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Experimental Study

A study solve problem

Similarities between Crimean-Congo hemorrhagic fever virus and Marburg virus in terms of symptoms, infection, diagnosis and treatment

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Abstract

Objectives: The aim of the study: to comparison and find similarity between two viruses that cause bleeding in human.

Study design: Systematic Review and Meta-Analysis study design

Background of Marburg virus: Marburg virus disease (MVD) is a severe, often fatal illness caused by the Marburg virus, virus is transmitted to people from fruit bats and then spreads in the human population through human to human transmission MVD is transmitted through animal to human transmission, in most cases, following stay in caves or mines inhabited by rousettine bats (Rousettus aegyptiacus) and through direct or indirect contacts with bats. Transmission from other wild animals such as primates to humans is possible but rare. Also transmission by human to human may then occur through direct contact with body fluids including stool , vomit , blood , urine , saliva , semen , breast milk of a sick person with MVD, direct contact with a MVD deceased person's body (body handling, involving funeral touching of the body and body fluids) contact with surfaces or equipment contaminated by the body fluids of a sick person with MVD and especially through unsafe injection practices. Secondary transmission from exposure to body fluids (semen) of people who recovered from MVD has been documented , although this remains a rare event.

The incubation period varies from 2-21 days. First symptoms are: abrupt high fever onset, severe headache and malaise, muscle aches and pains. These symptoms are usually followed by: severe watery diarrhea, abdominal pain and cramping, nausea and vomiting by day 3 Severe cases developing some forms of bleeding, generally from multiple areas sites including nose, gums, in vomitus and/or feces, vagina and venepuncture sites by day 5-7. Confusion, irritability and aggressivity can be noted in severe cases. In fatal cases, death occurs generally by day 8 and 9, generally following severe blood loss and shock. Symptoms are non-specific, clinical diagnosis may be difficult. Differential diagnosis includes other viral haemorrhagic fevers, yellow fever, malaria, typhoid fever, shigellosis and other viral and bacterial diseases. Definitive diagnosis requires

testing: reverse transcriptase polymerase chain reaction (RT - PCR) assay. Treatment Supportive drug therapy including: analgesics, antiemetics to treat vomiting, antianxiety drugs to treat agitation +/- antibiotics and/or antimalarial drugs.

Background of Crimean-Congo hemorrhagic fever virus: Congo hemorrhagic fever is a viral disease that affects humans in Africa, the Balkans, the Middle East and Asia in countries located south of 50 degrees north latitude. WHO EMRO The main reservoir and vector of CCHF is ticks of the genus Vitreous-eye, although other species of ticks can be infected with CCHF virus. Congo hemorrhagic fever virus is transmitted to humans, either through a tick bite or by coming into contact with the blood or tissues of an infected animal during or immediately after slaughter.Clinical features of Congo hemorrhagic fever, the incubation period ranges between two and 14 days, 70% of cases of Congo haemorrhagic fever have previously been exposed to a tick bite. It is estimated that 88% of infections are subclinical cases. The most common symptoms include sudden fever, chills, shivering, muscle pain, headache, weakness, vomiting, abdominal pain, and arthralgia . After a few days bleeding from the mucous membranes, hematoma, bruising, black stools, hematuria, nosebleeds, vaginal bleeding, bradycardia, thrombocytopenia, and leukopenia occur. Laboratory diagnosis requires the following tests reverse transcriptase-PCR assay, enzyme-linked immunosorbent assay with IgM antibodies and IgG total group antibodies. Antigen detection tests, Virus isolation by cell culture. Congo haemorrhagic fever treatment Early, intensive and active supportive care monitor fluid and electrolyte balance, renal function, blood pressure, oxygenation, and careful rehydration carefully. Supporting the coagulation system with blood components treatment. Supportive drug therapy including: analgesics, antiemetics to treat vomiting, antianxiety drugs to treat agitation +/- antibiotics and/or antimalarial drugs. The antiviral drug ribavirin can be given early in the disease. Kidney function Fluid and electrolyte balance Supportive drug therapy Ribavirin.

Keyword: Hematuria, antimalarial treatment and ribavirin.

Introduction

Marburg virus disease (MVD) is a severe, often fatal illness caused by the Marburg virus. The Marburg virus belongs to the Filoviridae family Rousettus aegyptiacus, fruit bats of the Pteropodidae family, are the natural hosts of Marburg virus. MVD is a zoonotic disease. Marburg virus is transmitted to people from fruit bats and then spreads in the human population through human to human transmission. The average MVD case fatality rate is around 50%, varying from 24% to 88% in past outbreaks depending on virus strain and case management.

Marburg virus was first detected in 1967 following exportation of Vervet monkeys (Cercopithecus aethiops) captured in Uganda and sent to Europe. Two simultaneous outbreaks were reported in, Marburg and Frankfurt in Germany; Belgrade, Yugoslavia (now Serbia) . The virus then caused outbreaks in South Africa, Kenya, Democratic Republic of the Congo, Angola, Uganda, Guinea and Ghana. In 2008, isolated cases were reported in the USA and the Netherlands in returned travelers who had visited caves inhabited by rousettine bats (Rousettus aegyptiacus) in Uganda.

MVD is transmitted through: Animal to human transmission: in most cases, following stay in caves or mines inhabited by rousettine bats (Rousettus aegyptiacus) and through direct or indirect contacts with bats. Transmission from other wild animals such as primates to humans is possible but rare. Human- to- human transmission may then occur through : direct contact with body fluids (stool, vomit, blood, urine, saliva, semen, breast milk) of a sick person with MVD. direct contact with a MVD deceased person's body (body handling involving funeral touching of the body and body fluids) contact with surfaces or equipment contaminated by the body fluids of a sick person with MVD , and especially through unsafe injection practices. Secondary transmission from exposure to body fluids (semen) of people who recovered from MVD has been documented, although this remains a rare event.

People working in mines or caves inhabited by rousettine bats (Rousettus aegyptiacus). People visiting caves inhabited by rousettine bats (Rousettus aegyptiacus). People in close contact with sick people exhibiting symptoms. Health care workers and medical personnel caring for MVD patients. Laboratory workers People handling bodies of people who died of MVD. Traditional healers caring for MVD patients.

The incubation period varies from 2 - 21 days. First symptoms are: abrupt high fever onset, severe headache and malaise, muscle aches and pains. These symptoms are usually followed by: severe watery diarrhea, abdominal pain and cramping, nausea and vomiting (by day 3) Severe cases developing some forms of bleeding, generally from multiple areas sites including nose, gums, in vomitus and/or feces, vagina, and venepuncture sites (by day 5-7). Confusion, irritability and aggressivity can be noted in severe cases. In fatal cases, death occurs generally by day 8 and 9, generally following severe blood loss and shock.

Symptoms are non-specific, clinical diagnosis may be difficult. Differential diagnosis includes other viral haemorrhagic fevers, yellow fever, malaria, typhoid fever, shigellosis, and other viral and bacterial diseases. Patient history is essential and should include, history of staying in mines or caves inhabited by rousettine bat Rousettus aegyptiacus) colonies > Contact with a suspected , probable or confirmed MVD patient.

Definitive diagnosis requires testing, reverse transcriptase polymerase chain reaction (RT - PCR) assay.

IgG and IgM with enzyme - linked immunosorbent antibody assay (ELISA) antigen detection tests virus isolation by cell culture Handling and processing specimen requires suitably equipped laboratories under maximum biological containment conditions and staff collecting samples should be trained.
While there is no specific therapeutics available for MVD, chances of survival can be improved through: early, aggressive, intensive supportive care such as monitoring fluids and electrolytes balance and vital signs, and careful rehydration Supportive

drug therapy including painkillers, antiemetic for vomiting, anxiolytic for agitation, +/antibiotics and/or antimalarial drugs if clinically indicated A range of investigational treatments are currently being evaluated. Psycho - social support and services.

Engage with communities to promote desired health practices and behaviours, particularly on caring for sick and/or deceased persons. Provide accurate and timely health advice and information on the disease.

Reducing the risk of bat - to - human transmission arising from prolonged exposure to mines or caves inhabited by fruit bat colonies. During work or research activities or tourist visits in mines or caves inhabited by fruit bat colonies, people should wear gloves and other appropriate protective clothing (including masks). During outbreaks all animal products (blood and meat) should be thoroughly cooked before consumption.

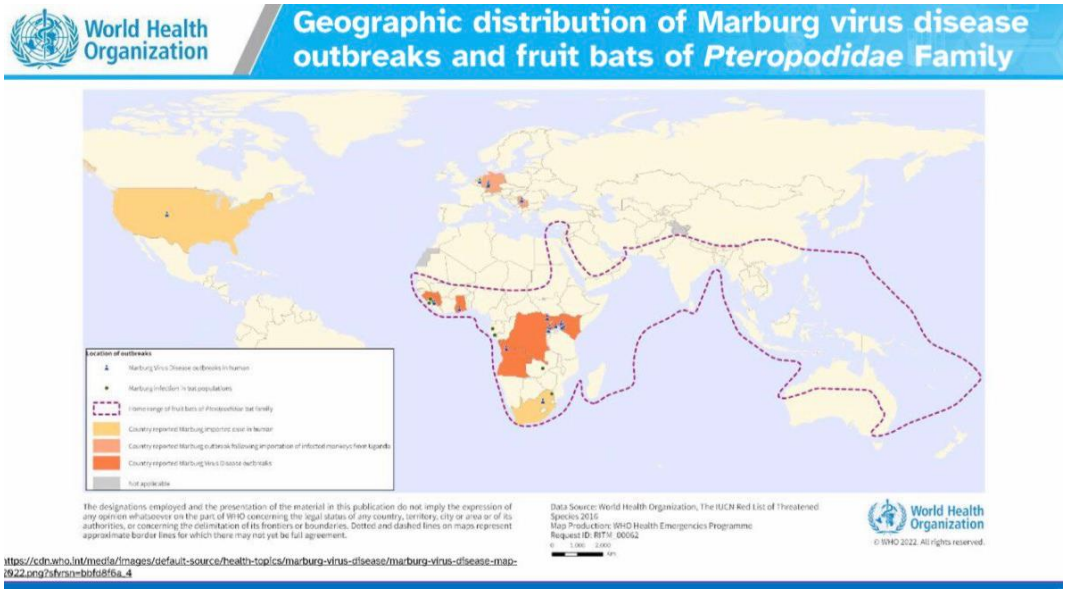
Reducing the risk of human-to-human transmission from direct or close contact with people with MVD symptoms, particularly with their bodily fluids. Avoid close contact with MVD patients and their body fluids and refer the patient early to an adequately equipped health facility. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. Safe and identified burial practices should be facilitated for suspected or confirmed MVD patients who died.

Implement Standard Precautions with all patients regardless of their diagnosis in all work practices at all times including safe injection https://www.who.int/publications/i/item/standard-precautions-in-health-care practices Health care workers treating a patient with MVD should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding. Laboratory workers are also at risk. Samples taken from suspected and confirmed MVD cases for diagnosis should be handled by trained staff and processed in suitably equipped laboratories.

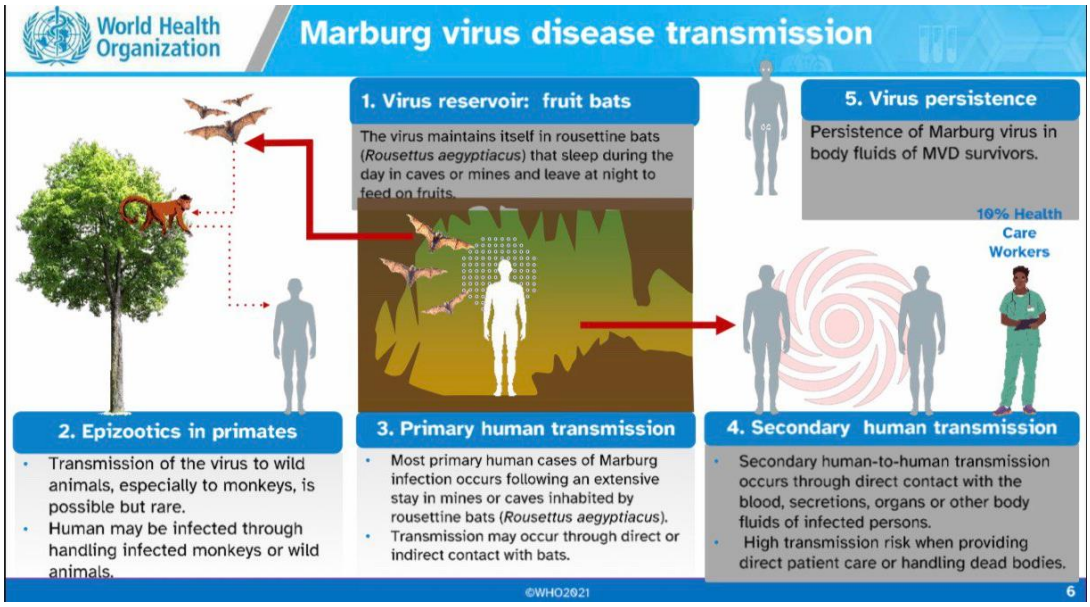
Good outbreak control relies on applying a package of interventions: Strong community engagement to empower communities in defining and adhering to outbreak control interventions. Surveillance and contact tracing Laboratory support for confirmation and patient management Case management Infection prevention and control in health facilities Safe and dignified burials.

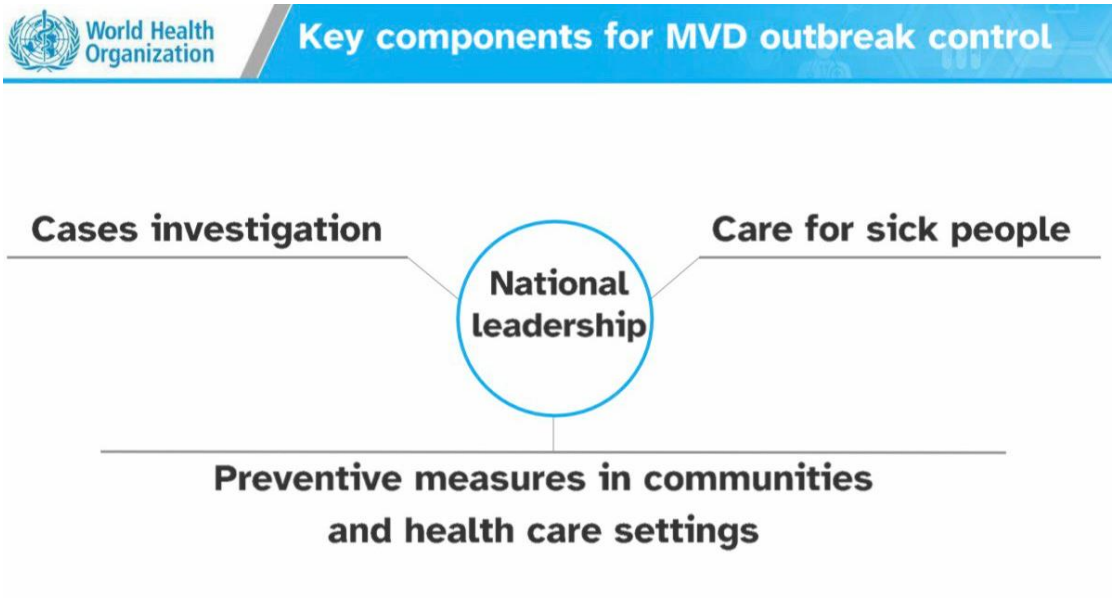
Table (1): Death percentage of Marburg in different country.

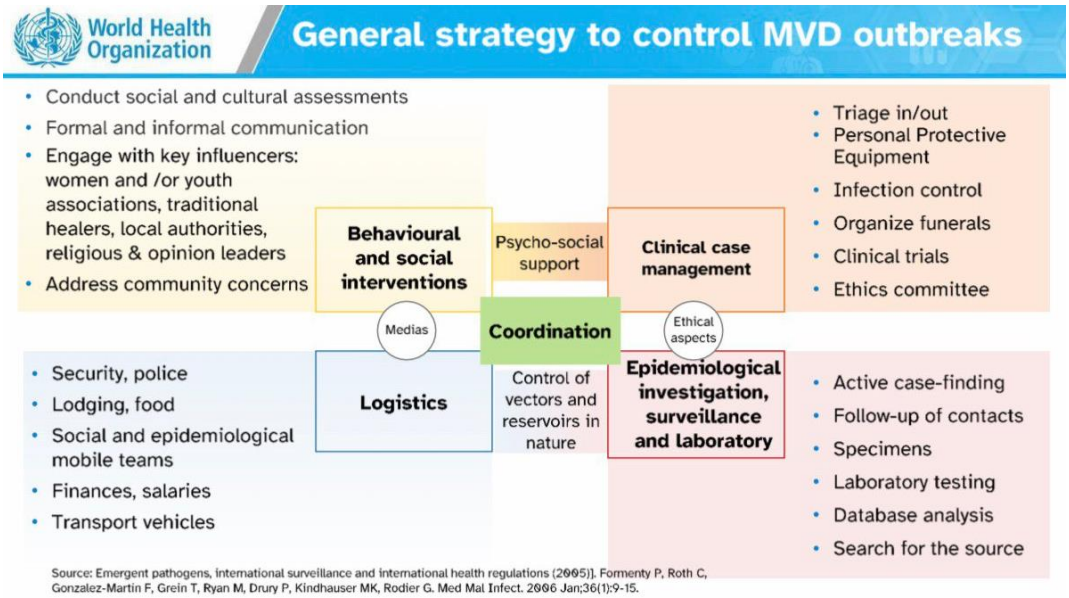
Year	Country	(confirmed and probable)	Death	CFR
2022	Ghana	3	2	66%
2021	Guinea	1	1	100%
2017	Uganda	4	3	100%
2014	Uganda	1	1	100%
2012	Uganda	15	4	27%
2008	Netherlands (ex-Uganda)	1	1	100%
2008	United States of America (ex-Uganda)	1	0	0%
2007	Uganda	4	2	50%
2005	Angola	374	329	88%
1998 to 2000	Democratic Republic of the Congo	154	128	83%
1987	Kenya	1	1	100%
1980	Kenya	2	1	50%
1975	South Africa (ex-Zimbabwe)	3	1	33%
1967	Yugoslavia	2	0	0%
1967	Germany	29	7	24%



https://cdn.who.int/media/images/default-source/health-topics/marburg-virus-disease/marburg-virus-disease-map-2022.png?sfvrsn=bbfa8f6a_4




World Health Organization
Key components for MVD outbreak control
Cases investigation
Care for sick people
National leadership
Preventive measures in communities and health care settings


World Health Organization
General strategy to control MVD outbreaks
Conduct social and cultural assessments
Formal and informal communication
Engage with key influencers: women and /or youth associations, traditional healers, local authorities, religious & opinion leaders
Address community concerns
Behavioural and social interventions
Psycho-social support
Clinical case management
Triage in/out
Personal Protective Equipment
Infection control
Organize funerals
Clinical trials
Ethics committee
Medias
Coordination
Ethical aspects
Security, police
Lodging, food
Social and epidemiological mobile teams
Finances, salaries
Transport vehicles
Logistics
Control of vectors and reservoirs in nature
Epidemiological investigation, surveillance and laboratory
Active case-finding
Follow-up of contacts
Specimens
Laboratory testing
Database analysis
Search for the source
Source: Emergent pathogens, international surveillance and international health regulations (2005)]. Formenty P, Roth C, Gonzalez-Martin F, Grein T, Ryan M, Drury P, Kindhauser MK, Rodier G. Med Mal Infect. 2006 Jan;36(1):9-15.

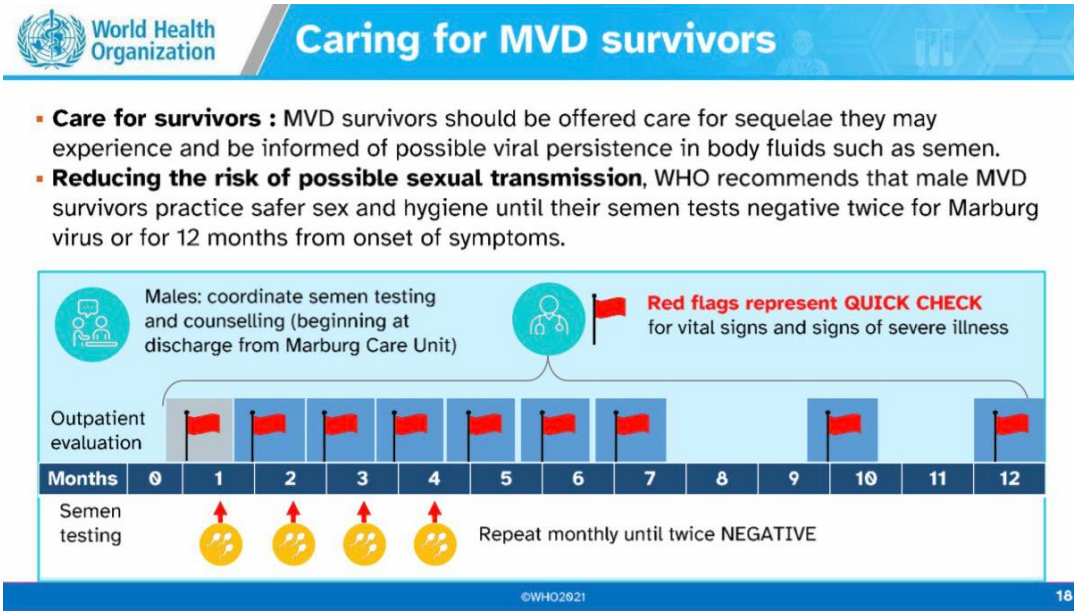


Figure (1): Marburg Virus disease.

Crimean-Congo hemorrhagic fever virus

Congo hemorrhagic fever is a viral disease that affects humans in Africa, the Balkans, the Middle East and Asia in countries located south of 50 degrees north latitude. . WHO EMRO The main reservoir and vector of CCHF is ticks of the genus Vitreous-eye, although other species of ticks can be infected with CCHF virus. - Crimean-Congo hemorrhagic fever virus is transmitted to humans; Either through a tick bite, or by coming into contact with the blood or tissues of an infected animal during or immediately after slaughter, 88% of infected people do not show sub-clinical symptoms, and one is the National Center for Influenza in South Africa / Robert. Swanepoel of eight people becomes severely ill. Clinical features of Congo hemorrhagic fever , the incubation period ranges between two and 14 days, 70% of cases of Crimean-Congo haemorrhagic fever have previously been exposed to a tick bite. It is estimated that 88% of infections are subclinical cases. The case fatality rate can be as high as 15% in patients who are hospitalized with severe symptoms. The most common symptoms include: sudden

fever, chills, shivering, muscle pain, headache, weakness, vomiting, abdominal pain, and arthralgia; . After a few days: bleeding from the mucous membranes, hematoma, bruising, black stools, hematuria, nosebleeds, vaginal bleeding, bradycardia, thrombocytopenia, and leukopenia occur.

Diagnosis of CCHF WHO EMRO Symptoms non-specific; It may be difficult to make a clinical diagnosis. The differential diagnosis includes other viral hemorrhagic fevers, malaria, typhoid fever, shigellosis, and other viral and bacterial diseases. The patient's medical history The patient's medical history is very important, and it must include the following:: Exposure to ticks (or exposure to wild animals and livestock) and/or the area/village is endemic for Crimean fever - Congo Alzvih < and/or contact with cases of Crimean fever - Congo Fawning.2018WHOO Differential Diagnosis OpenWHO.org.

Laboratory diagnosis of CCHF 10 Definitive definitive diagnosis requires the following tests: reverse transcriptase-PCR assay - enzyme-linked immunosorbent assay with IgM antibodies and IgG total group antibodies; - Antigen detection tests - Virus isolation by cell culture. . The handling personnel who collect the samples must be trained. WHO EMRO Sample handling and processing requires appropriately equipped laboratories under extreme biocontainment conditions.

Congo haemorrhagic fever: treatment Early, intensive and active supportive care Monitor fluid and electrolyte balance, renal function, blood pressure, oxygenation, and careful rehydration carefully. - Supporting the coagulation system with blood components treatment. Supportive drug therapy including: analgesics, antiemetics to treat vomiting, antianxiety drugs to treat agitation +/- antibiotics and/or antimalarial drugs. The antiviral drug ribavirin can be given early in the disease. Kidney function Fluid and electrolyte balance Supportive drug therapy Ribavirin.

Reduce the risk of tick-to-human transmission - protect yourself from tick bites, firstly, Avoid tick-infested areas. Secondly, wear light-colored clothing to easily find ticks on clothing. Thirdly, wear protective clothing e.g., long sleeves and long pants). Fourthly, Insert the ends of your pants into the socks so that ticks do not crawl into the pants. Finally, use a chemical insect repellent that contains a repellent substance for arthropods (diethyltoluamide) (on the skin), in addition to an acaricidal

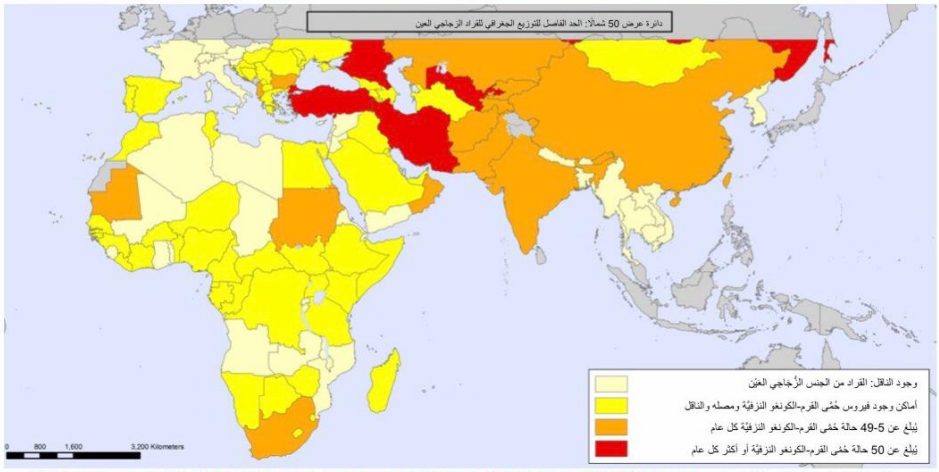
agent (acaricide) on shoes and clothes. Check daily for ticks: Clothes and skin should be checked regularly for ticks and removed.

Prevention of Crimean-Congo hemorrhagic fever: Get rid of ticks safely - use tweezers (or string). Remove the tick as close to the skin as possible. Do not bend or shake the tick. Gently pull the tick upwards until all parts of the tick have been removed. Wash hands with soap and water. Apply an antiseptic to the tick bite or clean the site with soap and water. Never crush ticks with your fingers. Avoid contact with patients infected with Crimean-Congo hemorrhagic fever and those who have died from it. Reducing the rate of transmission between humans. Wash hands with soap and water regularly. Encourage early treatment at the Congo Haemorrhagic Fever Treatment Center. . Avoid contact with others Seek medical help and advice immediately Be sure to drink plenty of fluids Ribavirin, the medicine Use gloves and a mask and keep hands clean when taking antiviral care Patients suspected of having Crimean-Congo hemorrhagic fever in patients suspected of having Congo hemorrhagic fever can be very effective if administered In the early stage of home disease.

WHO EMRO Prevention of Congo hemorrhagic fever in animal settings - Reduction of ticks in the surrounding environment: Use an acaricide (tick killer) on farms and in livestock production facilities, to reduce the spread of ticks on animals or in stables/pens. Controlling ticks with acaricides is a realistic and practical option for well-managed livestock production facilities. Quarantine animals before entering the slaughterhouse or routinely treat ruminants with acaricides 4 weeks before slaughter. This reduces the risk of infection of the animal with blood virus during slaughter. - Wear a mask, gloves and a protective gown when slaughtering and cutting animals in the slaughterhouse or at home to prevent skin contact with infected animal tissues or blood.

منظمة الصحة العالمية
المكتب الإقليمي لشرق المتوسط

التوزيع الجغرافي لحُمَّى القرم-الكونغو النزفيَّة



الخريطة متاحة على الموقع الإلكتروني: http:/www.who.int/csr/disease/crimean_congoHF/Global_CCHFRisk_2017.jpg?ua=1

منظمة الصحة العالمية
المكتب الإقليمي لشرق المتوسط

مرض حُمَّى القرم والكونغو النزفيَّة

- حُمَّى القرم-الكونغو النزفيَّة مرض فيروسي يصيب البشر في أفريقيا والبلقان والشرق الأوسط وآسيا في بلدان تقع جنوب دائرة العرض 50 درجة شمالًا.
- المستودع والناقل الرئيسي لحُمَّى القرم-الكونغو النزفيَّة هو القراد من الجنس **الزُّجَاجِي العَيْن**، وإن كانت أجناس القراد الأخرى يمكن أن تُصاب بفيروس حُمَّى القرم-الكونغو النزفيَّة .
- ينتقل فيروس حُمَّى القرم-الكونغو النزفيَّة إلى البشر؛ إما عبر لدغة القراد، وإما بملامسة دم أو أنسجة حيوان مصاب بالعدوى في أثناء الذبح أو بعده مباشرةً.
- 88% من المصابين لا تظهر عليهم أعراض دون سريرية، واحد من كل ثمانية أشخاص يُصاب بمرض وخيم.

المركز الوطني المعني بالإنفلونزا بجنوب أفريقيا/ روبرت. سوانيول

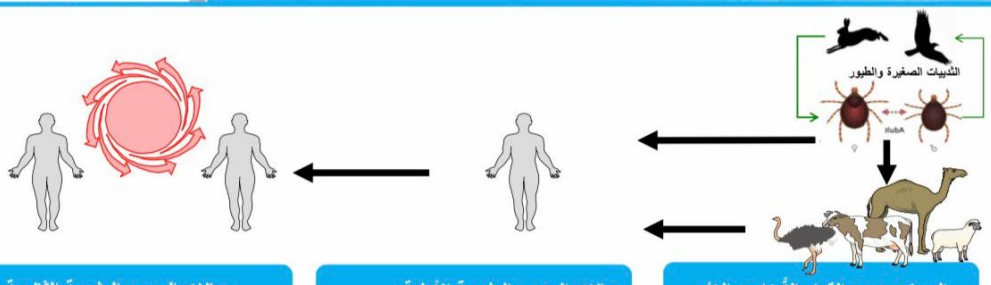
عبء حُمَّى القرم-الكونغو النزفيَّة

- 3 مليارات نسمة عرضة للخطر
- يُقدَّر بخمسمائة وفاة كل عام

المرض متوطن في أفريقيا، والبلقان، والشرق الأوسط، وآسيا

- يُقدَّر بما بين 10000 و15000 حالة عدوى بمرض حُمَّى القرم والكونغو النزفيَّة كل عام

حُمَّى القرم-الكونغو النزفيَّة: انتقال المرض



المستودع هو القراد الزُّجاجيّ العَيْن

- يُبقي فيروس حُمَّى القرم-الكونغو النزفيَّة على نفسه في الطبيعة في دورة تشمل القراد والفقاريات.
- معظم الحيوانات لا تظهر عليها أعراض.

حالات العدوى البشرية الأولية

ما بين 80 و90% من البشر يُصابون بهذا المرض عبر:

- لدغات القراد أو ملامسة مباشرة لدم القراد المصاب،
- الاتصال المباشر بدم/ أنسجة الحيوانات البرية والماشية المصابة.

حالات العدوى البشرية الثانوية

- يحدث الانتقال الثانوي للفيروس بين البشر بالملامسة المباشرة لدم شخص مصاب أو إفرازاته أو أعضاء جسمه، أو غير ذلك من سوائل الجسم الأخرى. ويكون خطر انتقال المرض مرتفعًا عند تقديم الرعاية المباشرة للمريض أو التعامل مع جثث الموتى (الجنازات).

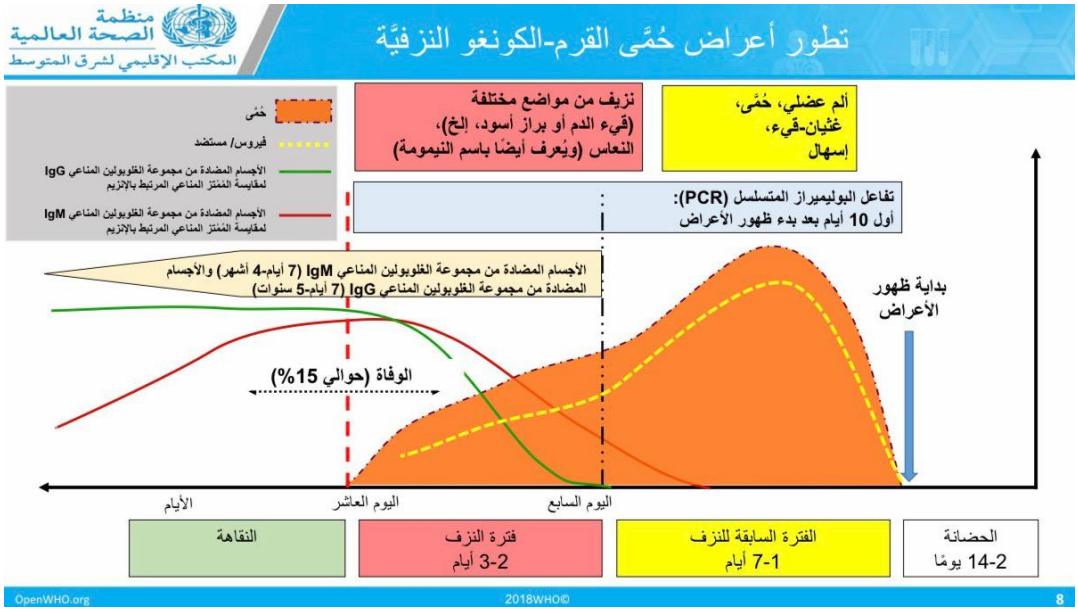


Figure (2): Congo virus fever, disease, symptoms, diagnosis and treatment.

Methodology

Study design

Meta-Analysis study design and Systematic review

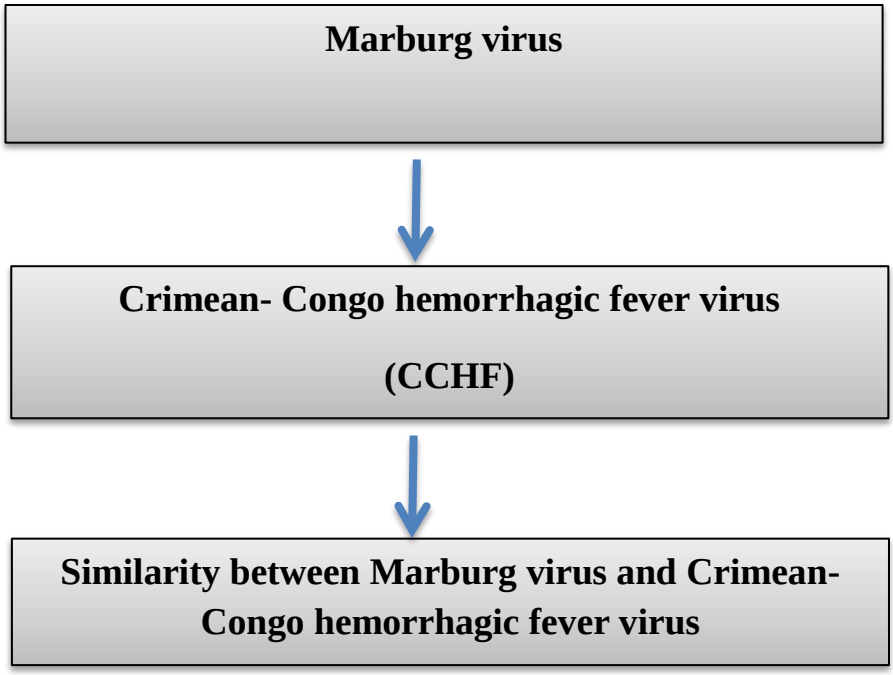


Figure (3): Scheme for this study.

Conclusions:

First: Both types of viruses Marburg Virus and Crimean-Congo hemorrhagic fever virus cause hemorrhage.

Second: The beneficial treatment for both viruses is anti-malarial treatments such as ribavirin.

Third: The diagnosis of the disease using molecular methods, as in the use of the PCR device.

About author

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Scientific assistant of Atwar Academy for scientific and research development

The best Arabic scholar

Editorial Director of the Journal of Articles and Inventions, Goidi American Journal

International Invention Executive Ambassador from America

Head of the Planning and Follow-up Department at the Arab Council for Training and E-Learning

Rapporteur of the Department of Anesthesia and Intensive Care

Representative of the International Commission for Investment, Invention and American Development in Iraq

Researcher, creator, scientist, inventor, author, expert in medical laboratories, consultant in medical laboratories, and one of the pioneers of invention in America

PhD in Biotechnology / Molecular Genetics / Genetic Engineering

Master's degree Microbiology / Molecular Biology

Bachelor's degree in Microbiology / Biology

Professional Doctorate in Quality

Professor Emeritus of World Sciences

Mini Master in Business Administration

Distinguished publisher of more than 150 research, articles and

Author of books and translator books

Inventor of more than 13 patents accepted in Iraq and published in America

٦ strains are registered in the American Genome Bank NCBI

Iraqi bacterial strains named after Nebras Rada Mohammed

holds gold medals and decorations for more than 150 medals and gold medals

She holds books of thanks and appreciation for more than 100 books of thanks and appreciation and certificates of appreciation

Member of more than 60 international and local associations

Recipient of many awards in different countries around the world, including

Best Community Personality Award 2020

Best Arab Woman Award in the Middle East 2020

WIPO World Intellectual Property Award

Best Research Award in the Middle East 2020

Best Research Award 2019 in Egypt / Sharm El-Sheikh

٤ awards from Toronto, Canada

First place award for invention from America for the patent of clot treatment

First place award from America for the patent of propolis purification

First place award from America for patent colistin gene

Honoring the best Arab scientist from the Atwar Academy for Scientific and Research Development

Wissam Mashoua is a scientist from Malaysia and Britain / London

Best distinguished inventor from America

Scientific creativity

Scientific excellence

The best Arab scientist

PhD in free media

A doctorate in postgraduate studiesa professional doctorate

An honorary doctorate

A professional doctorate in medical quality

Editor-in-chief of Atwar magazine for Arab women

A scientific assistant at Atwar Academy

The account of the researcher, Dr. Nebras Rada Mohammed

1-Researchgate account

https://www.researchgate.net/profile/Nebras-Mohammed-2

2-Publons account

/ https://publons.com/wos-op/p/44212198

3-ORCID account

https://orcid.org/0000-0003-1566-0995

4-Google Scholar account

https://scholar.google.com/citations?h/=en&user=JBmiuBYAAAAAJ

5-Researchid account

https://researchid.co/nebrasradamohammed

6-Scientific platform account

arid.my/0004-3323

7-Facebook account

https://www.facebook.com/nebrasrada

8-My LinkedIn account

https://www.linkedin.com/in/nebras-rada-mohammed-525060247

9-My YouTube channel link

youtube.com/channel/UCsM4STS9xb4ItLcT_hCHRzg

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https://portal.issn.org/resource/ISSN/2694-5460

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3-Mohammed, N. R. Inhibition gene expression MexAB-OprM and MexXY efflux pumps of Pseudomonas aeruginosa (XDR) by Novel inhibitors Levofloxacin, Silver nanoparticles and Beta rays. infection, 6, 7.