROGNOSIS

Most patients with cholangiocarcinoma are diagnosed at stages III and IV at the time of diagnosis. [7] Cholangiocarcinoma has a poor prognosis with a 5-year survival rate of approximately 5% in the type intrahepatic and 17% in the perihiliar and distal cholangiocarcinoma. [9]

Conflict of interest

The authors declare that they have no conflict of interest.

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