



सत्यमेव जयते

Ministry of Health & Family Welfare
Government of India

A Comprehensive Learning Guide

Crimean-Congo Hemorrhagic Fever



**NATIONAL CENTRE FOR DISEASE CONTROL
DIRECTORATE GENERAL OF HEALTH SERVICES**
Ministry of Health & Family Welfare, Government of India



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National Centre for Disease Control
Directorate General of Health Services
Ministry of Health & Family Welfare,
Government of India

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स्वास्थ्य सेवा महानिदेशक

DIRECTOR GENERAL OF HEALTH SERVICES



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Government of India
Ministry of Health & Family Welfare
Directorate General of Health Services



Message

Zoonotic diseases pose a significant and ongoing threat to biodiversity, human and public health and economic stability. Given India's diverse ecosystem, high population density and increasing human-animal action, the country remains particularly susceptible to zoonotic outbreaks. Past occurrences of plague, Nipah virus, avian influenza, leptospirosis, and Kyasanur Forest Disease emphasizes a critical need for robust surveillance, early detection, and a coordinated, intersectoral response.

Recognizing the importance of addressing zoonotic diseases as a public health priority, the Centre for One Health, under the National Centre for Disease Control (NCDC), is committed for strengthening surveillance, prevention, and response mechanisms through an integrated One Health approach. As part of this effort, the Centre for One Health has developed comprehensive learning guides on Priority Zoonotic Diseases. These modules provide scientifically validated, evidence-based guidance on the epidemiology, diagnosis, treatment, and prevention of key zoonotic diseases.

Strengthening disease surveillance, ensuring early diagnosis, and implementing timely interventions through a coordinated and multi-sectoral approach are critical to mitigating the risks associated with zoonotic diseases.

I am pleased to release these learning guides as a significant step in our ongoing efforts to combat zoonotic diseases. I urge all healthcare professionals, veterinary experts, and community leaders to actively utilize these resources to enhance their clinical index of suspicion for zoonosis and eventually contribute towards strengthening our health care system for responding timely and more efficiently to future outbreaks.

(Atul Goel)



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MESSAGE

It is my pleasure to know that the Centre for One Health at NCDC has prepared **Comprehensive Learning Guides** on 10 priority zoonotic diseases, which is now being shared with all concerned.

These resources become relevant in considering; India has encountered multiple zoonotic disease outbreaks in recent years, highlighting their persistent and evolving threat to public health. The re-emergence of **Nipah virus** in Kerala, **Kyasanur Forest Disease (KFD)** in Karnataka, and **avian influenza** across several states underscores the complex interconnections between human, animal, and environmental health. The rising cases of **leptospirosis** and **scrub typhus**, driven by climatic changes and ecological disruptions, further illustrate the unpredictable nature of zoonotic spillovers. With the additional challenges posed by **emerging coronaviruses** and **antimicrobial resistance (AMR)**, there is an urgent need for a **cohesive, evidence-based approach** to mitigate these risks effectively.

In recognition of this pressing need, the **National Centre for Disease Control (NCDC)** has intensified its efforts to fortify **zoonotic disease surveillance, outbreak preparedness, and intersectoral coordination**. As part of this initiative, the **Centre for One Health, NCDC**, has meticulously curated **Comprehensive Learning Guides** on priority zoonotic diseases. These guides, underpinned by the latest scientific insights and global best practices, serve as indispensable resources for **healthcare professionals, veterinarians, and epidemiologists**, equipping them with the knowledge to anticipate, detect, and mitigate zoonotic threats with precision.

To effectively curtail the impact of zoonotic diseases, a **harmonized One Health approach** is paramount—one that transcends disciplinary boundaries and fosters synergies across the human, animal, and environmental health sectors. I urge all stakeholders to **leverage these scholarly resources, enhance disease intelligence networks, and champion research-driven interventions**. By embracing a proactive and interdisciplinary ethos, we can **bolster pandemic preparedness, fortify national health security, and avert future spillover events**.

I sincerely **appreciate** my colleagues at the Centre for One Health, NCDC for their dedication to strengthening zoonotic disease control. Their efforts in enhancing surveillance, preparedness, and public health response are crucial in preventing and managing emerging health threats.

I am glad to see their commitment translating into evidence-based interventions and capacity-building initiatives that enhance zoonotic disease surveillance, outbreak preparedness, and overall health system resilience.

Through continuous innovation, collaboration, and unwavering dedication, we can fortify our health systems and safeguard our nation against zoonotic threats.

Wishing you all happy learning and skill enhancement wherever possible.

रंजन दास 19/3/25
Prof. (Dr.) Ranjan Das



Antibiotic resistance Containment Stewardship: Our Role, Our Responsibility
Judicious Use of Antibiotic: Key to Contain Antibiotic Resistance





भारत सरकार

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Message

Zoonotic diseases of public health importance continue to pose significant challenges to public health. These diseases, often driven by intricate human-animal-environment interactions, present substantial health risks, particularly to vulnerable populations, and demand a coordinated and robust response from the health sector.

In recognition of the pivotal role healthcare providers play in addressing these challenges, the **Centre for One Health** has developed a **Comprehensive Learning Guide for Priority Zoonotic Diseases**. This guide is designed to build capacity across the health sector, equipping professionals with the essential knowledge and skills needed to identify, manage, and prevent these diseases effectively. By enhancing surveillance systems, fostering rapid and accurate diagnostics, and implementing targeted prevention and control measures, healthcare providers can play a transformative role in mitigating the impact of zoonotic diseases.

The guide emphasizes the importance of building a resilient health workforce capable of responding to outbreaks, engaging communities, and collaborating across disciplines. Through these efforts, we aim to reduce the burden of zoonotic diseases, improve health outcomes, and contribute to the creation of a safer and healthier future.

I encourage all healthcare professionals to utilize this guide as a resource for improving their understanding and response to zoonotic diseases. Together, let us strengthen our health systems and work towards a future free from the threats posed by zoonotic diseases.

Dr. Simmi Tiwari
Joint Director and Head
Centre for One Health



Antibiotic Resistance Containment Stewardship: Our Role, Our Responsibility
Judicious Use of Antibiotic: Key to Contain Antibiotic Resistance



Acknowledgement

The **Comprehensive Learning Guide** for Crimean-Congo Haemorrhagic Fever (CCHF) has been developed to address the significant public health challenges posed by zoonotic diseases, which have serious health, economic, and social implications, particularly for vulnerable populations. The priority zoonotic diseases necessitate robust surveillance, timely diagnosis, and effective prevention and control measures. This guide aims to strengthen the capacity of healthcare professionals by equipping them with the requisite knowledge and skills to mitigate these public health threats and improve health outcomes.

We acknowledge with deep appreciation the valuable contributions of the **subject matter experts** from leading medical institutions and research organizations, whose guidance and technical expertise has been critical in shaping this **Comprehensive Learning Guide**.

The Centre for One Health, NCDC, expresses its sincere gratitude to Ms. Punya Salila Srivastava, Secretary, Health and Family Welfare, Government of India; Ms. L.S. Changsan, Additional Secretary, Ministry of Health and Family Welfare, Government of India; Prof. (Dr.) Atul Goel, Director General of Health Services (DGHS), Government of India; Ms. Latha Ganapathy, Joint Secretary, Department of Health & Family Welfare, Government of India for their leadership, guidance, and support.

Lastly, we acknowledge the USAID-funded RISE project team, implemented by Jhpiego, for their technical support in drafting and finalizing this guide. Their collaboration has been pivotal in ensuring the quality and relevance of this resource.

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Preface

CCHF is a severe tick-borne viral disease that affects both animals and humans. The disease is primarily transmitted to humans through direct contact with the blood or other bodily fluids of infected animals, or through the bite of infected ticks. With its potential for rapid transmission and high fatality rate, CCHF poses a significant public health concern in many parts of the world, particularly in regions where the disease is endemic. Understanding the disease, its transmission, and effective preventive measures are crucial for minimizing the risk of outbreaks and ensuring timely and accurate diagnosis.

This scientific guide aims to equip learners with the knowledge and tools necessary to educate and train individuals involved in various aspects of CCHF management. It provides a comprehensive overview of the disease, covering its epidemiology, clinical presentation, laboratory diagnosis, treatment options, and preventive measures.

The guide is structured in a user-friendly manner, allowing learners to effectively communicate complex scientific concepts to their audience. It contains detailed explanations to enhance understanding and engagement. The content is supported by the latest scientific research and public health guidelines, ensuring the information presented is accurate and up to date.

It is our sincere hope that this guide will serve as a valuable resource for learners and educators, enabling them to grasp essential knowledge and skills. By equipping professionals and individuals at risk with the necessary information, we can enhance our collective ability to detect, prevent, and respond to CCHF outbreaks, thereby safeguarding public health.

We would like to express our gratitude to all the experts, researchers, and contributors who have provided their invaluable insights and expertise in developing this scientific module. Their dedication and commitment to public health have been instrumental in creating a comprehensive resource that will contribute to the effective management of CCHF.

We hope you find this module informative, engaging, and ultimately, empowering. Together, let us work towards building a safer and healthier future by combating CCHF through knowledge and preparedness.

Abbreviations

ABG	Arterial Blood Gas
AD	Additional Director
ARDS	Acute Respiratory Distress Syndrome
ALT	Alanine Transaminase
APTT	Activated Partial Thromboplastin Time
ASHA	Accredited Social Health Activist
AST	Aspartate Transaminase
BT	Blood Transfusion
BSL	Biosafety Level
CBC	Complete Blood Count
CCHF	Crimean-Congo Haemorrhagic Fever
CCHF	Crimean-Congo Haemorrhagic Fever Virus
CCF	Crimean-Congo Fever
CDHO	Chief District Health Officer
CHC	Community Health Centre
CMO	Chief Medical Officer
CPK-MM	Creatine Phosphokinase Muscle Isoenzyme
CPK Total	Total Creatine Phosphokinase
CRP	C-Reactive Protein
CRYO	Cryoprecipitate
CFR	Case Fatality Rate
CSF	Cerebrospinal Fluid
DD	Deputy Director
DEET	Diethyltoluamide
DH	District Hospital
EDTA	Ethylenediaminetetraacetic Acid
EIA	Enzyme Immunoassay
ELISA	Enzyme-Linked Immunosorbent Assay
FFP	Fresh Frozen Plasma
FNAC	Fine Needle Aspiration Cytology
HAV	Hepatitis A Virus
HCW	Health Care Worker
HEPA	High-Efficiency Particulate Air
HEV	Hepatitis E Virus
HSADL	High Security Animal Disease Laboratory
ICAR	Indian Council of Agricultural Research
ICMR	Indian Council of Medical Research
ICU	Intensive Care Unit
IDSP	Integrated Disease Surveillance Program
IEC	Information, Education, and Communication
IFA	Immunofluorescence Assay
IgG	Immunoglobulin G
IgM	Immunoglobulin M

INR	International Normalized Ratio
KFD	Kyasanur Forest Disease
LDH	Lactate Dehydrogenase
LFT	Liver Function Test
MCQ	Multiple Choice Questions
MICU	Medical Intensive Care Unit
MO	Medical Officer
MPHW	Multi-Purpose Health Worker
NAAT	Nucleic Acid Amplification Test
N-95	N95 Respirator Mask
NCDC	National Centre for Disease Control
NIV	National Institute of Virology
NSAID	Non-Steroidal Anti-Inflammatory Drugs
NS1	Non-Structural Protein 1
OPD	Outpatient Department
PCV	Packed Cell Volume
PEP	Post-Exposure Prophylaxis
PHC	Primary Health Centre
PPE	Personal Protective Equipment
PRP	Platelet-Rich Plasma
PT	Prothrombin Time
RBS	Random Blood Sugar
RDT	Rapid Diagnostic Test
RDD	Regional Deputy Director
RNA	Ribonucleic Acid
RMO	Resident Medical Officer
RRT	Rapid Response Team
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SDP	Single Donor Platelet
SGOT	Serum Glutamic-Oxaloacetic Transaminase
SGPT	Serum Glutamic-Pyruvic Transaminase
sRNA	Small RNA
TLC	Total Leukocyte Count
USG	Ultrasonography
USSR	Union of Soviet Socialist Republics
VHF	Viral Haemorrhagic Fever
WHO	World Health Organization
ZPHI	Zoonotic and Public Health Importance

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Introduction to Learning Guide for Crimean-Congo Haemorrhagic Fever (CCHF)

Zoonotic diseases have played a critical role in human evolution, particularly in populations that domesticated animals for food and clothing. These diseases continue to pose a major global threat, transcending ecological and geopolitical boundaries. Their impact on public health and the global economy is considerable, influencing international trade through disease transmission and regulatory restrictions. Effective control necessitates robust global surveillance and coordinated response systems.

Controlling zoonoses remains a priority for international agencies, addressing the specific health and economic challenges of each region. Despite being poorly documented, zoonotic diseases pose a significant public health problem in India. They equally impact animal, human, and environmental sectors, causing substantial damage to the nation's economy. To protect all sectors, it is essential for India to rapidly identify, diagnose, and manage these diseases. The One Health approach plays a crucial role in this endeavor, as we have learned valuable lessons from the COVID-19 pandemic regarding the need for strong surveillance and diagnostic preparedness to handle future pandemic situations.

To provide comprehensive training, the Center for One Health, NCDC has developed Learning Guide. These packages serve as both trainers' guides and self-directed learning resources. The training focuses on zoonoses and zoonotic diseases of public health importance in India (ZPHI) and emphasizes the One Health approach to responding to zoonotic diseases. By the end of the training, participants should have a solid understanding of the core principles of CCHF, its outbreak potential, health emergencies, risk communication, diagnostic procedures, laboratory safety, surveillance, data reporting, and their applications.

The guide is based on national and international guidelines and serve as a comprehensive training resource for individuals involved in zoonotic disease diagnosis and surveillance activities. They provide a deeper insight into the understanding of CCHF. The curriculum is designed to enable facilitators and learners to undergo step-by-step learning within a specified time frame, ensuring a thorough understanding of each module.

The guide caters to various audiences, including medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel who are expected to acquire knowledge and competencies beyond their regular field of work.

The learning resource guide consists of a Facilitators' Guide (FG), which provides instructional processes and supports educators in facilitating and assessing learning. Each module follows a standardized structure, including a session outline, detailed session plans, slide decks, and a wide range of references and resources for further reading. These resources offer comprehensive information on the respective topics.

The learning guide aims to provide a comprehensive education for medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel. It helps them understand, identify, and differentiate between zoonotic diseases and equips them with the necessary knowledge and orientation for diagnostics procedures and surveillance systems.

Course Description

Course Design

This comprehensive CCHF training guide is tailored for medical professionals including doctors, veterinarians, paramedical staff and laboratory personnel. The course is designed to enhance their understanding and expertise in dealing with CCHF cases, spanning various aspects of prevention, diagnosis, and treatment. The training approach emphasizes practical application, aiming to equip participants with hands-on skills and competencies that can be directly applied in their professional roles.

Evaluation Approach

The evaluation approach for the CCHF preparedness and response training guide includes a comprehensive pre- post-training quiz questionnaire designed to assess participants' knowledge and learning progression. The questionnaire utilizes multiple-choice questions (MCQs) to gauge participants' understanding of CCHF related concepts before and after the training. This approach allows for a clear measurement of knowledge enhancement and provides valuable insights into the effectiveness of the training program.

- ***Pre-Training Quiz:***

Before the training begins, participants will be administered a pre-training questionnaire. This questionnaire serves as a baseline assessment of participants' existing knowledge and awareness of CCHF. The pre-training quiz will consist of MCQs that cover various aspects of CCHF, including its etiology, modes of transmission, clinical manifestations, prevention measures, and response strategies. The purpose of the pre-training quiz is to establish a starting point and identify areas where participants may require more focused training.

- ***Post-Training Quiz:***

Upon completion of the CCHF preparedness and response training guide, participants will be given a post-training quiz questionnaire. This questionnaire will contain a similar set of MCQs as the pre-training quiz, covering the same topics related to CCHF. The aim of the post-training quiz is to evaluate participants' knowledge advancement and to measure the effectiveness of the training in enhancing their understanding of CCHF related concepts and procedures.

Course Syllabus

Course Goals

Foster an in-depth comprehension of CCHF and its diverse forms.

- Equip participants with skills for CCHF diagnosis, management, and prevention.
- Emphasize the importance of the One Health approach in addressing zoonotic diseases.
- Develop proficiency in risk communication, laboratory safety, and surveillance strategies.

Participant's Learning Objectives

By the course's conclusion, participants will be able to:

- Identify various CCHF forms and their clinical characteristics.
- Apply diagnostic and treatment protocols for CCHF management.
- Implement preventive strategies and outbreak management tactics.

Participant Selection Criteria

Participants for this CCHF response and preparedness training should be professionals from various fields involved in emergency response and public health:

- Emergency Responders: Including public health experts, medical personnel, and first responders.
- Laboratory and Biosafety Staff: Those experienced in handling biohazards.
- Government and Decision-Makers: Officials with authority in emergency coordination.
- Community Leaders and Experts: Community influencers, researchers, and mental health specialists.

Using the Resource Guide

All training activities in this course will be conducted in an interactive, participatory manner using the training guide appropriately as suggested in the course outline in the facilitators' guide. To accomplish this, the trainer will have to change roles throughout the course. For example, the trainer is a facilitator when conducting small group discussions and finally, when objectively assessing performance, the trainer serves as an evaluator.

Composition of Participants

The training is intended for 15-20 participants hailing from various state and healthcare fraternities. There can be a single facilitator as an expert of the disease.

Course Schedule

Morning Session

Introduce and welcome participants

- Discuss participant expectations and prior knowledge
- Outline the objectives of the course and learning outcomes

Review the course schedule and its components

- Provide an overview of the training guide materials
- Conduct a pre-course knowledge assessment to gauge participants' baseline understanding
- Distribute course materials, including handouts and resources

Interactive presentations

- Take Sessions 1-4 and discuss in detail about basics of CCHF, its epidemiology, bioweapon potential, clinical disease and its significant features in humans and animals.
- Interactive discussion and Q&A session after the lecture

Afternoon Session

Interactive presentations

- Take Sessions 5-10 and discuss in detail about frequently asked questions, diagnosis of CCHF, its treatment, prevention & control, outbreak management and surveillance.

Debriefing and group discussions on simulation outcomes

- Interactive discussion and Q&A session after the lecture

Review, Assessment, and Closing

- Comprehensive review of key concepts covered during the training
- Interactive quiz to reinforce learning
- Final assessment to measure participants' understanding of course material
- Reflection session: Participants share insights and takeaways from the course
- Closing remarks, thanking participants for their engagement

Course Outline

The course outline presented here follows a model structure for the training curriculum. It delineates the enabling objectives necessary to achieve the participant learning goals outlined in the course syllabus. The outline offers recommendations for suitable learning activities and essential resources and materials for each enabling objective. Depending on specific participant requirements, the trainer has the option to introduce supplementary practice activities, devise case studies, role-play scenarios, or tailor learning situations accordingly.

The course outline comprises four columns:

- **Duration:** This column specifies the estimated time allocated for each learning activity. This allocation ensures an equitable distribution of time across the diverse training components.
- **Learning Objectives:** This column lays out the enabling objectives and their alignment with corresponding learning activities. The objectives are sequenced to provide guidance on the training structure. The interplay of objectives and activities—ranging from icebreakers and interactive group tasks to practical exercises and breaks—constitutes the overall training progression.
- **Pre-requisite Knowledge/Skill:** This column addresses the foundational knowledge or skills that participants should possess prior to the session. It underscores the importance of existing competencies for effective engagement in the training.
- **Competencies to be Achieved:** The fourth column enumerates the competencies participants are expected to acquire by the conclusion of the session. It underscores the practical outcomes that participants will attain through engagement in the training.

AGENDA		
S. No	Topic	Duration
1.	Welcome & Introduction of the training agenda and setting ground rules	15 min
2.	Ice breaker: Talk about yourself • Contribution to the management & control of zoonoses • Expectations from the training	30 min
3.	Training objectives	15 min
4.	Pre-Test Quiz	15 min
5.	Session 1: Introduction to CCHF	15 min
6.	Session 2: Epidemiology of CCHF	30 min
7.	Session 3: Etiology, Transmission & Emergence of CCHF	20 min
8.	Session 4: Case Definition & Disease Progression	20 min
9.	Session 5: Clinical Manifestations & Differential Diagnosis	15 min
10.	Session 6: Laboratory Diagnosis of CCHF	20 min
11.	Session 7: Case Study, Treatment & Prevention of CCHF cases	20 min
12.	Session 8: Outbreak Management	20 min
13.	Session 9: Surveillance & Risk Communication	15 min
14.	Session 10: Sample Collection, Storage and Transportation	15 min
15.	Post - Test Quiz	15 min
16.	Q/A session, review and discussion	15 min
17.	Group activity: Understanding priorities, concerns and challenges of state on zoonoses	15 min
18.	Closing remarks	5 min

Session-1

Introduction to CCHF

Course No. 001	Session 1: Introduction to CCHF
Duration	15 minutes
Learning Objective	• Define CCHF • Understand historical background and key milestones in understanding CCHF • Describe disease overview
Pre-requisite knowledge/skill	• Basic understanding of infectious diseases and epidemiology. • Knowledge of biosafety and infection prevention practices. • Familiarity with zoonotic diseases and tick-borne transmission.
Competencies to be achieved	• Learners would gain knowledge of the basic characteristics and features of CCHF • Learners would understand the historical context and significant milestones in the study and understanding of CCHF • Learners would be able to describe the key aspects of CCHF

INTRODUCTION

CCHF (Crimean-Congo Hemorrhagic Fever) is a zoonotic disease that remains a significant public health concern in numerous countries. Its global distribution spans across Asia, ranging from China's Xinjian region to the Middle East and southern Russia, and includes focal areas in Africa and parts of southeastern Europe. Consequently, the CCHF is currently recognized as the most widely prevalent cause of severe hemorrhagic fevers. Like other zoonotic agents transmitted by ticks, the CCHF naturally circulates in an enzootic cycle involving ticks, vertebrates, and ticks again. Primarily affecting livestock such as cattle, sheep, and goats (acting as reservoirs), humans become infected through direct contact with blood or tissues from infected animals or through tick bites. Therefore, pastoral communities are particularly vulnerable to this disease.

Although CCHF cases are sporadic in nature, the case fatality rates (CFR) among hospitalized patients have varied from 9% to as high as 50%. CCHF outbreaks pose a threat to public health services due to their potential for epidemics, high CFR, and the possibility of nosocomial outbreaks. Additionally, the challenges associated with treatment and prevention further compound the burden on the healthcare sector. Consequently, the country's health system may become overwhelmed, leading to significant economic challenges as well.

Introduction

- The common vector for CCHF virus is ticks of the genus *Hyalomma*.
- The virus is transmitted to humans either directly by *Hyalomma* ticks or by contact with blood or secretions of infected domestic animals or their meat.
- CCHF virus is primarily a zoonotic virus, which means that the transmission cycle mainly involves ticks and wild or domestic animals.
- Hard ticks are the reservoir and the vector for CCHF virus. In addition, infected animals may also act as reservoir during the period of viraemia.
- Cattle, sheep and goats do not become ill after infection but are viraemic for about one week.
- During this period of time the virus may be transmitted to humans who have close contact to these animals such as agricultural workers, slaughterhouse workers, cooks and veterinarians.

Source: www.reliefweb.int/report/afghanistan/operational-guidelines-prevention-and-control-cCHF-afghanistan-2012



Centre for One Health, NCDC, MoHFW

CRIMEAN-CONGO HAEMORRHAGIC FEVER

Notes

Introduction contd...

- The virus may be spread into other geographical regions via infected livestock.
- The virus may also be transmitted from human to human via blood and secretions. This might occur primarily in the hospital setting and the health care workers are mainly at risk in this situation
- Case fatality rates (CFR) in hospitalized patients have ranged from 9% to as high as 50%
- WHO classified CCHF as its priority A disease considering its risk to both public health as well as national security
- It is a notifiable disease in India and is classified as an Emerging zoonotic disease of public health importance



Image source: https://www.researchgate.net/publication/264148481_Crimean-Congo_Haemorrhagic_Fever_in_Afghanistan, <https://www.dailymail.co.uk/health/article-2388883>

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Session-2

Epidemiology of CCHFV

Course No. 002	Session 2: Epidemiology: Distribution and Case Fatality
Duration	30 minutes
Learning Objective	• Understand epidemic potential of CCHFV • Describe seasonality and case fatality rate of CCHFV • Understand geographical distribution of CCHFV in India • Understand overview of global distribution and prevalence of CCHFV
Pre-requisite knowledge/skill	• Understanding of CCHF transmission dynamics, epidemic potential, and seasonality. • Knowledge of case fatality rates and geographical distribution of CCHF in India. • Awareness of global distribution and prevalence of CCHF.
Competencies to be achieved	• Epidemic potential assessment of CCHFV • Analysis of seasonality and understanding its implications. • Analysis of case fatality rate and its significance. • Assessment of geographical distribution of CCHFV in India. • Explain global distribution and prevalence of CCHFV

HISTORICAL BACKGROUND

Crimean-Congo Hemorrhagic Fever (CCHF) was initially identified and documented during the Spring and Summer of 1944 when around 200 Soviet army troops and agricultural workers in Crimea exhibited symptoms of a febrile illness. Subsequent to this initial observation, small clusters of similar cases continued to be reported annually in the same geographical region. The investigation and documentation of the inaugural outbreak were conducted by military physicians and later by a scientific expedition led by Professor Mikhail Chumakov of the USSR Academy of Medical Science. Notably, Chumakov played a crucial role in the development of the oral polio vaccine. Prior to his involvement in CCHF research, he had been part of a team that uncovered the viral cause of tick-borne encephalitis (TBE). This discovery came about unexpectedly when Chumakov himself contracted the infection during an autopsy, resulting in a permanent loss of hearing and paralysis of his right arm.

Chumakov and his collaborators coined the term Crimean Haemorrhagic Fever (CCHF) to characterize a syndrome marked by fever and various haemorrhagic complications, predominantly affecting the gastrointestinal system, accompanied by hypotension and shock. In the initial report in 1944, the case fatality rates stood at 8%. The emergence of CCHF in Crimea during this period is attributed to favorable environmental conditions exacerbated by wartime circumstances, including neglected agricultural lands, the influx of a non-immune population, and a local surge in the hare population due to reduced hunting.

Russian investigators noted the resemblance between CHF and a severe febrile illness in the 12th-century documented reports by the Tadjik physician and philosopher Dzhurdzhani. Additionally, in Uzbekistan, a comparable haemorrhagic disease was referred to as 'karakhalak,' translating to black death.

Initial attempts by Russian scientists to establish an animal model and identify the cause of CHF proved unsuccessful across various species, including white mice, guinea pigs, rabbits, monkeys, and cats. In 1945-46, psychiatric patients were directly injected with samples from clinical cases in Crimea as a form of pyrogenic therapy. Injection of a pulverized and filtered suspension from *Hyalomma marginatum* nymphs induced a characteristic CHF illness.

The first reliable USSR animal model emerged in 1967 at the Institute of Poliomyelitis and Viral Encephalitis in Moscow, utilizing newborn white mice brains for serial passage and isolation. Russian investigators noted a high incidence of cases among milkmaids and agricultural workers, many of whom frequently removed and crushed engorged ticks from cattle with their fingers. They also highlighted ground-feeding birds as tick hosts, acknowledging the potential risk of introducing and establishing CCHF in new geographical areas.

CCHF is endemic across Africa, the Balkans, the Middle East, and parts of Asia located south of the 50th parallel north, which marks the geographic range of its primary tick vector, the *Hyalomma* genus. The virus (CCHF) is widely spread throughout Asia, from western China's Xinjiang region to the Middle East and southern Russia.

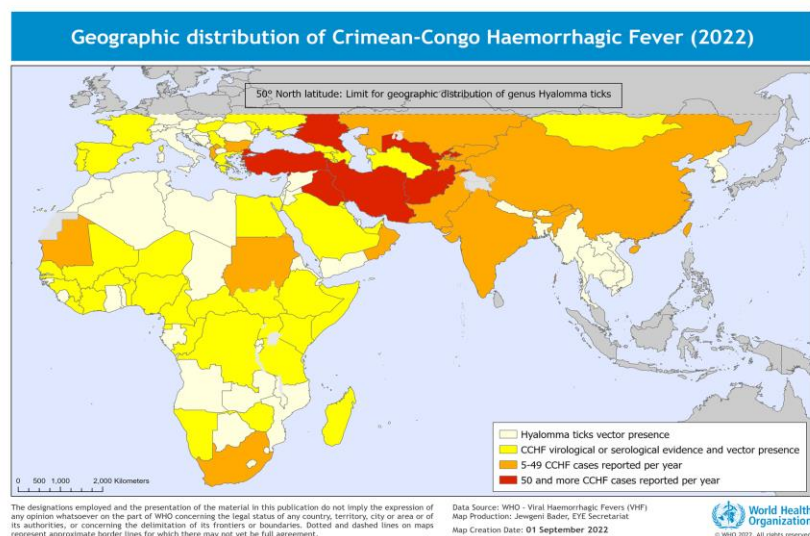


Fig 1- Geographic distribution of CCHF (2022)

Reported CCHF cases span several regions:

1. **Southeastern Europe and Russia:** Countries affected include Ukraine, Bulgaria, Albania, Serbia & Montenegro (Kosovo), Turkey, North Macedonia, and the Russian Federation.
2. **Asia:** Cases have been recorded in China, Kazakhstan, Tajikistan, Pakistan, Afghanistan, and India.
3. **Middle East:** Iraq, Iran, the United Arab Emirates (UAE), Saudi Arabia, and Oman have all reported cases. In 2022, Iraq experienced a large outbreak, with 212 cases and 27 deaths reported to the WHO.
4. **Africa:** The virus has been found in Mauritania, Senegal, Burkina Faso, the Republic of Congo, the Democratic Republic of Congo, Uganda, Kenya, Tanzania, South Africa, and Namibia.

In addition, Greece recorded its first clinical case of CCHF in July 2008.

Table 1: Geographic distribution of CCHF according to S-segment analysis.

Genotype	Countries
Africa 1	Western Africa (Senegal, Mauritania)
Africa 2	Central Africa (Uganda, Democratic Republic of Congo)
Africa 3	South Africa, Nigeria, Uganda
Asia 1	The Middle East (Iran, Iraq, Oman, United Arab Emirates), Pakistan, Afghanistan
Asia 2	Far East and Central Asia (Tajikistan, Uzbekistan, Kazakhstan, China), Iran
Europe 1	Eastern Europe (Albania, Kosovo, Bulgaria, Russia, Turkey, Greece), Iran
Europe 2	Greece (AP92 strain), Turkey

The phylogenetic grouping of S RNA segments illustrates that the pattern of genetic diversity observed is largely related to the geographical distribution of the with distinct clades or lineages found in Africa, Asia, the Middle East, and Europe, often associated with the presence of Hyalomma ticks.

India

India's first laboratory confirmed outbreak of CCHF was reported in January 2011 in Ahmedabad, Gujarat, where nosocomial transmission was identified. This initial outbreak resulted in 7 confirmed cases and 2 fatalities. Since then, Gujarat has consistently experienced annual CCHF outbreaks, making it a key region for the disease in India.

Other states have also reported CCHF cases, indicating the spread of the virus beyond Gujarat:

1. **Rajasthan:** Between 2014 and 2019, multiple outbreaks were recorded in the districts of Chittorgarh, Jodhpur, and Sirohi. The repeated occurrences highlight the ongoing risk of CCHF in this region.
2. **Uttar Pradesh (2015):** In 2015, an outbreak occurred in Moradabad, marking the first significant instance of CCHF in this state.
3. **Kerala (2018):** A single case was reported in Thrissur district, involving an expatriate who had returned from the UAE. This suggests a possible link between international travel and the spread of the virus.
4. **Gujarat (2023):** The most recent cases were recorded in 2023, with one in Kutch district and two in Amreli district, indicating that despite public health interventions, CCHF remains a persistent threat in Gujarat.

While Gujarat is considered endemic for CCHF in India, cases have also emerged sporadically in other states like Rajasthan and Uttar Pradesh. Although serological studies suggest the presence of CCHF antibodies in humans, comprehensive data on seroprevalence remains limited. Studies have shown CCHF IgG seropositivity in cattle (5.4%) and sheep/goats (10.99%) nationwide, indicating that the virus may be more widespread across India than previously understood.

Despite the presence of vector species and domestic reservoir animals across the country, CCHF cases and outbreaks are primarily reported in Gujarat. This is linked to ticks, particularly those from Dermacentor, Hyalomma, and Rhipicephalus genera. Hyalomma marginatum is a key vector in Europe. Climatic factors, changes in reservoir species, and human activities, such as neglecting agricultural land or deforestation, can impact tick habitats. Migratory birds contribute to tick spread, demonstrated in Turkey and suspected in Russia. Antibody production and transient viraemia have been observed in various vertebrates, with cattle, sheep, and goats showing high seroprevalence.

Global epidemiology of CCHF



The first clinical case of CCHF was reported in Greece in July 2008.

- The first outbreak - 1944 when soviet troops re-occupying areas of Crimean Peninsula developed an acute febrile illness with symptoms like shock and bleeding (Grashchenkov, 1944).
- In 1969, this agent was found identical to that isolated in Belgian Congo in 1956 (Casals, 1969). Hence, led to the disease being named as Crimean Congo Hemorrhagic fever.
- CCHF is widely distributed in Asia, extending from the Xinjiang region of western China to the Middle East and southern Russia.
- There are endemic areas over many parts of south-eastern Europe, and the Middle East. Cases are less commonly identified from Africa, with the exception of South Africa.

- **Cases have been reported in the following countries:**
- **South-eastern Europe and Russian Federation** - Ukraine, Bulgaria, Albania, Serbia & Montenegro (Kosovo), Turkey, Macedonia, Russian Federation.
- **Asia** - China, Kazakhstan, Tajikistan, Pakistan, Afghanistan
- **Middle East** - Iraq, Iran, the United Arab Emirates (UAE), Saudi Arabia, Oman.
- **Africa** - Mauritania, Senegal, Burkina Faso, Congo (Republic and Democratic Republic), Uganda, Kenya, Tanzania, South Africa, Namibia.

[\[ARCHIVED CONTENT\] WPA - Global epidemiology of CCHF \(introduction.pptx\)](#)

Overview of CCHF in India

First Confirmed Outbreak:

- January 2011 in Ahmedabad, Gujarat, with nosocomial transmission
- **Cases and Fatalities:** 7 confirmed cases, 2 deaths.
- **Endemicity in Gujarat:** Persistent outbreaks occur annually, with Gujarat as a hotspot.

Regional Outbreaks Beyond Gujarat:

- **Rajasthan (2014-2019):** Multiple outbreaks in Chittorgarh, Jodhpur, and Sirohi districts.
- **Uttar Pradesh (2015):** Significant outbreak in Moradabad, showing spread beyond Gujarat.
- **Kerala (2018):** Single case in Thrissur, possibly imported from UAE.
- **Gujarat (2023):** Recent cases in Kutch and Amreli reinforce CCHF's ongoing threat.

Seroprevalence and Vector Ecology:

- **Serological Findings:** CCHF antibodies in livestock across India.
- **IgG Seropositivity:** 5.4% in cattle, 10.99% in sheep/goats.

Tick Vectors:

- **Dermacentor, Hyalomma, Rhipicephalus** species are primary vectors.

Environmental Drivers:

- Deforestation and land-use changes contribute to habitat expansion, increasing tick-borne transmission risks.

Note: CCHF's endemicity in Gujarat and sporadic cases in other regions suggest a broader presence in India than reported.

Notes

Session-3

Etiology, Transmission & Emergence of CCHF

Course No. 003	Session 3: Epidemiology, Transmission & Emergence of CCHF
Duration	20 minutes
Learning Objective	• Identification and characterization of CCHF • Describing reservoir hosts • Understanding the mode of transmission • Identification of vectors
Pre-requisite knowledge/skill	• Knowledge of CCHF identification, diagnosis, and pathogen characterization. • Understanding of reservoir hosts and their role in disease ecology. • Familiarity with modes of transmission and identification of tick vectors.
Competencies to be achieved	• Skill in recognizing and describing the CCHF • Familiarity with the reservoir host that carry the CCHF • Understanding how CCHF spreads from person to person • Identify the agents responsible for transmitting CCHF • Understanding the emergence factors for CCHF

CAUSATIVE AGENT

Crimean-Congo Hemorrhagic Fever Virus (CCHF) is an enveloped, tri-segmented, single-stranded, negative-sense RNA virus belonging to the genus *Orthonairovirus*, order *Bunyavirales*, and family *Nairoviridae*. The viral genome is composed of three single-stranded, negative-sense RNA segments: the large (L), medium (M), and small (S) segments.

Replication of the tri-segmented genome is inherently error-prone, which contributes to antigenic drift, resulting in the emergence of seven distinct genotypes of the virus. While the exact cell receptor for CCHF remains unknown, the low-density lipoprotein receptor (LDLR) has recently been proposed as a critical factor for CCHF cell entry.

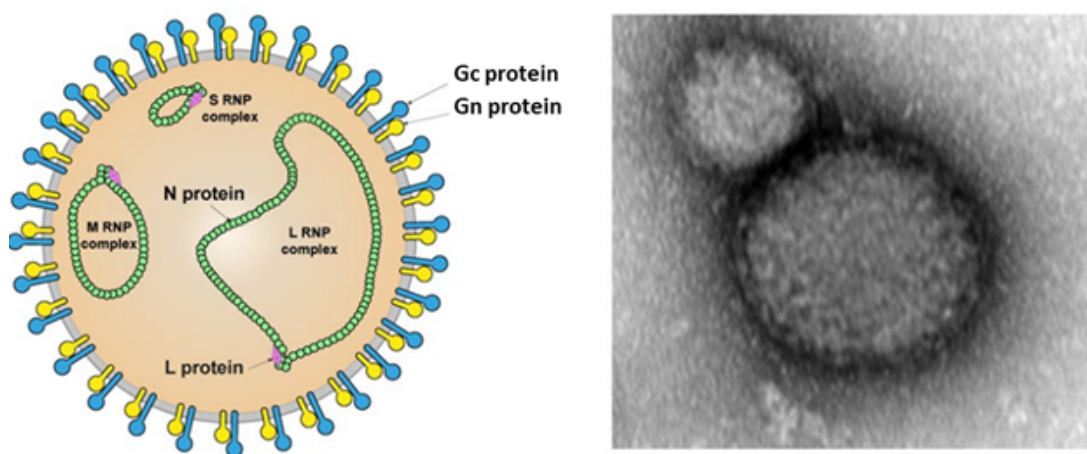


Fig 2- Structure of CCHF Virus

(Image Source: *Nairoviridae. Electron micrograph of a Crimean-Congo hemorrhagic...* / Download Scientific Diagram (researchgate.net))

Vector: Ticks, specifically those from the *Hyalomma* genus in the *Ixodidae* family, are the primary vectors of CCHF. These arthropods feed on the blood of animals and humans. Various tick genera can become infected with the CCHF, but *Hyalomma* ticks are the most efficient and common vectors. These ticks also serve as natural reservoirs for the virus. *Hyalomma* ticks can be identified by their four pairs of legs in adults and lack of clear body segmentation. The adult ticks are flat and oval shaped. The ticks have four life stages: eggs, larvae, nymphs, and adults. Larvae and nymphs primarily feed on lower vertebrates such as rodents, rabbits, and hares, while adult ticks feed on larger vertebrates such as cattle, goats, and sheep. Both male and female ticks can act as vectors for disease transmission. Transovarial transmission (from infected female ticks to offspring via eggs) and trans-stadial transmission (from larvae to nymph to adult) have been observed among some vector species, contributing to the circulation of the virus in the nature.

Reservoir: Hard ticks, including those from the *Hyalomma* genus, serve as the reservoir for the CCHF. Infected animals can also act as reservoirs during the viraemic period. They can infect a wide range of wild animals and domestic ruminants such as hares, rats, camels, cattle, sheep, and goats.

While many bird species are resistant to infection, ostriches are susceptible and may have a high prevalence of infection in endemic areas. Animals acquire the CCHF from the bites of infected ticks. Infected small vertebrates, on which immature *Hyalomma* ticks feed, are believed to be the primary source of acquisition by ticks. Domestic ruminant animals, including cattle, sheep, and goats, experience viremia for approximately one week after becoming infected.

ENVIRONMENTAL FACTORS

Several environmental factors have contributed to increased transmission of the CCHF. These include ecological changes, poverty, social instability, poor health services, and the absence of standard infection control practices.

Transmission of CCHF can occur through both animal-to-human and human-to-human routes.

Tick to Animal: The CCHF can be present in various wild and domestic animals, and it has been identified in multiple species such as cattle, sheep, goats, hares, hedgehogs, dogs, and mice.

Animal-to-Human/Ticks-to-Human Transmission: Human infection with the CCHF can occur through direct contact with blood or other tissues of infected livestock. This can happen during activities such as slaughtering, butchering, or handling of infected animals. Another mode of transmission is through tick bites, where infected ticks transmit to humans. Additionally, crushing an infected tick can also result in transmission. It is important to note that consuming meat from infected animals does not pose a risk, as the virus is inactivated during post-slaughter acidification and does not survive cooking.

Human-to-Human Transmission: Human transmission of the CCHF can occur when there is contact with blood, body fluids, or waste products from patients who have the disease. This can happen when broken skin or mucous membranes come into contact with these infectious materials. Healthcare workers are at risk, particularly if they experience accidental exposure to patient's body fluids while caring for infected individuals. In advance stages of the disease, risk of transmission from patient is higher due to high viraemia. So far breastfeeding has not been associated with transmission.

It should be noted that human-to-human transmission is not as common as animal-to-human transmission in the case of CCHF.

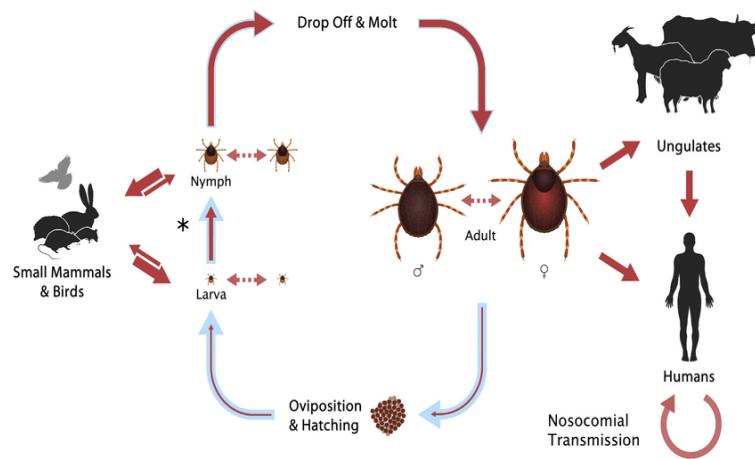


Fig 3: Life cycle of *Hyalomma* spp. ticks and vertical and horizontal.

(Image Source: Download Scientific Diagram -researchgate.net)

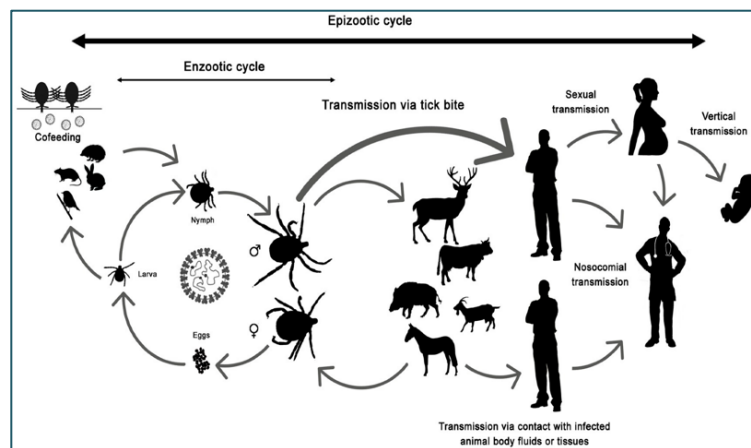


Fig 4: Crimean-Congo hemorrhagic fever virus (CCHF) cycle and its routes of transmission.

(Image Source: <https://doi.org/10.3390/microorganisms9030649>)

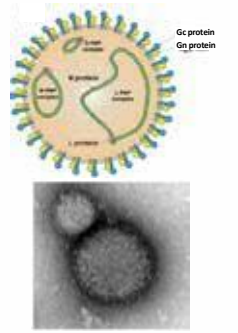
POPULATION AT RISK

The population at greatest risk of CCHF infection in endemic countries includes individuals involved in the livestock industry, such as agricultural workers, slaughterhouse workers, veterinarians, Campers and hikers in forests. Healthcare workers who provide care to suspected, probable, or confirmed CCHF cases without following proper contact precautions are also at high risk of infection.

Furthermore, nosocomial outbreaks (hospital-acquired infection outbreaks) have been reported in several countries, emphasizing the importance of implementing effective infection control measures to prevent the spread of CCHF within healthcare settings.

CCHF structure

- Crimean-Congo Hemorrhagic Fever Virus (CCHF) is an enveloped, tri-segmented, single-stranded, negative-sense RNA.
- The virus belongs to the genus *Orthobunyavirus*, order *Bunyvirales*, and family *Nairoviridae*.
- The viral genome is composed of three single-stranded, negative-sense RNA segments: the large (L), medium (M), and small (S) segments.
- Replication of the tri-segmented genome is inherently error-prone, which contributes to antigenic drift, resulting in the emergence of seven distinct genotypes of the virus.
- While the exact cell receptor for CCHF remains unknown, the low-density lipoprotein receptor (LDLR) has recently been proposed as a critical factor for CCHF cell entry.



[Nairovirus: Electron micrograph of a Crimean-Congo hemorrhagic virus. | Download Scientific Diagram | Researchgate.net](#)

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CCHF Vector: Hyalomma Ticks

Overview:

- Primary Vector:** *Hyalomma* ticks (Family: Ixodidae) are the most efficient and common vectors of CCHF.
- Transmission:** Both male and female ticks can transmit the virus.

Key Features of *Hyalomma* Ticks:

- Physical Traits:** Four pairs of legs, flat and oval-shaped, no clear body segmentation.
- Life Stages:** Egg → Larva → Nymph → Adult
- Larvae & Nymphs** feed on small vertebrates (rodents, rabbits, hares).
- Adults** feed on larger animals (cattle, goats, sheep).

Disease Cycle:

- Reservoir Role:** *Hyalomma* ticks are natural reservoirs of CCHF.
- Transmission Modes:**
 - Transovarial:** Virus passed from female tick to offspring via eggs.
 - Trans-stadial:** Virus carried through tick life stages (larva → nymph → adult).

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Reservoirs of CCHF

Primary Reservoirs

- Hard Ticks:** *Hyalomma* genus ticks act as natural reservoirs.
- Infected Animals (During Viremia):** Wild animals and domestic ruminants (e.g., hares, rats, camels, cattle, sheep, goats) serve as reservoirs while viremic.

Transmission to Ticks

- Small Vertebrates:** Infected small animals on which immature *Hyalomma* ticks feed are believed to be a primary source for the virus in ticks.
- Domestic Ruminants:** Infected cattle, sheep, and goats show viremia for approximately one week, supporting virus transmission to ticks.

Susceptibility Among Birds

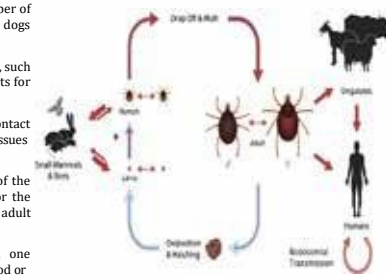
- Resistant Species:** Many bird species are resistant to CCHF.
- Susceptible Species:** Ostriches can harbor high infection rates in endemic areas.

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Tick lifecycle and CCHF transmission

- Tick to Animal:** CCHF can be found in many wild and domesticated animals and has been isolated from a number of species including cattle, sheep, goats, hares, hedgehogs, dogs and mice.
- Animal to Human:** Numerous wild and domestic animals, such as cattle, goats, sheep and hares, serve as amplifying hosts for the virus.
 - Transmission to humans occurs through direct contact with infected animal blood/tissues (Slaughtering/butchering).
- Ticks to Human:** Ixodid (hard) ticks, especially those of the genus, *Hyalomma*, are both a reservoir and a vector for the CCHF virus. Transmission occurs by tick bite or handling adult infected ticks
- Human to Human:** CCHF can be transmitted from one infected human to another by contact with infectious blood or body fluids (e.g Nosocomial infection are common)



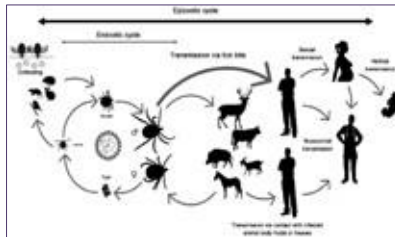
[Source: Life cycle of Hyalomma spp. ticks and vertical and horizontal... | Download Scientific Diagram | researchgate.net](#)

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Notes

Transmission of CCHF among species



Intrinsic Incubation period: (In definitive host-Humans)

The incubation period of the virus ranges from 2 to 9 days and depends on host, route of exposure and viral inoculum.

The time to onset of the disease:

- 1-3 days after tick-bite,
- 5-6 up to 9 days after contact with infected livestock/human blood, tissue and excreta
- Some reports even suggest IIP to be 2 to 14 days

Extrinsic Incubation period: (In intermediate Host-ticks/animals)

There are no reports of the EIP

Meat itself is not a risk because the virus is inactivated by post-slaughter acidification of the tissues and would not survive cooking

Source: <https://reliefweb.int/report/afghanistan/operational-guidelines-prevention-and-control-cchf-afghanistan-2012> Source: <https://www.unicef.org/uganda/crimean-congo-hemorrhagic-fever>
Source: www.researchgate.net/figure/Life-cycle-of-the-tick-and-transmission-pathway-of-Crimean-Congo-hemorrhagic-fever-virus_fig2_284209106

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People at Risk



Animal handlers



Farmers



Veterinarians



Abattoir workers



Campers and Hikers



Healthcare providers

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CCHF infected organisms pose risk of disease transmission

Humans may acquire the CCHF from



infected livestock



tick bite



crushing an infected tick



blood or other tissues



other infected humans

- Humans can become infected if blood, body fluids and wastes from patients with the disease come into contact with broken skin or mucous membranes

- In advanced stages of the disease, aerosol contact of blood of the patient can also lead to transmission of the virus.

- Hospital acquired infection outbreaks (Nosocomial spread) have been reported in many countries including India

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Notes

Session-4

Case Definition

Course No. 004	Session 4: Case Definition
Duration	20 minutes
Learning Objective	• Identifying suspected, probable and confirmed case in humans
Pre-requisite knowledge/skill	• Understanding case definitions for suspected, probable, and confirmed CCHF cases. • Ability to recognize clinical signs and epidemiological links in suspected cases. • Knowledge of laboratory confirmation methods for diagnosing CCHF.
Competencies to be achieved	• Capability to explain the signs and symptoms experienced by humans with CCHF. • Proficiency in recognizing and classifying human cases of CCHF (suspected, probable, and confirmed)

CASE DEFINITIONS

CASE DEFINITION (as per revised IDSP definition 2019)

Suspect case: A patient presenting with a sudden onset of high fever ($>38.5^{\circ}\text{C}$) accompanied by one or more of the following symptoms:

- Severe headache, muscle pain (myalgia), nausea, vomiting, and/or diarrhea
AND/OR
- A history of insect (tick) bite within 14 days before the onset of symptoms
OR
- Contact with tissues, blood, or other biological fluids from a potentially infected animal (e.g., abattoir workers, livestock owners, veterinarians) within the 14 days prior to symptom onset
OR
- Exposure to a suspect, probable, or laboratory-confirmed CCHF case (including contact with a patient, healthcare workers, or others) within 14 days before symptom onset.

Probable case: A suspected CCHF case presenting with two or more of the following haemorrhagic symptoms:

- Petechiae, purpuric rash, nosebleed (rhinorrhagia), vomiting blood (hematemesis), coughing up blood (haemoptysis), gastrointestinal bleeding, gum bleeding (gingival haemorrhage)
- Any other haemorrhagic manifestation without any known precipitating factors.

Confirmed case: A presumptive case confirmed by one or more of the following:

- Detection of the CCHF virus genome through validated RT-PCR in a clinical specimen
AND/OR sequencing
- OR
- Demonstration of seroconversion by ELISA or IFA, with specific IgM antibodies against CCHF virus
OR
- A 4-fold increase in specific IgG antibodies against CCHF virus between two specimens collected during the acute and convalescent phases
OR
- Isolation of the CCHF virus

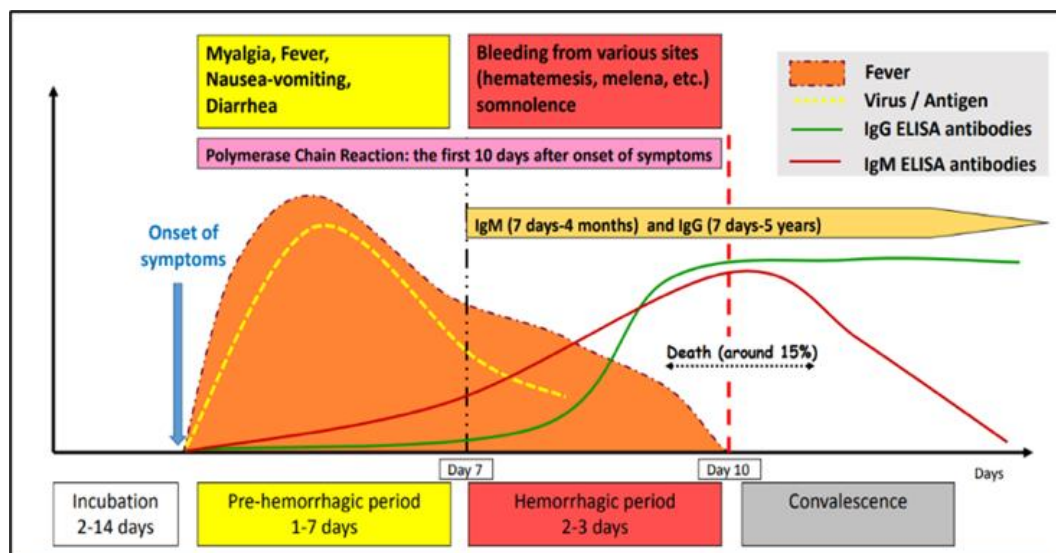


Fig 5.-Natural History

(Image Source: <https://openwho.org/courses/crimean-congo-haemorrhagic-fever-introduction>)

Case Definition

Suspected Case

- Abrupt onset of high fever ($>38.5^{\circ}\text{C}$)
- Severe headache, myalgia, nausea, vomiting, diarrhoea
- History of any of the following within 14 days prior to symptom onset
 - tick bite
 - contact with tissues, blood, or other biological fluids from a possibly infected animal
 - exposure to a suspect, probable, or laboratory-confirmed CCHF case

Probable Case

- Thrombocytopenia $< 50,000/\text{cmm}$.
- Two or more of the following haemorrhagic manifestations:
 - Hematoma at an injection site, petechiae, purpuric rash, rhinorrhagia, hematemesis, haemoptysis, gastrointestinal haemorrhage, gingival haemorrhage.
 - Any other haemorrhagic manifestation in the absence of any known precipitating factor for haemorrhagic manifestation

Confirmed Case

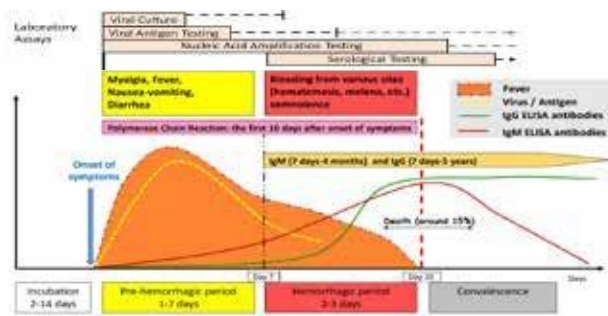
- Meets criteria for suspected/probable cases & laboratory-confirmed with one of the following assays.
- RT-PCR
- Detection of specific IgM antibodies by ELISA or IFA, or a 4-fold increase in specific IgG antibodies in two specimens collected in the acute and convalescence phases.
- Virus isolation

Source: <http://dx.doi.org/10.1186/14752875-2012-111.pdf> (pdf)

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Natural History



Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2800000/>

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Notes

Session-5

Clinical Management & Differential Diagnosis

Course No. 005	Session 5: Clinical Management & Differential Diagnosis
Duration	5 minutes
Learning Objectives	• Describe clinical signs and symptoms in humans • Differential Diagnosis
Pre-requisite knowledge/skill	• Knowledge of signs and symptoms of CCHF in humans • Understand how to differentiate CCHF from other similar diseases • Awareness of clinical presentation, disease severity and progression.
Competencies to be achieved	• Capability to distinguish CCHF from other similar clinical diseases through a thorough differential diagnosis

CLINICAL MANIFESTATION IN HUMANS

CCHF typically presents with a sudden onset of symptoms. 88% of infections may be sub-clinical.

Pre-Hemorrhagic Phase: (1-7 days post incubation period) The initial phase is characterized by fever, myalgia, dizziness, neck pain, stiffness, backache, headache, sore eyes, and sensitivity to light (photophobia). Early on, there may be accompanying symptoms such as nausea, vomiting, sore throat, diarrhea, and generalized abdominal pain.

As the illness progresses, patients may experience mood swings, confusion, and aggression. After a few days, these symptoms may give way to sleepiness, depression, and fatigue. Abdominal pain may localize to the right upper quadrant, and hepatomegaly (enlargement of the liver) may be detectable.

Hemorrhagic Phase: (7 to 10 days after first period. Lasts for 2-3 days) Patients in this phase have rapid heart rate (tachycardia), swelling of lymph nodes (lymphadenopathy), and the presence of a petechial rash on internal mucosal surfaces. Ecchymoses, which are larger areas of skin discoloration similar to a petechial rash, may also be observed. Other haemorrhagic manifestations can occur, such as melaena (blood in the stool), hematuria (blood in the urine), epistaxis (nosebleeds), and bleeding from the gums. Hepatitis is often evident. Severe cases may progress to hepatorenal and pulmonary failure after the fifth day of illness.

Convalescent Phase: (10-20 days after onset of illness, lasts for one month) During the convalescence period, which begins about 10-20 days after the onset of illness, survivors may experience symptoms such as labile pulse, tachycardia, temporary or complete hair loss, polyneuritis, difficulty breathing, dry mouth (xerostomia), vision problems, hearing loss, and memory loss.

The mortality rate of CCHF ranges from approximately 9% to 50%, with fatal outcomes typically occurring in the second week of illness. Patients who survive usually begin to show improvement around the ninth or tenth day after symptom onset.

CLINICAL DIAGNOSIS

Early diagnosis plays a crucial role in the management of CCHF cases and the prevention of outbreaks. It is important to consider differential diagnosis for other diseases with similar symptoms, including bacterial, viral, and non-infectious diseases. When evaluating a patient, clinical diagnosis of CCHF should be considered if the following criteria are met:

1. Presence of compatible clinical manifestations such as fever, myalgia, and bleeding.
2. Epidemiological risk factors, including a history of tick bite, exposure to infected livestock, or crushing a tick between two exposed body parts.
3. Contact with suspected cases of CCHF, engaging in outdoor activities in outbreak areas, or residing/traveling in regions with known CCHF prevalence.
4. Compatible laboratory findings, such as thrombocytopenia (low platelet count), leukopenia (low white blood cell count), and elevated levels of certain enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase, and creatine phosphokinase. Elevated levels of inflammatory cytokines

Differential Diagnosis

CCHF is difficult to distinguish from a host of other febrile illnesses, at least early in the course of disease. When awaiting laboratory confirmation, several diseases should be considered in the differential diagnosis. These include malaria, leptospirosis, rickettsial diseases, meningococemia, typhoid disease, viral hepatitis, meningococemia, dengue hemorrhagic fever, hemolytic uremic syndrome, thrombocytopenic purpura, KFD, Lassa fever and EBOLA.

WHEN TO SUSPECT

- History of tick bite in last 14 days
- History of unprotected/accidental contact with animal blood, tissue or excreta or infected person
- History of travel to high animal density population area/thick forest
- Exposure to suspected or confirmed case of CCHF
- History of travel to endemic areas or ongoing outbreak

Table 2: Key distinguishing features to aid in diagnosing CCHF

Disease	Key Clinical Differences	Epidemiological Clue	Sample	Tests and Expected Results
CCHF	Sudden high fever , haemorrhagic symptoms (petechiae, epistaxis, hematemesis).	Tick bites or contact with livestock fluids; outbreaks in endemic regions (e.g., Africa, Asia).	Blood	RT-PCR: Positive for CCHF RNA.
	Rapid hepatic dysfunction.			ELISA: IgM/IgG positive.
				Biochemical: Elevated ALT, AST; thrombocytopenia .
Dengue	Retro-orbital pain , severe myalgia ("breakbone fever").	Mosquito bites in urban areas, associated with monsoon seasons .	Blood	NS1 antigen: Positive in early stages.
	Haemorrhagic signs, shock in severe dengue.			IgM serology: Positive after Day 5.
				Thrombocytopenia , elevated hematocrit.
Ebola/ Marburg Virus	High fatality rate , severe hemorrhage , and multi-organ failure.	Recent outbreaks in Africa , exposure to bats or infected individuals.	Blood, body fluids	RT-PCR: Positive for viral RNA.
				Serology: IgM/IgG positive.
				Coagulation profile: DIC markers (prolonged PT/ aPTT).
Leptospirosis	Jaundice , conjunctival suffusion, renal failure , and muscle tenderness ("Weil's disease" in severe cases).	Exposure to contaminated water , often during floods or through animal urine.	Blood, urine	MAT: Positive for antibodies.
				PCR: Positive for <i>Leptospira</i> DNA.
				Biochemical: Elevated ALT, AST, and bilirubin.
Malaria	Cyclic fever (tertian or quartan), chills, splenomegaly, and severe anemia in complicated cases.	Travel to malaria-endemic areas , particularly tropical and subtropical regions ; mosquito bites.	Blood (thick and thin smears)	Blood Smear: Visible <i>Plasmodium</i> species.
				RDT: Positive for malaria antigens (HRP2 or pLDH).
				LDH elevated .

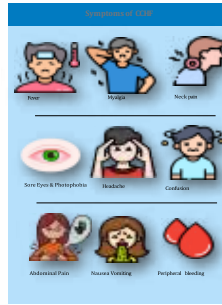
Disease	Key Clinical Differences	Epidemiological Clue	Sample	Tests and Expected Results
Scrub Typhus	Eschar at bite site, fever, lymphadenopathy, and multi-organ failure in severe cases.	Tick/mite bites, endemic regions in Asia-Pacific ("Tsutsugamushi Triangle").	Blood	PCR: Positive for <i>Orientia tsutsugamushi</i> DNA.
				Weil-Felix test: Positive for OX-K antigen.
				Elevated ALT, AST, bilirubin.
Lassa Fever	Gradual onset of fever, facial swelling , pleural effusion, and hearing loss as a late complication.	Endemic in West Africa , exposure to rodents or contact with infected fluids.	Blood, urine	RT-PCR: Positive for Lassa RNA.
				Serology: IgM positive.
				Biochemical: Elevated ALT, AST, bilirubin, and albuminuria.
Meningococcal Disease	Stiff neck, photophobia, altered mental status, and purpuric rash.	Close contact outbreaks (e.g., dorms, barracks); no vector/animal exposure.	CSF, blood	CSF Analysis: Elevated WBC, low glucose, high protein.
				PCR: Positive for <i>Neisseria meningitidis</i> .
Typhoid/Paratyphoid	Step-ladder fever, abdominal pain, rose spots, and hepatosplenomegaly.	Contaminated food/water , common in regions with poor sanitation ; prolonged fever with GI focus.	Blood, stool	Blood Culture: Positive for <i>Salmonella typhi</i> .
				Widal Test: Positive (rising O and H titers).
				Pathogen in stool.
Lyme Disease	Erythema migrans ("bull's-eye rash"), arthralgia, and neurological manifestations in disseminated disease.	Exposure to ticks , typically in temperate regions (e.g., North America, Europe).	Blood	PCR: Positive for <i>Borrelia burgdorferi</i> DNA.
				ELISA: Positive IgM (early); IgG (late stage).

Clinical Manifestation in Humans

Clinical Course: Pre-hemorrhagic period

Period: 1-7 days post incubation period

Signs and Symptoms : fever, myalgia, dizziness, neck pain, stiffness, backache, headache, sore eyes, photophobia, nausea, vomiting, sore throat, diarrhea and generalized abdominal pain

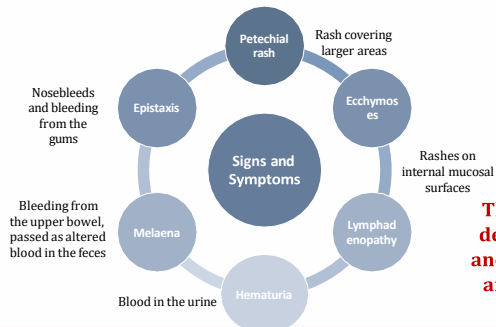


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Clinical Course: Hemorrhagic period

Period: 7-10 days after first period. Last for 2-3 days



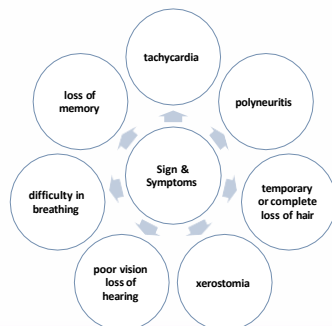
The severely ill may develop hepatorenal and pulmonary failure after the fifth day of illness

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Clinical Course: Convalescent period (In survivors)

Period: 10-20 days after the onset of illness, lasts for month



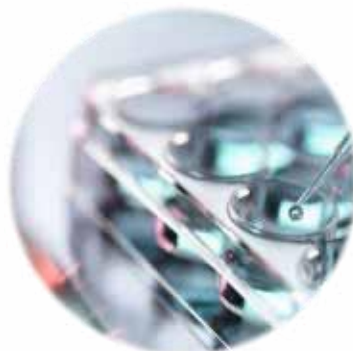
- **Incubation period:** In case of tick bite-1 to 3 days, maximum to 9 days, in case of contact with infected blood: 5 to 6 days, maximum to 13 days.
- The mortality rate from CCHF is approximately 9-50% with death occurring in the second week of illness.
- In patients who recover, improvement generally begins on the ninth or tenth day after the onset of illness.

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Laboratory Investigations

- Laboratory abnormalities may include low platelet and high white blood cell count, raised levels of aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase and creatinine phosphokinase
- Prothrombin time and activated partial thromboplastin time are prolonged and fibrinogen is decreased, whereas fibrin degradation products are elevated



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Notes

There are a number of tropical infection which presents similar clinical manifestations and hence should be suspected and ruled out while making a diagnosis of CCHF. The following diseases are to be considered in differential diagnosis:

[illegible][illegible]

Session-6

Laboratory Diagnosis

Course No. 006	Session 6: Laboratory Diagnosis
Duration	20 minutes
Learning Objectives	• Describe diagnostic algorithm of CCHF • Understand laboratory requirements for diagnosis of CCHF
Pre-requisite knowledge/skill	• Knowledge of the diagnostic algorithms • Understanding of laboratory biosafety levels and infrastructure • Familiarity with molecular and serological methods
Competencies to be achieved	• Proficiency in explaining the step-by-step diagnostic process for identifying and confirming cases of CCHF • Comprehension of the various diagnostic tests employed to detect and validate the presence of CCHF • Knowledge of the specific laboratory prerequisites and conditions necessary for effectively diagnosing CCHF

LABORATORY DIAGNOSIS

Laboratory diagnosis plays a crucial role in confirming cases of CCHF. It helps to confirm CCHF cases and differentiate them from other diseases with similar symptoms. It enables early detection and appropriate management of patients.

Sample Collection

For diagnosing CCHF, samples may include serum, plasma, or tissue from various organs such as the liver, spleen, bone marrow, kidneys, lungs, and brain.

- **Ante-mortem:** Blood samples, specifically serum or plasma.
- **Post-mortem:** Tissue samples from the liver, spleen, bone marrow, kidneys, lungs, and brain.

During the initial days of illness, diagnosis can be made through the detection of the virus or its genome in blood or tissue samples.

Collection Protocol

Samples must be collected following all biosafety precautions and should be accompanied by a detailed patient history on a form available from the testing laboratory. Before dispatching the samples, disinfect the outer surface of the container using a 1:100 dilution of bleach or a 5% Lysol solution.

Sampling Window

Table 2: Summary of the time frame, symptoms, sample type, and diagnostic tests.

Time (Days/Weeks)	Symptoms	Sample	Diagnostic Tests
Day 1-5 (Acute Phase)	Sudden onset of fever, myalgia, headache, nausea, vomiting, diarrhoea, abdominal pain	Blood (serum or plasma)	RT-PCR: Detects viral RNA during early viremia. Antigen ELISA: Detects CCHF viral antigens.
Day 5-7 (Transition Phase)	Progressive symptoms: worsening fever, severe headache, abdominal pain, muscle aches, bleeding (petechiae, ecchymosis), and organ dysfunction	Blood (serum/plasma) or tissue	IgM ELISA: Detects recent infection (antibody production starts around day 5).

Time (Days/Weeks)	Symptoms	Sample	Diagnostic Tests
Day 8-14 (Recovery Phase)	Symptom resolution, but potential for complications (e.g., neurological issues)	Blood	IgG ELISA: Indicates past or ongoing infection (elevated levels suggest recovery phase).
Post-Mortem	-	Tissue (e.g., liver biopsy)	Histopathology: Examines tissue for viral inclusion bodies. RT-PCR: Confirms CCHF viral RNA.
Beyond 14 Days	-	Blood	IgG ELISA: Detects persistent IgG antibodies.

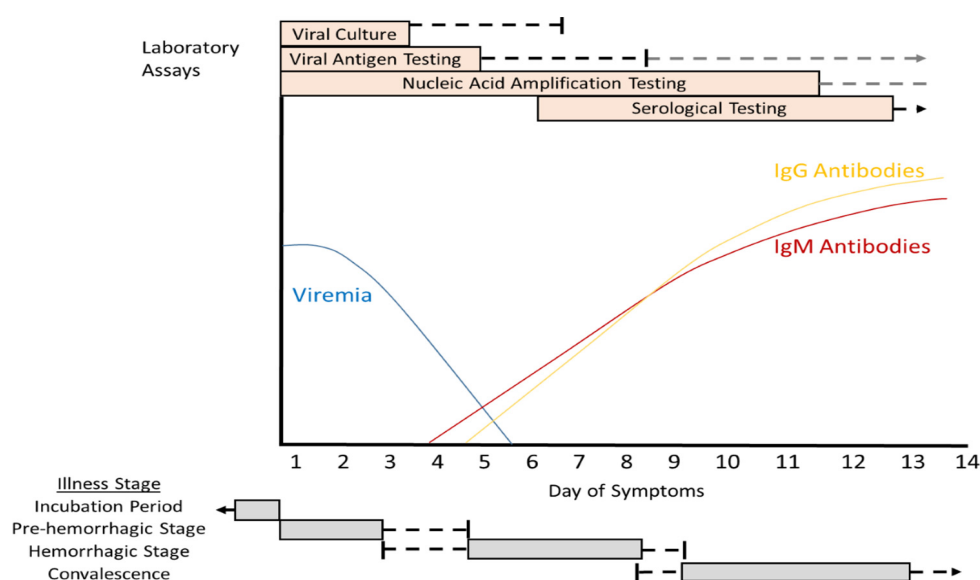


Fig 6: Overview of diagnostic testing for acute illness due to Crimean-Congo hemorrhagic fever virus in a non-fatal human infection.

(Image Source: <https://pubmed.ncbi.nlm.nih.gov/32024724/>)

Various methods are employed in specially equipped, high biosafety laboratories for this purpose. These methods include serological assays

Serology

Antibody detection using enzyme-linked immunosorbent assays (ELISA) or enzyme-linked immunoassays (EIA). IgM (5-8 days) and IgG (10-14 days) antibodies can be detected in serum/plasma/urine/whole blood using these assays, with IgM antibodies becoming undetectable after about 4 months, while IgG antibodies can remain detectable for years, indicating long-lasting immunity.

Molecular methods

Reverse transcriptase polymerase chain reaction (RT-PCR) is a preferred method for rapid laboratory diagnosis. It is highly sensitive, specific, and provides quick results.

Virus Isolation

Isolation for CCHF should always be conducted in a maximum bio-containment laboratory,

specifically, a BSL-4 facility. During the first five days of illness, they can be isolated from blood or tissue specimens and cultured in cell lines. Viral antigens can also be detected in tissue samples using immunofluorescence or EIA.

Due to the high-risk nature of CCHF, clinical samples should be handled in specially equipped laboratories with high biosafety levels, such as BSL 3 plus or 4 facilities. In case of high suspicion, sample should be sent to referral laboratory.

Sample collection for CCHF diagnosis involves obtaining blood samples during the ante-mortem phase of the illness. Serum or plasma is collected for further testing.

Table 3: Laboratory Diagnostic Methods: Sample Types, Timing, and Biosafety Requirements

Test	Incubation Period	Sample Type	Inactivation of Specimen	Method	BSL Requirements
Molecular Diagnosis	Within 10-12 days	Plasma, Serum, Urine, Whole blood	Done	RT-PCR, Real time RT-PCR	BSL 2 or 3
Serological Diagnosis (IgM ELISA)	7 days to 4 months	Plasma, Serum, Whole blood, saliva	Done	IgM ELISA	BSL 2 or 3
Serological Diagnosis (IgG ELISA)	7 days to 3-5 years	Plasma, Serum, Whole blood, saliva	Done	IgG ELISA	BSL 2 or 3
Viral Culture	1-3 days	Serum, Plasma	Not done	Using cell lines, Inoculation of mice	BSL 3 or 4
Viral Antigen Detection	2-5 days	Plasma or serum	Done	ELISA	BSL 2 or 3

The tests can be chosen based on the facility available. In postmortem cases, tissue samples are collected from various organs including the liver, spleen, bone marrow, kidney, lung, and brain.

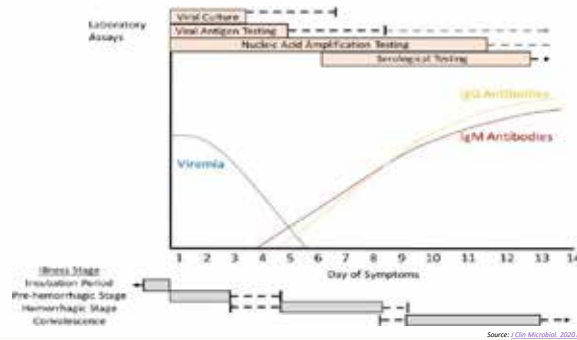
Diagnostic Tests and Sample Type

This table outlines the ideal days for sample collection and corresponding specimen types for accurate CCHF diagnosis using various laboratory methods.

Table 4: *Optimal Timing and Sample Types for CCHF Laboratory Testing*

Test	Optimal Days for Sample Collection	Sample Type
Viral Culture	1-3	Blood, tissue
Viral Antigen Testing	2-5	Blood, Serum, Plasma
Nucleic Acid Amplification Testing (NAAT)	1-7	Blood, tissue
Serological Testing (IgM)	7-14	Blood, Serum, Plasma
Serological Testing (IgG)	14+	Blood, Serum, Plasma

Which Test to Choose?



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Sampling Window

Time (Days/Weeks)	Symptoms	Sample	Diagnostic Tests
Day 1-5 (Acute Phase)	Sudden onset of fever, myalgia, headache, nausea, vomiting, diarrhoea, abdominal pain	Blood (serum or plasma)	- RT-PCR: Detects viral RNA during early viremia. Antigen ELISA: Detects CCHF viral antigens.
Day 5-7 (Transition Phase)	Progressive symptoms: worsening fever, severe headache, abdominal pain, muscle aches, bleeding (petechiae, ecchymosis), and organ dysfunction	Blood (serum/plasma) or tissue	- IgM ELISA: Detects recent infection (antibody production starts around day 5).
Day 8-14 (Recovery Phase)	Symptom resolution, but potential for complications (e.g., neurological issues)	Blood	- IgG ELISA: Indicates past or ongoing infection (elevated levels suggest recovery phase).
Post-Mortem	-	Tissue (e.g., liver biopsy)	- Histopathology: Examines tissue for viral inclusion bodies. - RT-PCR: Confirms CCHF viral RNA.
Beyond 14 Days	-	Blood	- IgG ELISA: Detects persistent IgG antibodies.

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CCHF virus infection can be diagnosed by several different laboratory tests:

- IgM and IgG ELISA ;
- Antigen detection;
- Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) assay; and
- Virus isolation by cell culture or mice inoculation.

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Diagnostic Tests

Test	Incubation Period	Sample Type	Inactivation of Specimen	Method	BSL Requirement
Molecular Diagnosis (PCR)	Within 10-12 days	Plasma, Serum, Urine, Whole blood	Done	RT-PCR, Real time RT-PCR	BSL 2 or 3
Serological Diagnosis (IgM ELISA)	7 days to 4 months	Plasma, Serum, Whole blood, saliva	Done	IgM ELISA	BSL 2 or 3
Serological Diagnosis (IgG ELISA)	7 days to 3-5 years	Plasma, Serum, Whole blood, saliva	Done	IgG ELISA	BSL 2 or 3
Viral Culture	1-3 days	Serum, Plasma	Not done	Using cell lines, Inoculation of mice	BSL 3 or 4
Viral Antigen Detection	2-5 days	Plasma or serum	Done	ELISA	BSL 2 or 3

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Notes

Measures to improve CCHFV laboratory preparedness and response

Improving molecular tests to overcome the lack of sensitivity due to the high variability of the CCHFV genome;

Providing a positive control panel for molecular diagnostics, including the different CCHFV genotypes in order to support the improvement of diagnostic capability of clinical laboratories;

Enrolling in EQA programs by diagnostic laboratories

Improvement of diagnostic algorithms building on clinical experiences;

Validation of procedures to inactivate infectivity of clinical samples;

Establishing of an international biorepository for the collection and storing of clinical samples, with the aim of validating new diagnostic tests and supporting pathogenicity studies.

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Notes

Reference Laboratories

The diagnostic facilities are available at

National Institute of High-Security Animal Diseases (Formerly HSADL), Bhopal

National Center for Disease Control (NCDC), Delhi

National Institute of Virology (NIV), Pune



Image Source: <https://www.shutterstock.com/image-vector/chemistry>

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Session-7

Case Study and Treatment

Course No. 007	Session 7: Case Study and Treatment
Duration	20 minutes
Learning Objectives	• Describe a sample case of CCHF • Understand treatment options
Pre-requisite knowledge/skill	• Knowledge of symptoms and disease progression • Understanding of available treatment options and supportive care measures • Awareness of challenges in clinical management
Competencies to be achieved	• Comprehension of the case study and general understanding of handling of CCHF cases • Explanation of strategies for treatment of CCHF

CASE STUDY

CASE PRESENTATION

A 35-year-old male farmer and cattle handler from rural Gujarat presented with a four-day history of high-grade fever accompanied by chills, headache, myalgia, and vomiting. He subsequently developed hematuria and experienced oral and nasal bleeding, for which he received a platelet transfusion.

EXAMINATION FINDINGS

On examination, the patient was febrile with a temperature of 39°C and exhibited diffuse muscle tenderness. Systemic examination was otherwise unremarkable at presentation.

Parameter	Value
Haemoglobin	15 g/dL
TLC	1,400/ μ L
Platelet count	33,000/ μ L
SGPT	49 U/L
SGOT	120 U/L
Bilirubin (Total/Direct)	5.3 mg/dL / 0.78 mg/dL
Serum Creatinine	1.3 mg/dL
Blood Urea	79.2 mg/dL
Prothrombin Time (INR)	1.69

PROVISIONAL DIAGNOSIS: ACUTE VIRAL HEMORRHAGIC FEVER

Differential Diagnosis:

1. Dengue Fever
2. Crimean-Congo Hemorrhagic Fever (CCHF), based on epidemiological suspicion
3. Other Tropical Fevers: Malaria, Scrub Typhus

Diagnostic Workup

- Dengue NS1 antigen test: Negative
- Malaria Rapid Diagnostic Test and Peripheral Smear: Negative
- Scrub Typhus IgM ELISA: Negative

Subsequently, a sample was sent for Crimean-Congo Hemorrhagic Fever evaluation, and RT-PCR confirmed CCHF.

Progression:

On the 8th day of illness, the patient developed tachypnea and type 1 respiratory failure. Examination revealed basal crepitations, and further evaluation indicated Acute Respiratory Distress Syndrome (ARDS). The patient was placed on mechanical ventilation as his clinical condition and laboratory parameters continued to deteriorate.

TREATMENT

Treatment: Is primarily supportive, requiring careful monitoring of fluid and electrolyte balance. Supportive therapy involves administering thrombocytes, fresh frozen plasma, and erythrocyte preparations.

Antiviral Chemotherapy: Ribavirin is the recommended antiviral agent due to its demonstrated inhibitory effects on CCHF virus replication. Optimal results are achieved when ribavirin is started within 5 days of symptom onset. However, the level of evidence supporting use of Ribavirin is limited. Ribavirin is recommended as possible treatment by WHO.

Ribavirin Dosage: Refer to the table below for specific dosage guidelines.

RIBAVIRIN DOSAGE

Table 5: Ribavirin Dosing Regimen for CCHF in Adults and Children

Adults				
Administration	Dosage	Loading Day 1	Day 2-4	Day 5-10
Intravenous	Dose (mg/kg)	17 mg/kg (max 1000 mg per dose)	17 mg/kg (max 1000 mg per dose) every 6 hours	8 mg/kg (max 500 mg per dose) every 8 hours
Oral	Dose (mg)	2000 mg	1000 mg every 6 hours	500 mg every 6 hours
Children				
Intravenous	Dose (mg/kg)	17 mg/kg every 6 hours	30 mg/kg every 6 hours	-
Oral	Dose (mg/kg)	30 mg/kg every 6 hours	30 mg/kg every 6 hours	7 mg/kg every 6 hours

ADVERSE EFFECTS

The most frequent side effect of ribavirin is mild to moderate hemolytic anemia, which is reversible. The anemia associated with ribavirin treatment is often asymptomatic and can be managed by regular monitoring of blood counts and serum biochemistry. When administered intravenously as a bolus, ribavirin has been reported to cause rigors; therefore, it is recommended that the drug be given as an infusion over 10-15 minutes. Cases of pancytopenia and pancreatitis have also been reported with intravenous ribavirin.

CONTRA-INDICATIONS AND PRECAUTIONS

Pregnant Women: Ribavirin is contraindicated in pregnant women due to its significant teratogenic and embryocidal effects observed across all adequately studied animal species. It may only be administered to pregnant women if the benefits of treatment outweigh the potential risks to the fetus. Given the high mortality risk of CCHF for both pregnant women and their fetus, ribavirin might still be recommended.

It is also contraindicated in patients with chronic anemia (hemoglobin levels below 8 g/dl) and those with severe renal impairment (creatinine clearance <30 ml/min), as the drug may accumulate and cause toxicity. These patients should be closely monitored during ribavirin therapy for signs of toxicity, such as anemia.

Ribavirin treatment is indicated for severe cases, while mild cases do not require the use of ribavirin.

IN THE TRIAGE

Patients are divided into 3 categories:

Categories	Presentation	Treatment
Category A	Relatively mild disease No bleeding manifestation	Supporting therapy, do not require Ribavirin
Category B	Severely ill, local and systemic bleeding manifestation, (first 5 days of illness)	Aggressive therapy, Administration of Ribavirin immediately
Category C	Comatose/terminal state with DIC and multi-organ failure (after day 5)	Intensive treatment Ribavirin Poor prognosis

Category-A

Those who have relatively mild disease (fever < 38.5°C, no systemic bleeding, Alanine Transaminase (SGPT) levels < 150 IU, Platelet count > 50,000). These patients improve spontaneously by about day 10 of illness. The patient can be managed with supportive therapy and regular monitoring for worsening of symptoms. These patients do not require Ribavirin.

Category-B

Those who are in the first 5 days of illness and are severely ill with high grade fever (> 38.5°C), local and systemic bleeding manifestations, having Alanine Transaminase (SGPT) levels of 150 IU or more, aspartate aminotransferase (SGOT) of 200 IU or more, platelets (< 50,000) or Activated Partial Thromboplastin Time (APTT) of 60 seconds or more. Even if the patients still look comparatively well at this stage these clinical path values are markers of poor prognosis if recorded during the

first 5 days of illness and persons in this group should be treated as soon as possible with Ribavirin. Those who are recognized and treated early enough respond remarkably well to ribavirin.

Category C

Patients first seen/recognized as CCHF after day 5 and are in comatose/terminal state with DIC and multi organ failure. Treatment with ribavirin is indicated but the prognosis is very poor. Category B & C patients, even if they subsequently test negative, should receive the full course of ribavirin.

Pre-hospital Care

Supportive care is based on the patient's physiologic condition. Because most patients requiring prehospital evaluation and transport are in the early stages of the disease, universal precautions should be adequate. In patients with respiratory symptoms (e.g., cough, rhinitis), use face shields and N-95 masks (2). The ambulance should be disinfected after patient transportation with bleach/ sodium hypochlorite solution.

Care in Hospital Settings

Supportive therapy

Team of dedicated trained staff should treat the patients. General supportive therapy is the mainstay of patient management in CCHF. Intensive monitoring to guide volume and blood component replacement is required. Supportive care includes fluid management by intravenous crystalloids, oxygen, cardiac monitoring and administration of blood and blood products as clinically indicated. Avoid intramuscular injections and the use of aspirin or other anticoagulants. Minimize invasive procedures because of the risk associated with viral transmission from sharp objects.

OTHER DRUGS/CRITICAL CARE SUPPORT

In cases of hypotension and hemodynamic instability, patients should be treated according to standard protocols for shock management, including resuscitation, fluid supplementation (crystalloids/colloids), and inotropic support. Blood product replacement should be performed after evaluating the patient's complete blood count.

For suspected secondary bacterial infections, treatment should follow standard guidelines for community-acquired or nosocomial infections. Proton pump inhibitors may be considered on a case-by-case basis to manage potential bleeding in patients with peptic ulcers.

Steroids have no confirmed role in managing this illness. Correction of coagulation abnormalities with fresh frozen plasma (FFP) or cryoprecipitate may be considered in cases of active bleeding or if an invasive procedure is planned (normally, coagulation abnormalities are not corrected without these indications).

Platelet Transfusion: Platelet transfusion (random donor platelets (RDP) or single donor platelets (SDP)) should be considered in cases of significant bleeding due to thrombocytopenia.

Fever Management: Use paracetamol to manage fever, and avoid other NSAIDs.

Ventilator/Renal Support: Provide ventilator or renal support according to standard guidelines when needed.

Precautions: Avoid intramuscular injections and medications that affect the coagulation system.

Breastfeeding: Breastfeeding is not recommended during the acute phase of CCHF due to the established risk of transmitting the virus to the infant.

CHEMOPROPHYLAXIS

Prophylactic administration of oral Ribavirin to contacts of CCHF patients is *not* recommended. Symptomatic contacts may receive therapeutic doses as previously outlined. Full therapeutic doses of Ribavirin should be considered for healthcare workers (HCWs) who have experienced significant exposure, such as a needle stick injury or direct contact with blood or body fluids. For those with mild exposure, close observation and monitoring for symptoms are advised.

CCHF Case Presentation

Patient History

35-year-old male farmer and cattle handler from rural Gujarat
4-day history of:

- High-grade fever
- Chills
- Headache
- Myalgia
- Vomiting

Subsequent development of:

- Hematuria
- Oral and nasal bleeding

Physical Examination

Fever (39°C)
Diffuse muscle tenderness

Laboratory Findings

Haematological:

- Thrombocytopenia
- Leukopenia

Liver Function Tests:

- Elevated liver enzymes

Renal Function Tests:

- Elevated creatinine and urea

Coagulation Profile:

- Prolonged prothrombin time (INR 1.69)

Provisional Diagnosis: Acute Viral Hemorrhagic Fever

Differential Diagnosis: Dengue Fever, CCHF, based on epidemiological suspicion and Other Tropical Fevers like Malaria, Scrub Typhus

Clinical Course

Day 8: Tachypnea, Type 1 respiratory failure, Basal crepitations, ARDS, Mechanical ventilation

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Antiviral Chemotherapy



1

Ribavirin is the recommended antiviral agent, although its mechanism of action is not clear.

2

Ribavirin has shown inhibitory effects on CCHF virus replication, while other drugs tested had limited or no antiviral activity.

3

Adverse events related to ribavirin therapy have not been noted among CCHF patients, but it is contraindicated in pregnant women.

Image source: www.pharmtech.com/files/public-trial-in-medicine-quality-as-public-health-challenges-emerge

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Ribavirin Dosage

Adults				
Administration	Dosage	Loading Day 1	Day 2-4	Day 5-10
Intravenous	Dose (mg/kg)	17 mg/kg (max 1000 mg per dose)	17 mg/kg (max 1000 mg per dose) every 6 hours	8 mg/kg (max 500 mg per dose) every 8 hours
Oral	Dose (mg)	2000 mg	1000 mg every 6 hours	500 mg every 6 hours
Children				
Intravenous	Dose (mg/kg)	17 mg/kg every 6 hours	17 mg/kg every 8 hours	-
Oral	Dose (mg/kg)	30 mg/kg every 6 hours	15 mg/kg every 6 hours	7 mg/kg every 6 hours

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Adverse effects:

- The most common side effect of Ribavirin is mild to moderate hemolytic anemia which is reversible.
- Anemia associated with ribavirin therapy is often asymptomatic and can be managed by monitoring blood count and serum biochemistry.
- Ribavirin administered as an intravenous bolus has been reported to induce rigors; consequently, it is recommended that the drug be administered as an infusion over 10-15 minutes. There have been reports of pancytopenia and pancreatitis associated with use of intravenous ribavirin.

Contra-indications and precautions:

- Ribavirin is contraindicated for treatment in pregnant women.
- Ribavirin is contraindicated in patients with chronic anemia and hemoglobin levels below 8 g/dl, and in patients with severe renal impairment (creatinine clearance <30 ml/min).
- Patients should be carefully monitored during therapy with ribavirin for signs and symptoms of toxicity, such as anemia.

Source: <http://pub.medicines.gov.in/medicines/ribavirin/24107727.pdf>

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Notes

Triage

In the triage patients are divided into 3 categories:

Categories	Presentation	Treatment
Category A	Relatively mild disease No bleeding manifestation	Supporting therapy, do not require Ribavirin
Category B	Severely ill, local and systemic bleeding manifestation, (first 5 days of illness)	Aggressive therapy, Administration of Ribavirin immediately
Category C	Comatose/terminal state with DIC and multi-organ failure (after day 5)	Intensive treatment Ribavirin Poor prognosis

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Other drugs / Critical care support

In case of hypotension and hemodynamic instability

- patient treatment should include resuscitation, fluid supplements (crystalloids/ colloids) and inotropic support.

There is no definite role of steroids for managing this illness per se.

- Correction of coagulation abnormalities (only if present) with the use of PRP/SDP; FFP, cryoprecipitate, as per indications may be considered.

In suspected secondary bacterial infection

- patient should be treated on standard guidelines / practice for community acquired/ nosocomial infections. Proton pump inhibitors can be considered on case-to-case basis.

Platelet transfusion may be considered if there is significant bleeding with thrombocytopenia

- Use Paracetamol for fever, avoid other NSAID.
- Ventilator/ renal support may be provided as per standard guidelines.

Source: <https://ncdc-mohfw.gov.in/WhiteBoardData/LinkImages/Annex%20456%20273.pdf>

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Chemoprophylaxis:

- Symptomatic contacts can be given therapeutic dose as mentioned above.
- Consider full therapeutic dose of Ribavirin for Health Care Workers with severe exposure (Needle stick injury, direct contact with blood /body fluids).
- For person with mild exposure observe and closely monitor HCW for any symptoms.

Prophylactic administration of oral Ribavirin to contacts of CCHF patients is NOT recommended

Source: <https://ncdc-mohfw.gov.in/WhiteBoardData/LinkImages/Annex%20456%20273.pdf>

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Treatment

- Meticulous monitoring of fluid and electrolyte balance is necessary.
- Severe cases should be defined and treated, while mild cases do not require ribavirin treatment.

Supportive therapy is essential and includes the administration of thrombocytes, fresh frozen plasma, and erythrocyte preparations.

Replacement therapy with blood products should be done after checking the patient's complete blood count.

Conservative measures should be taken to address potential bleeding foci, such as using histamine receptor blockers for peptic ulcer patients

Passive immunotherapy using convalescent plasma has been suggested but lacks control groups and has limited evidence.

Avoid intramuscular injections and drugs that affect the coagulation system.

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Notes

Session-8

Outbreak Management & Prevention

Course No. 008	Session 8: Outbreak Management & Prevention
Duration	15 minutes
Learning Objectives	• Describe outbreak management and case classification • Understand outbreak situation in India • Understanding public health scenario • Describe outbreak response and • Describe prevention and control measures • Describe collaboration between healthcare providers and public health authorities
Pre-requisite knowledge/skill	• Knowledge of CCHF outbreak management, case classification, and public health implications. • Understanding of the outbreak situation in India and the national response framework. • Familiarity with prevention, control measures, and coordination between healthcare providers and public health authorities.
Competencies to be achieved	• Understanding potential sources of outbreak • Describing reported CCHF outbreaks in India • Understanding roles of departments in combatting outbreaks • Explain measures to improve outbreak response and preparedness • Competency in effectively managing outbreaks of CCHF

OUTBREAK CASE DEFINITIONS

For any surveillance system there should be a defined uniform case definition to detect the cases.

Suspected case: Any person with clinical features suggestive of CCHF (such as fever, chills, myalgia, headaches, nausea, vomiting, etc.) and at least one of the following exposures within 15 days before symptom onset:

1. Tick bite or crushing a tick with bare hands
2. Direct contact with animal blood or tissues during or immediately after slaughter
3. Direct contact with blood, secretions, or excretions of a CCHF case
4. Residing in or visiting an endemic or outbreak-affected area where exposure to livestock or ticks was possible.

Even single suspected case of CCHF will be termed as an outbreak

Probable case: Any deceased suspected case (where laboratory confirmation is not possible) with an epidemiological link to a confirmed CCHF case.

Confirmed case: Any suspected or probable case

1. With a positive laboratory result, which includes:
2. Detection of the by RT-PCR
3. Positive IgM or IgG seroconversion
4. Positive antigen detection test
5. isolation

Discarded case: Any suspected or probable case with a negative laboratory result, showing no specific antibodies, RNA, or specific detectable antigens.

Clinical features suggestive of CCHF may include:

Sudden onset of fever ($>38^{\circ}\text{C}$), chills, myalgia, headaches, dizziness, neck pain and stiffness, backache, sore eyes, and photophobia.

Additional symptoms may include nausea, vomiting, diarrhoea, abdominal pain, sore throat, mood swings, confusion, sleepiness, depression, lassitude, hepatomegaly, hepatitis, tachycardia, lymphadenopathy, petechial rash, ecchymoses, melena, hematuria, nose bleeding, and unusual vaginal bleeding.

Severe cases may experience rapid deterioration of kidney function, liver failure, or pulmonary failure.

OUTBREAKS IN INDIA

The first outbreak in India was reported in 2011 from Gujarat killing four people including a doctor and a nurse who were either involved in the treatment or were the close contacts of patient. Subsequently, every year outbreaks of CCHF have been reported from different districts of Gujarat. Recently, outbreaks of CCHF have also been reported from Jodhpur, Rajasthan and Moradabad, Uttar Pradesh.

In 2011, the first confirmed outbreak of CCHF occurred in a tertiary care hospital in Ahmadabad, Gujarat. The investigation revealed the circulation of the Tajikistan strain of the CCHF in this outbreak. Collaborating with the Integrated Disease Surveillance Programme (IDSP) and ICMR-NIV, the epidemiological links of CCHF cases were confirmed. Another significant outbreak occurred in 2013 in Karyana village, Amreli district, Gujarat, where secondary cases were observed among close contacts performing last rituals of CCHF cases.

A survey of antibodies in domestic animals in Gujarat revealed a high prevalence of anti-CCHF IgG antibodies in 15 districts. Gujarat experienced a high prevalence of CCHF cases during 2011-2014, resulting in several fatalities.

In 2014, the outbreak of CCHF was reported in Rajasthan, raising concerns about the spread of the to the state. Subsequently, a nosocomial outbreak occurred in Jodhpur in 2015, with genetic analysis suggesting a new strain of CCHF. To assess the prevalence of CCHF in the rest of the country, a countrywide survey was conducted in collaboration with the Indian Council of Agricultural Research (ICAR), which showed the presence of CCHF antibodies in various states and union territories.

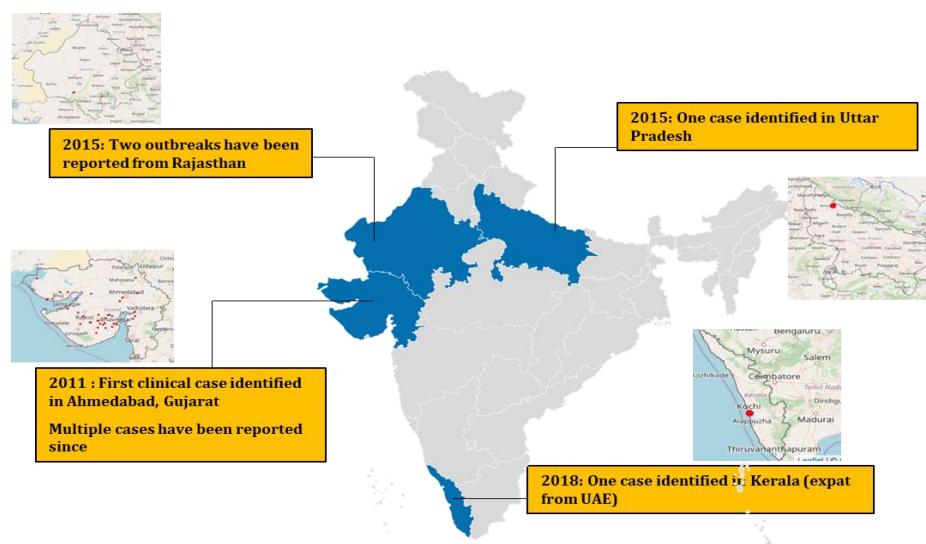


Fig 7: Outbreaks in India.

(Map Source: mapchart.net)

Imported cases of CCHF were also reported in India, including a case from Muscat, Oman, in

2016, and a case from Dubai, United Arab Emirates, in 2019. The surveillance system under IDSP contributed to the detection of CCHF cases in the country.

From 2011 to 2020, a total of 125 CCHF cases were confirmed in India, with a case fatality rate of 42.40%. The affected states included Gujarat, Rajasthan, and imported cases from other countries. The One Health approach, emphasizing the interconnectedness of human, animal, and environmental health, is crucial for controlling and preventing zoonotic diseases like CCHF in India.

Source: (https://journals.lww.com/ijmr/Fulltext/2021/03000/Experiences_of_Indian_Council_of_Medical_Research.15.aspx)

Potential sources of Outbreaks

CCHF outbreaks can occur through various transmission routes. Infected animals, such as cattle, goats, sheep, and rodents, can carry the virus and transmit it to humans through contact with their blood, tissues, or bodily fluids. Laboratory accidents can also lead to infections if proper safety protocols are not followed. While rare, person-to-person transmission can occur through direct contact with the blood or body fluids of an infected individual, especially in the later stages of the illness. Occupational exposure is a significant risk factor for individuals working closely with livestock, including farmers, animal handlers, and veterinarians. Nosocomial transmission can occur in healthcare settings through contact with infected patients' blood or body fluids or due to improper infection control practices.

OUTBREAK PREPAREDNESS AND RESPONSE

CCHF outbreaks constitute a threat to public health services due to its epidemic potential, high CFR and potential for nosocomial outbreaks and the adversities of treatment and prevention. This might over burden the health sector of the country and bring a remarkable economical hindrance as well.

Preparedness and response to an outbreak involve coordinated efforts from different departments. The following steps outline the actions to be taken.

1. Identify a Rapid Response Team (RRT) for investigation of an outbreak
2. Develop emergency response plans and protocols for outbreak situations.
3. Coordinate with the relevant departments and agencies to mobilize resources and manpower.
4. Establish emergency operation centers for effective coordination and decision-making.
5. Conduct drills and simulations to test the response capacity and identify areas for improvement.
6. It is important for these departments to work in a coordinated manner, sharing information, resources, and expertise to effectively respond to outbreaks

7. There should be a incident command system for dissemination of information, reporting to authorities and media information
8. Any suspected case of CCHF in a Human should trigger response
9. Immediate contact tracing of the individuals
10. Identification of animal contacts
11. Vector control measures (Health, Animal and Environment)

It is important for these departments to work in a coordinated manner, sharing information, resources, and expertise to effectively respond to outbreaks and minimize their impact on public health.

Table 6: Multisectoral Response Framework for CCHF Outbreak Management

Steps	Description	Health	Agriculture	Forest	Environment
Activate the Intersectoral Response Team	Establish an intersectoral team with representatives from the health department, agriculture department, forest department, and environmental agency.	Lead coordination and overall response	Provide expertise on livestock management	Provide expertise on wildlife surveillance	Provide expertise on wildlife surveillance
Provide expertise on wildlife surveillance	Promptly report and share information on suspected cases between health and agriculture sectors.	Collect and analyse health-related data	Gather information on livestock exposure	Assist in identifying potential vectors	Assist in identifying potential vectors
Joint Case Investigation and Data Collection	Conduct joint investigations to collect data on symptoms, exposure history, and relevant factors involving representatives from multiple sectors.	Lead the case investigations	Assist in collecting exposure data	Provide insights on potential animal reservoirs	Contribute to understanding environmental impact
Laboratory Testing and Diagnosis	Collaborate between health and agriculture sectors to collect and test samples for accurate diagnosis of the specific pathogen causing the outbreak.	Coordinate sample collection and testing	Assist in sample collection and transportation	Provide expertise on wildlife disease testing	Ensure environmental sample testing

Steps	Description	Health	Agriculture	Forest	Environment
Communication and Public Awareness	Develop joint communication strategies to disseminate information and educate the public on preventive measures involving health and agriculture sectors.	Lead public communication efforts	Collaborate in public awareness campaigns	Assist in disseminating information on vectors	Contribute to environmental health messaging

CCHF OUTBREAK MANAGEMENT

CCHF outbreaks require a robust response strategy to contain the spread of the virus and minimize its impact. The management approach involves several key steps:

- **Case Identification and Isolation:** Prompt identification of suspected, probable, and confirmed CCHF cases is crucial. Infected individuals should be isolated to prevent further transmission.
- **Sample Collection and Testing:** Samples are collected for laboratory testing to confirm the diagnosis. WHO guidelines should be followed for sample collection and testing.
- **Contact Tracing:** Identifying and monitoring human contacts of the infected individual is essential to prevent secondary infections.
- **Animal Contact Management:** Identifying and quarantining animal contacts, especially livestock, is important as ticks can transmit the virus between animals and humans.
- **Infection Prevention and Control:** Strict adherence to infection prevention and control measures, including the use of personal protective equipment and proper disposal of contaminated materials, is crucial for healthcare workers and those in contact with infected individuals.
- **Dead Body Disposal:** Safe disposal of the bodies of individuals who have died from CCHF is essential to prevent further transmission.
- **Community Engagement:** Public health education and awareness campaigns are crucial to inform the community about the risks of CCHF, prevention measures, and the importance of seeking medical attention early.

PREVENTION AND CONTROL

IN AREAS AFFECTED BY THE DISEASE

- Conduct public education campaigns to raise awareness about the mode of transmission and personal protective measures.
- Collaborate with the Animal Husbandry Department to implement tick control measures in affected areas, particularly for cattle, and coordinate with Krishi Vikas Kendra to coordinate efforts with District Level Zonal Coordinators.

- Promote personal protection practices, such as wearing light clothing that covers the legs and arms, tucking pants into socks, regularly checking clothing and skin for ticks, and applying tick repellents like DEET or permethrin.
- Individuals working with livestock or animals in endemic areas should use repellents on their skin and clothing, wear gloves or protective clothing to prevent contact with infected tissues or blood.
- Ensure safe handling of dead bodies using appropriate personal protection measures.

INFECTION PREVENTION AND CONTROL IN HEALTH FACILITIES

- Capacity building of the healthcare provider on proper use of PPE including training of laboratory staff for safe handling of the samples
- Training of laboratory personnel on the packaging of samples if transportation is needed
- Health-care workers caring for patients with suspected or confirmed CCHF, or handling related specimens, should follow standard infection control measures, including hand hygiene, PPE, safe injection, and burial practices. Adherence to universal infection prevention protocols is essential in facilities managing CCHF cases
- Promptly identify and separate patients with signs and symptoms consistent with CCHF at the point of entry into the healthcare facility.
- Manage patients with suspected or confirmed CCHF in isolation rooms and follow barrier- nursing techniques to prevent nosocomial infections.
- Availability and accessibility of PPE, along with a separate designated area for donning and doffing with restricted access, should be ensured, while limiting entry to the patient's room to only designated medical and para-medical staff and attendants, excluding non-essential staff and visitors.
- IEC materials on proper donning and doffing procedures, along with a spill management kit, should be readily available at all necessary locations.

NON-PHARMACEUTICAL INTERVENTIONS

- Adhere to adequate infection control measures, including barrier nursing, when patients with CCHF are admitted to the hospital to prevent nosocomial spread of infection.
- Isolate patients in a designated room, with consideration for negative pressure rooms if patients have prominent cough, vomiting, diarrhea, or hemorrhage.
- Ensure that all staff entering the patient's room wear personal protective equipment.
- Practice regular hand washing/hand sanitization before and after clinical examinations or procedures on the patient.
- Staff coming within 3 feet of the patient should wear face shields or surgical masks with eye protection. Use HEPA filter masks if patients have respiratory, gastrointestinal, or hemorrhagic symptoms.
- Collect and handle blood or tissue specimens for diagnostic purposes using universal precautions.
-

- Implement proper sharps management protocols to prevent accidental needlestick injuries and exposure to contaminated instruments.

SAFE DISPOSAL OF BODY WASTES AND DECONTAMINATION PROCEDURES SHOULD BE FOLLOWED

- Standard Waste Management guidelines should be followed
- Properly dispose of body wastes using appropriate decontamination procedures.
- Cover legs/shoes if large amounts of blood or other body fluids in the environment.
- Discard all used protective barriers and clean shoes with a hospital disinfectant or a solution of household bleach before exiting the room.
- Consider using an anteroom for putting on and removing protective barriers and storing supplies.
- Treat hospital clothing, bed sheets, and other linen used in patient care as infectious, and autoclave send to common treatment facility for management.
- Collect all used materials such as syringes, gloves, cannulas, tubing, etc., in an autoclavable bag, autoclave them, and incinerate them.
- Decontaminate and autoclave all instruments and equipment before reuse.
- Clean surfaces with liquid bleach for decontamination.
- CCHF can be inactivated by disinfectants including 1% hypochlorite and 2% glutaraldehyde.

Take precautions to avoid spills, needle pricks, injuries, and accidents during case management.

- Healthcare workers who have had contact with tissue or blood from patients with suspected, probable, or confirmed CCHF should be monitored daily for temperature and symptoms for at least 14 days after potential exposure.
- Follow standard guidelines for hospital waste management practices.
- Examine the patient and attendants for ticks using universal precautions. Use acaricidal agents if there is evidence of tick infestation.

DEAD BODY DISPOSAL

- Use rubber gloves or double surgical gloves when handling a dead body. The personnel handling the dead body in hospitals should also wear masks/PPE.
- Spray the dead body with a 1:10 solution of liquid bleach. Wrap it with a winding sheet and spray the sheet with bleach solution.
- Place the wrapped and bleached body in a plastic bag, seal it with adhesive tape, and transport it.
- Disinfect the ambulance or transport vehicle.
- Maintain a safe and clean patient environment.
- Educate medical and para-medical staff and attendants to follow universal infection prevention and control practices.
- Take precautions to avoid spills, pricks, injuries, and accidents during patient management. Needles should not be recapped but discarded properly.

- Staff members should report to management if they are exposed to a patient's blood or body fluids, sustain a sharps injury, or develop fever, body aches, or bleeding tendencies.
- Display signs, posters, and other educational materials on infection prevention and control practices prominently in hospitals.
- Inform the designated laboratory in advance about the sample and transport it to the designated laboratory with caution to avoid breakage or spills.
- After the patient is discharged, clean and wipe down room surfaces with an appropriate disinfectant to kill the virus.

Note: It is important to consult and follow the specific guidelines and protocols issued by relevant health authorities and departments for effective implementation of these measures.

HOW TO REMOVE A TICK

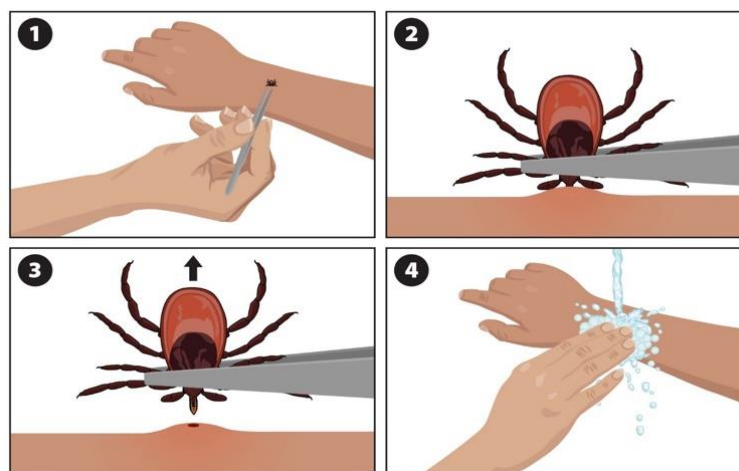


Fig 7: How to remove a tick?

(Source: <https://www.cdc.gov/ticks/after-a-tick-bite/index.html>)

- Use clean, fine-tipped tweezers to grasp the tick as close to the skin's surface as possible.
- Pull upward with steady, even pressure. Don't twist or jerk the tick; this can cause the mouth- parts to break off and remain in the skin. If this happens, remove the mouth- parts with tweezers. If you cannot remove the mouth easily with tweezers, leave it alone and let the skin heal.
- After removing the tick, thoroughly clean the bite area and your hands with rubbing alcohol or soap and water.
- Never crush a tick with your fingers. Dispose of a live tick by putting it in alcohol, placing it in a sealed bag/container, wrapping it tightly in tape, or flushing it down the toilet.

DESIGNATED AREA IN CASUALTY/TRAUMA CENTER

- Primary call to be attended by the CMO or Resident on duty.
- Confirmed, probable, or strongly suspected cases should be transferred directly to the isolation ward.

- Isolate the patient.
- Check for any tick bite marks and, if found, remove the tick using universal precautions.
- Avoid intramuscular injections.
- Administer oral and IV fluids and correct electrolyte imbalances.
- Conduct routine and special investigations as clinically indicated.
- Rule out other common differential diagnoses and transfer the patient to the isolation ward.
- Even if a Dengue test is positive, if clinically consistent with CCHF, isolate, investigate, and manage the patient accordingly.

Table 6: Comprehensive Diagnostic Workup for Suspected CCHF Cases

Category	Tests
Routine Tests	CBC, ESR, RBS, CT, BT, PT, aPTT, LFT, RFT, blood grouping, and cross- matching.
Blood Examinations	Malaria, Dengue, Chikungunya, Zika, and Leptospirosis (PCR, Leptocheck, MAT, or ELISA, especially in endemic areas like South Gujarat), if the patient tests negative for CCHF.
Other Specific Tests	S. LDH, CPK Total, CPK-MM, S. Ferritin, D-Dimer.
Additional Serology	HBsAg, anti-HAV antibody, anti-HEV antibody.
Urine Analysis	Routine, microscopic, and for hemoglobinuria/myoglobinuria.
Stool	Occult blood test.
Arterial Blood Gas Analysis	ABG Analysis.
Pregnancy Test	If indicated.
Imaging	X-ray chest, USG of the abdomen, chest, and pericardium.
Biopsies	Bone marrow aspiration and biopsy, lymph node FNAC.
Inflammatory Markers	Interleukin (IL)-6, IL-10, and Tumor Necrosis Factor-Alpha.

CARE OF CASES IN ISOLATION WARD

1. Upon admission, collect a sample for CCHF testing and send it to ICMR-NIV, Pune, via the medical college's Microbiology Department. Classify the patient as Category A/B/C and initiate Ribavirin if not previously started or contraindicated.
 - **Routine Case Management:**
 - Manage haemorrhage/shock with inotropic drugs, PCV, FFP, CRYO, PRP/SDP, or whole blood as needed.
 - Provide ventilatory support or dialysis as indicated.
 - Treat any associated conditions.
2. Dedicated Staff: The resident and faculty of the admitting unit will manage admissions.

3. Staff will rotate weekly.
4. Notify the Nodal Officer for Medicine/Community Medicine and higher authorities.
5. Complete the Ribavirin course, even if CCHF test results are negative.
6. Follow universal precautions and hospital waste management as per standards, supervised by the Infection Control Committee.
7. Handle dead body disposal according to Government of India guidelines.

DEPARTMENT-WISE RESPONSIBILITIES

Table 7: Department-Wise Roles and Responsibilities for CCHF Preparedness and Response

Department	Responsibilities
Anatomy	Special handling of any donated bodies from suspected haemorrhagic fever cases.
Biochemistry, Pathology, & Microbiology	Maintain a 24/7 laboratory facility. Provide PPE training for all staff, including universal precautions, waste management, and post-mortem protocols.
Microbiology	Collect, package, and transport CCHF samples to ICMR-NIV, Pune. Communicate results from ICMR-NIV to the treating hospital. Monitor infection control practices in isolation. Send patient details of each sample to appropriate authorities.
Blood Bank	Ensure availability of blood and blood products.
Community Medicine	Prepare a contact list, monitor contacts' health for 14 days post-contact, maintain line listings, and perform verbal autopsies.
Forensic Medicine	Conduct post-mortem examinations if necessary (ideally to be avoided).
Clinical Departments	Medicine, Paediatrics, Anaesthesiology, and ICU departments prepare to treat cases. Suspected cases may arise from MICU, general OPD, fever clinics, and other OPDs. Actively screen for and manage suspected cases.
RMO	Arrange dead body disposal in liaison with the Municipal Corporation or competent authority. Train class IV staff and sweepers.
Matron	Schedule nursing staff on a seven-day rotation, train for dedicated care, and ensure fumigation of patient cabins.
Sanitary Inspector	Assign class IV staff and sweepers on a seven-day rotation.
Medical Superintendent	Oversee overall management. Conduct training for relevant staff, procure Ribavirin, PPE, and other supplies for the isolation ward. Communicate with higher authorities and coordinate media briefings.

COMMUNICATION PROTOCOL FOR INFORMATION SHARING OF VHF

Table 7: Communication Protocol and Responsibilities for Suspected VHF Cases

Protocol Step	Description
Communication by Paramedics & ASHA	Report suspected VHF cases identified by MPHWS (M/F) or ASHA workers during field visits to the MO PHC via phone.
	Based on guidance, refer the patient to the nearest PHC or CHC.
Communication by PHC & CHC	For suspected VHF cases at PHC/CHC requiring referral to DH or Medical College:
	Transport the patient in a designated government vehicle with a referral slip detailing symptoms, investigations, and treatments.
	Inform the referral hospital and CDHO.
	CDHO maintains close communication with the referral hospital to monitor the patient's status.
Communication by DH or Medical College Hospital	For suspected VHF cases at DH or Medical College (direct or referral):
	Admitting unit informs the RMO or Medical Superintendent.
	RMO/Superintendent notifies the CDHO.
	Designate a nodal officer for the isolation ward and share contact with CDHO.
	Nodal officer updates CDHO on patient's status at 9:00 a.m. and 5:00 p.m. via email.
	If a sample is sent to ICMR-NIV Pune, Microbiology Dept informs CDHO and shares results.
	For advanced referrals, transport in a government vehicle with a detailed referral slip; inform referral hospital and CDHO.
Communication & Role of CDHO	Notify AD (Public Health), DD (Epidemic), and RDD.
	Submit daily reports on VHF cases.
	Convene intersectoral coordination meetings as needed.
	Maintain close contact with the patient's health facility.
	Conduct active fever surveillance in affected villages.
	Trace contacts with 14-day temperature monitoring.
	Promptly refer symptomatic contacts to a tertiary center.
	Ensure close supervision of all high-risk contacts.

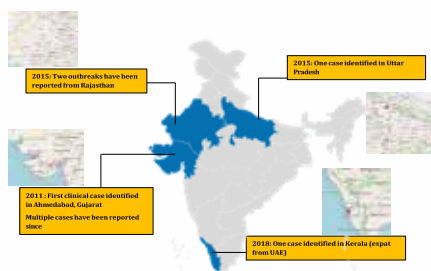
CCHF outbreak case classification

CCHF discarded case	CCHF confirmed case	CCHF suspected case	CCHF probable case
- Laboratory test(s) negative suspected or probable case, by: - ELISA (IgG or IgM), OR - Antigen detection test, OR - Detection of virus by RT PCR, OR - Virus isolation	- Laboratory test(s) positive suspected or probable case, by: - ELISA (IgG or IgM), OR - Antigen detection test, OR - Detection of virus by RT PCR, OR - Virus isolation	- Clinical features suggestive of CCHF + any 1 symptom in past 15 days of: - Bitten by a tick or crushed a tick with bare hands, OR - Direct contact with animal blood or other tissues during/immediately after slaughter, OR - Direct contact with blood, secretion or excretions of a CCHF case, OR - Resided in or visited an endemic or outbreak-affected area, where exposure to livestock or ticks was possible	- Deceased suspected case, where: - Epidemiologically linked with confirmed case(s) of CCHF - Has not been possible to collect samples for laboratory investigations for CCHF

Source: www.who.int/emergencies/outbreaks/diseases/cchf/cchf-outbreak-and-case-management/cchf-outbreak-and-case-management.pdf

Reported CCHF outbreaks in India

The first outbreak in India was reported in 2011 from Gujarat killing four people



Subsequently, every year outbreaks of CCHF have been reported from different districts of Gujarat. Recently, outbreaks of CCHF have also been reported from Jodhpur, Rajasthan and Muradabad, Uttar Pradesh

Potential sources of the outbreak :

Infected Animals Cattle, goats, sheep, and rodents can carry the CCHF virus. Contact with infected animals or their blood, tissues, or bodily fluids can lead to transmission.	Laboratory Accidents Accidental exposure or lapses in safety protocols in laboratories can result in laboratory-acquired infections.
Person-to-Person Transmission Although rare, direct contact with the blood or body fluids of an infected person can lead to transmission. This is more likely in the later stages of the illness.	
Occupational Exposure Individuals working closely with livestock are at higher risk. Farmers, animal handlers, and veterinarians may come into direct contact with infected animals or their products. People involved in transport and trading animals.	
Nosocomial Transmission CCHF can spread in healthcare settings. Contact with infected patients' blood or body fluids can lead to transmission. Improper infection control practices and mishandling of medical waste or equipment can contribute to nosocomial transmission.	

CCHF Outbreak Management: Key Strategies

Strategy	Description
Rapid Response Team (RRT)	Establish a dedicated team to swiftly investigate and respond to outbreaks.
Emergency Response Plans	Develop and update comprehensive plans and protocols for effective response.
Inter-departmental Coordination	Foster collaboration among relevant departments and agencies.
Emergency Operation Centers	Establish centers for centralized coordination and decision-making.
Drills and Simulations	Conduct regular exercises to test response capabilities.
Case Management and Contact Tracing	Promptly identify and isolate cases, trace contacts, and monitor for symptoms.
Animal Contact Management	Identify and quarantine animals that may be carrying the virus.
Vector Control	Implement measures to reduce the population of ticks.
Infection Prevention and Control	Adhere to strict infection prevention and control measures.

Notes

CCHF outbreak management

CCHF suspected case

- Isolate patient and manage as active CCHF case
- Samples for investigation using WHO guidelines

CCHF probable case

- Dead body disposal using Universal Infection Prevention and Control Practices

CCHF confirmed case

- Isolate patient and manage as active CCHF case
- PCR confirmation if not done

CCHF discarded case

- Isolate patient and manage as infectious etiology
- PCR confirmation if not done
- Investigate for pathogens presenting with similar symptoms

Human contacts

- Identify and isolate all in contact
- Test for CCHF
- Management as per protocol

Animal contacts

- Identify and quarantine animals
- If livestock, use acaricides for tick control

Source: www.who.int/emergencies/diseases/nipah-virus/crimean-congo-haemorrhagic-fever

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Prevention

In Disease Affected Areas

Intervention	Description
Educate public	- Inform the public about the mode of transmission and personal protective measures.
Tick Control	- Undertake tick control in affected areas in consultation with the Animal Husbandry Department.
Personal protection	- Wear light clothing that covers legs and arms. - Tuck pants into socks. - Regularly examine clothing and skin for ticks. - Apply tick repellent (e.g., DEET or permethrin) to the skin or clothing.
Protection for persons working with animals	- Use repellents on the skin and clothing. - Wear gloves or other protective clothing to prevent skin contact with infected tissues or blood.
Safe handling of dead bodies	- Use personal protective measures when handling dead bodies.

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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Prevention

Infection Prevention and Control in Health Facilities

Universal Infection Prevention and Control practices Strictly adhere to universal infection prevention and control practices in healthcare facilities dealing with suspected, probable, and confirmed cases. Identify and separate patients with signs and symptoms consistent with CCHF as quickly as possible upon entry to the healthcare facility. Patient identification and isolation Manage suspected or confirmed CCHF cases in isolation rooms & follow barrier-nursing techniques to prevent nosocomial infections. Only designated medical/para-medical staff and attendants should attend to the patient. Restricted access to patient rooms Non-essential staff and visitors should not be allowed to enter the room. Place patients in isolation rooms & Restrict nonessential staff and visitors from entering patient rooms. Non-Pharmaceutical Interventions Use personal protective equipment when entering patient rooms & maintain a clean and safe patient environment. Follow hand hygiene protocols & proper disposal of sharps and wastes. Handle dead bodies using rubber gloves or double surgical gloves. Spray the body with a bleach solution & Wrap it in a winding sheet sprayed with bleach. Dead body disposal Place the wrapped body in a plastic bag and seal it. Disinfect the ambulance/transport vehicle. Clean the patient's room after discharge.	
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CRIMEAN-CONGO HAEMORRHAGIC FEVER

Preventive Measures for CCHF Outbreak

Community	Patient	Patient Attender	Health Care Staff	Animal Handler
- Avoid contact with blood or body fluids of sick animals. - Wear protective clothing (gloves, masks) when handling animals or their tissues. - Practice good personal hygiene, including frequent handwashing with soap and water. - Use insect repellent to prevent tick bites. - Promote environmental cleanliness and proper waste management to	- Isolate the patient to prevent transmission to others. - Follow strict infection control practices, including wearing personal protective equipment (PPE). - Maintain good respiratory hygiene, such as covering the mouth and nose when coughing or sneezing. - Receive appropriate medical care and follow prescribed treatments.	- Limit close contact with the patient's blood or body fluids. - Follow infection prevention practices, including hand hygiene and proper disposal of contaminated items. - Use personal protective equipment (PPE) when in close contact with the patient.	- Adhere to strict infection prevention and control protocols. - Wear appropriate personal protective equipment (PPE) when in contact with the patient or their specimens. - Follow safe waste management procedures for disposing of contaminated materials. - Practice proper hand hygiene before and after patient contact.	- Wear protective clothing (gloves, masks) when handling animals or their tissues. - Avoid direct contact with blood or body fluids of animals. - Implement tick control measures, such as using insect repellents and regular inspection of animals. - Practice good personal hygiene, including frequent handwashing after handling animals. - Report any sick animals or unusual deaths to the appropriate authorities.
Implementing these preventive measures can significantly reduce the risk of transmission and help control the outbreak of CCHF effectively for each respective group.				

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Reducing the risk of infection in people

Reducing the risk of tick- to-human transmission	Reducing the risk of animal-to-human transmission	Reducing the risk of human-to-human transmission	Controlling infection in health-care settings
• Wear protective clothing (long sleeves, long trousers); • Wear light colored clothing for easy detection of ticks on the clothes; • Use approved acaricides to kill ticks on clothing; • Use approved repellent on the skin and clothing; • Regularly examine clothing and skin for ticks; if found, remove them safely; • Avoid ticks-infested areas	• Wear mask, gloves and gowns when slaughtering and butchering animals in slaughterhouses or at home to prevent skin contact with infected animal tissue or blood; • Quarantine animals before they enter slaughterhouses or routinely treat animals with pesticides two weeks prior to slaughter; • Use acaricide (tick killer) in farms and livestock production facilities to decrease tick infestations on animals	• Avoid close physical contact with CCHF-infected people; • wear gloves and protective equipment when taking care of ill people; • wash hands regularly after caring for or visiting ill people; • Encourage early treatment in CCHF Treatment Center	• Strictly adhered universal Infection Prevention and Control practices dealing with suspected, probable and confirmed cases. • Patients with suspected or confirmed CCHF should be managed in an isolation room. • Only designated medical / para-medical staff and attendants should attend the patient. • All staff entering the room should wear personal protective equipment (PPE). • Hand washing before and after clinical examination on the patient.

Center for Disease Control, CDC, Atlanta

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Procedure to remove the Tick

- Use clean, fine-tipped tweezers to grasp the tick as close to the skin's surface as possible.
- Pull upward with steady, even pressure. Don't twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin. If this happens, remove the mouth-parts with tweezers. If you cannot remove the mouth easily with tweezers, leave it alone and let the skin heal.
- After removing the tick, thoroughly clean the bite area and your hands with rubbing alcohol or soap and water.
- Never crush a tick with your fingers. Dispose of a live tick by putting it in alcohol, placing it in a sealed bag/container, wrapping it tightly in tape, or flushing it down the toilet.



Source: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5811a1.htm>

Steps of outbreak response

```
graph LR; A[Prepare for Field Work:  
Gather necessary tools,  
resources, and background  
information to facilitate the  
investigation.] --> B[Confirm the Diagnosis:  
Verify the diagnosis of the  
suspected disease through  
laboratory tests and clinical  
assessments.]; B --> C[Determine the Existence of  
an Outbreak: Assess  
whether the number of cases  
exceeds expected levels for  
that area and timeframe.]; C --> D[Identify and Count Cases:  
Develop a case definition and  
create a line listing to track  
both confirmed and  
suspected cases  
systematically.]; D --> E[Plan for Systematic  
Studies: Prepare for more  
detailed epidemiological  
studies to gather additional  
data and verify initial  
findings.]; E --> F[Develop and Test  
Hypotheses: Formulate  
hypotheses regarding the  
source and transmission of  
the outbreak and test them  
through data analysis.]; F --> G[Consider Control  
Measures: Evaluate the  
feasibility of implementing  
immediate control measures  
while planning for further  
interventions.]; G --> H[Implement and Evaluate  
Control Measures: Put  
control measures into action  
and continuously assess their  
effectiveness to mitigate the  
outbreak's impact.]; H --> I[Communicate Findings:  
Summarize the  
investigation's results for  
relevant authorities and  
prepare comprehensive  
reports for stakeholders.];
```

Prepare for Field Work: Gather necessary tools, resources, and background information to facilitate the investigation.

Confirm the Diagnosis: Verify the diagnosis of the suspected disease through laboratory tests and clinical assessments.

Determine the Existence of an Outbreak: Assess whether the number of cases exceeds expected levels for that area and timeframe.

Identify and Count Cases: Develop a case definition and create a line listing to track both confirmed and suspected cases systematically.

Plan for Systematic Studies: Prepare for more detailed epidemiological studies to gather additional data and verify initial findings.

Develop and Test Hypotheses: Formulate hypotheses regarding the source and transmission of the outbreak and test them through data analysis.

Consider Control Measures: Evaluate the feasibility of implementing immediate control measures while planning for further interventions.

Implement and Evaluate Control Measures: Put control measures into action and continuously assess their effectiveness to mitigate the outbreak's impact.

Communicate Findings: Summarize the investigation's results for relevant authorities and prepare comprehensive reports for stakeholders.

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Session-9

Surveillance and Risk Communication

Course No. 009	Session 9: Surveillance and Risk Communication
Duration	10 minutes
Learning Objectives	• Understand surveillance of CCHF • Describe risk communication and public awareness
Pre-requisite knowledge/skill	• Understanding of CCHF surveillance systems and reporting mechanisms. • Knowledge of effective risk communication strategies. • Awareness of public education approaches to enhance CCHF prevention and awareness.
Competencies to be achieved	• Comprehension of the various methods employed for surveillance and monitoring of CCHF cases. • Description of strategies for risk communication and raising public awareness about CCHF • Understanding the importance of collaboration between healthcare providers and public health authorities in addressing CCHF cases

SURVEILLANCE AND RISK COMMUNICATION

Effective surveillance is crucial for monitoring the spread of CCHF and implementing timely control measures. This involves surveillance of humans, animals, and ticks in endemic and bordering non-endemic areas. As infected animals often remain asymptomatic, active surveillance and human case detection are key strategies for identifying the circulation of the virus. In India, testing and surveillance for viral hemorrhagic fevers, including CCHF, have been ongoing. As the incidence of tick-borne diseases increases in a region, surveillance efforts are expanded to include humans and animals in adjacent areas. Additionally, whenever a CCHF-positive death is reported, immediate surveillance is conducted among community members, focusing on individuals with unusual fever symptoms. Serological testing of domestic animals and viral RNA detection in infested ticks are also performed to assess the extent of infection.

SURVEILLANCE & RISK COMMUNICATION

To strengthen CCHF surveillance in India, collaborative efforts between ICMR and ICAR have been initiated. These efforts include conducting surveys to assess the prevalence of CCHF antibodies in domestic animals across various states. Additionally, serosurveys in humans from endemic regions, such as Gujarat, have been conducted to understand the extent of human exposure to the virus. These surveillance activities play a crucial role in monitoring the spread of CCHF and implementing timely control measures.

Surveillance for CCHF involves coordinated efforts from various departments and stakeholders. Here are the steps in CCHF surveillance taken by different departments:

HEALTH SERVICES

- Establish and maintain a routine surveillance system for CCHF in collaboration with other departments and agencies. Develop guidelines and protocols for case detection, diagnosis, and reporting of CCHF cases.
- Train healthcare workers on recognizing and reporting suspected cases of CCHF.
- Ensure access to laboratory facilities for timely and accurate diagnosis of CCHF cases.
- Collect and analyse data on CCHF cases, including demographic information, clinical features, and outcomes.
- Monitor trends in CCHF cases and identify potential outbreaks.
- Coordinate with other departments to initiate appropriate control measures in response to CCHF outbreaks.

ANIMAL HUSBANDRY AND VETERINARY SERVICES

- Conduct surveillance of livestock, particularly cattle and other domestic animals, for CCHF infection.
- Implement measures to prevent and control tick infestation in animals.
- Collaborate with healthcare departments to investigate and respond to CCHF cases with a suspected link to animal exposure.
- Provide guidance on safe handling and disposal of animal carcasses to minimize the risk of transmission.

EPIDEMIOLOGY AND PUBLIC HEALTH

- Coordinate surveillance activities and data collection related to CCHF.
- Analyze surveillance data to identify patterns, risk factors, and geographical distribution of CCHF cases.
- Conduct outbreak investigations to determine the source of infection and modes of transmission.
- Assess the effectiveness of control measures and provide recommendations for improvement.
- Communicate surveillance findings and updates to relevant stakeholders and the public.

LABORATORIES

- Provide training and quality assurance programs for laboratory staff performing CCHF testing.
- Ensure availability of diagnostic tests for CCHF, such as RT-PCR, serology, antigen detection, and isolation.
- Establish a system for timely reporting of laboratory results to support case confirmation and surveillance.

COMMUNICATIONS AND INFORMATION

- Develop communication strategies to raise awareness about CCHF among the public, healthcare workers, and other relevant stakeholders.
- Disseminate information on CCHF prevention, symptoms, and reporting procedures through various channels, including media campaigns, websites, and social media.
- Respond to public inquiries and provide accurate and up-to-date information on CCHF.

EMERGENCY MANAGEMENT

- Develop and implement emergency response plans for CCHF outbreaks.
- Coordinate resources and personnel for rapid response to CCHF cases and outbreaks.
- Establish mechanisms for interdepartmental communication and coordination during emergencies.

- Collaboration and coordination between these departments, along with other relevant stakeholders, are crucial for effective CCHF surveillance, early detection of cases, and timely implementation of control measures to prevent the spread of the disease.

RISK COMMUNICATION

The hospital setting provides a conducive environment for risk communication. The outpatient department (OPD) can be utilized to educate patients on the animal-human-vector interface and simple preventive measures such as personal hygiene, handwashing, daily bathing, keeping domestic animals clean and free from ticks, maintaining general health and sanitation measures in the household and surroundings, and reporting of symptomatic cases.

Instructions for monitoring and laboratory testing for contacts of CCHF cases:

Contacts include family members, neighbours, and healthcare facility contacts.

Table 8: Definition, monitoring of contacts and laboratory testing for contacts of CCHF case

Protocol Step	Description
Definition of “Contact”	• Contacts include family, neighbourhood, and health care facility contacts.
Monitoring Contacts	• All contacts must self-monitor twice daily for clinical symptoms (e.g., fever, muscular pain, bleeding) for up to 14 days from the last known contact with the patient or infection source.
	• If symptoms arise, contacts must report immediately to the nearest health facility.
Testing Blood for CCHF	• Laboratory testing is recommended for individuals meeting the case definition criteria for CCHF.

MONITORING

All contacts should self-monitor twice daily for any clinical symptoms such as fever, muscular pain, or bleeding for a maximum of 14 days from the day of last contact with the patient or other sources of infection. If any symptom occurs, the contact should immediately report to the nearest health facility.

TESTING

Appropriate laboratory testing, specifically blood tests, is recommended for cases that meet the case definition for CCHF.

BARRIER NURSING

Isolation/barrier nursing is a set of infection control practices implemented to contain and

eliminate the spread of pathogenic organisms. It is performed either in the patient's own room or at home. Barrier nursing serves two purposes in infection prevention and control:

- a. Source isolation/barrier nursing: This practice aims to prevent the transmission of infection from the patient to others. It involves implementing measures to isolate the patient and create a barrier to minimize contact and exposure to infectious agents.
- b. Protective isolation/reverse barrier nursing: This practice is designed to prevent the transmission of infection from caregivers or healthcare providers to susceptible patients. It involves implementing measures to protect the vulnerable patient from potential sources of infection by healthcare personnel.

Both forms of barrier nursing play a crucial role in maintaining a safe environment and preventing the spread of infectious diseases.

WASTE MANAGEMENT

During CCHF outbreaks, proper waste management is crucial to minimize the risk of infection transmission. Here are important guidelines for waste management:

1. Waste triaging: Waste should be sorted and categorized appropriately to facilitate safe handling and disposal.
2. Sharps disposal: Sharp objects such as needles, syringes, and glass articles that have come into contact with the bloodstream should be placed in puncture-resistant containers located near the point of use.
3. Solid waste collection: Solid non-sharp medical waste should be collected using leak-proof waste bags and covered bins.
4. Controlled access to waste disposal area: The area designated for final treatment and disposal of waste should have controlled access to prevent entry by animals, untrained personnel, or children.
5. Personal protective equipment (PPE): When handling solid infectious waste, it is important to wear gloves, a gown, and closed shoes (e.g., boots) to protect against potential exposure.
6. Disposal of liquid waste: Faeces, urine, vomit, and liquid waste from washing can be disposed of in the sanitary sewer or pit latrine without further treatment.
7. When handling liquid infectious waste (e.g., secretions or excretions with visible blood), it is important to wear gloves, a gown, closed shoes, and facial protection to prevent contact with potentially infectious materials.
8. Preventing splashes: When disposing of liquid infectious waste, it is important to avoid splashing. Goggles provide better protection against splashes than visors, especially when pouring liquid waste from a bucket.

Adhering to these waste management practices helps ensure the safe handling and disposal of waste during CCHF outbreaks, minimizing the risk of infection transmission to healthcare workers and the community.

CCHF Surveillance

Surveillance programs for humans, animals and ticks in endemic and bordering non-endemic areas can be used to monitor the spread of disease.

As infected animals are usually asymptomatic, only active surveillance or human case detection will reveal CCHF in circulation.

In India, testing and surveillance of the viral haemorrhagic fever have been an ongoing activity.

As the incidence of tick-borne diseases increases in any area, surveillance in other/adjoining geographic areas is carried out among humans and animals at expanded level.

Whenever any deceased CCHF-positive patient is reported, immediate surveillance is conducted for members of the community, for unusual fever symptoms, as well as IgG antibody screening of domestic animals and viral RNA detection in infested ticks



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CCHF Surveillance contd...

- A joint initiative has been taken up by ICMR and the Indian Council of Agricultural Research (ICAR) to conduct a survey of IgG antibodies against CCHF in domestic animals in different states of India.
- In one of the country-wide survey was conducted with the Indian Council of Agricultural Research (ICAR), which showed that the prevalence of the CCHF in all the 22 states and one UT wherein samples were taken from bovine, sheep and goats.
- In a CCHF serosurvey conducted for 3 years (2015, 2016, 2017) in humans from the endemic state of Gujarat reported a low CCHF seropositivity for CCHF (0.5%) as against other endemic regions of the world.

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CCHF Outbreak Management: Intersectoral Collaboration- Departments and their Roles



Health Services

- Surveillance system establishment and maintenance, guideline and protocol development
- Healthcare worker training, laboratory diagnosis and data analysis
- Outbreak response coordination



Animal Husbandry and Veterinary Services

- Livestock surveillance
- Tick control measures
- Collaboration with health departments
- Safe animal handling and disposal guidelines



Epidemiology and Public Health

- Surveillance coordination and data analysis
- Outbreak investigation
- Assessment of control measures
- Public communication



Laboratories

- Diagnostic test availability
- Laboratory staff training
- Timely reporting of results



Communications and Information

- Public awareness campaigns
- Information dissemination
- Public inquiry response



Emergency Management

- Emergency response plan development
- Resource mobilization
- Interdepartmental coordination

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Risk communication

Hospital setting provides an enabling environment for risk communication.

OPD may be used as a venue for educating patients on animal-human vector interface and simple measures for disease prevention such as personal hygiene, hand washing, daily bath, keeping domestic animals clean and free from ticks, and general health and sanitation measures in the house and within the surroundings.

Self-reporting of symptomatic cases should be encouraged

Use of repellents on animals before the slaughter could reduce the number of infected slaughterhouse workers

Patients with suspected or confirmed CCHF should be managed in an isolation room for the period of communicability and barrier-nursing techniques should be followed to avoid nosocomial infection.

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Notes

Definition, monitoring of contacts and Laboratory testing for contacts of CCHF case

Definition of "Contact"	Contacts include family, neighbourhood, and health care facility contacts.
Monitoring Contacts	- All contacts must self-monitor twice daily for clinical symptoms (e.g., fever, muscular pain, bleeding) for up to 14 days from the last known contact with the patient or infection source. - If symptoms arise, contacts must report immediately to the nearest health facility.
Testing Blood for CCHF	- Laboratory testing is recommended for individuals meeting the case definition criteria for CCHF.

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Notes

Session-10

Sample Collection, Storage and Transportation

Course No. 010	Session 10: Sample Collection, Storage and Transportation
Duration	20 minutes
Learning Objectives	• Describe samples to be collected in humans and animals • Understand conditions required for storage of specimens • Explain procedure for transportation of sample to laboratory
Pre-requisite knowledge/skill	• Knowledge of appropriate samples to be collected from humans and animals for CCHF diagnosis. • Understanding of required storage conditions to maintain specimen integrity. • Familiarity with safe and compliant procedures for transporting samples to the laboratory.
Competencies to be achieved	• Proficiency in explaining the essential samples needed for diagnosing Crimean-Congo Hemorrhagic Fever (CCHF) in both humans and animals. • Comprehension of the necessary storage conditions to ensure the preservation of sample quality. • Familiarity with the correct protocol for transporting samples to the laboratory.

SAMPLE COLLECTION

Due to the high risk associated with CCHF, clinical samples should be handled in specially-equipped laboratories with high biosafety level, preferably BSL-3 plus or BSL-4.

Sample collection for CCHF diagnosis includes both ante-mortem and postmortem samples. Ante-mortem samples consist of blood samples, specifically serum or plasma. Postmortem samples involve the collection of tissue samples, including liver, spleen, bone marrow, kidney, lung, and brain.

During the early stages of illness, diagnosis is achieved by detecting the virus or its genome in blood or tissue samples.

When collecting samples, it is crucial to follow biosafety precautions. The samples should be accompanied by a detailed patient history form, which can be obtained from the testing laboratory. Before dispatching the samples, the outer surface of the sample container should be disinfected using a 1:100 dilution of bleach or a 5% Lysol solution.

SAMPLE TRANSPORTATION

For transportation, the samples should be safely packed in triple container packing and transported under cold chain conditions to the reference laboratory, with prior intimation. In situations where obtaining specialized containers is difficult, alternative methods can be used:

1. The case sheets should be filled with complete information and provided along with the samples in a separate case report form.
2. Blood samples (serum, plasma, or EDTA-treated blood) should be placed in screw cap plastic vials and properly labeled.
3. The vials containing the samples should be placed in high-quality plastic bags that are sealed by heat or tied with rubber bands to prevent leaks.
4. This plastic bag should then be placed in another sealed plastic container, which is further placed in a thermocol or vaccine carrier containing ice.
5. In cases where a plastic container is not available, a good quality of double plastic bags can be used as an alternative.
6. The case sheets containing complete information should be placed in a plastic bag or envelope and securely attached to the outer surface of the thermocol or vaccine container.
7. To ensure proper handling of the samples, the person responsible should wear gloves and a gown to avoid direct contact with the infectious material. After completing the packing of the samples, it is important to thoroughly wash hands with soap and water.
8. Before dispatching the container, the outer surfaces of the container should be disinfected. This can be done using a 1:100 dilution of bleach or a 5% Lysol solution to clean the container and minimize the risk of contamination.

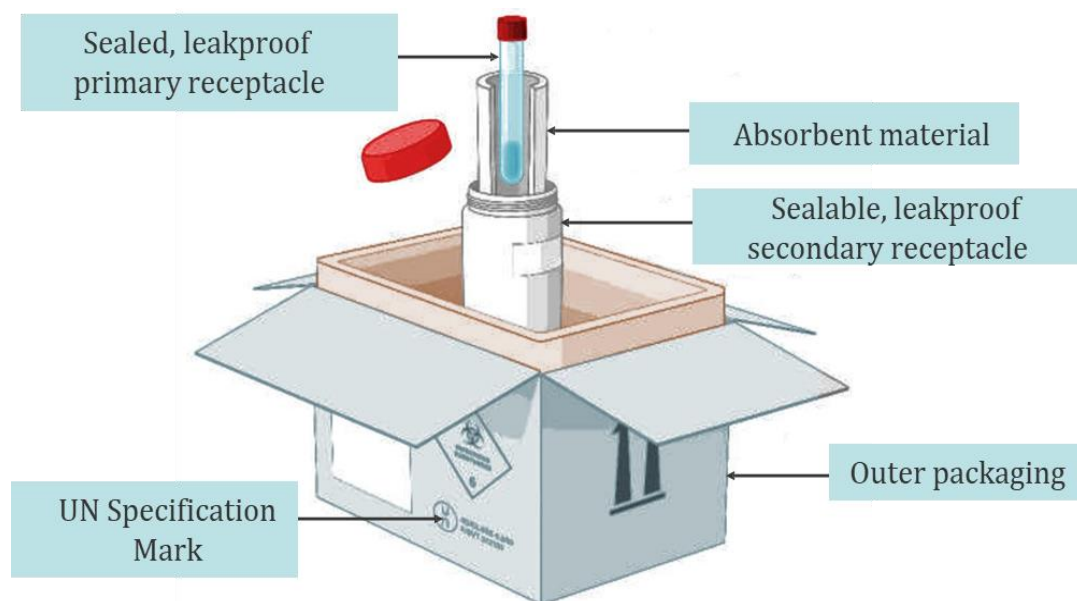


Fig 8: Triple layer packaging

(Image Source: Monkeypox Preparedness and response, OpenWHO.org)

SAMPLE STORAGE

The samples should be sent to the laboratory as soon as possible, preferably within 48 hours, and stored at a temperature between 4-8°C during transportation. If there is a delay beyond 48 hours, the specimens must be stored at a temperature of -70°C to maintain their integrity. It is important to avoid repeated freezing and thawing of the samples to prevent any potential degradation or loss of quality.

Sample Collection

Ante-mortem

- Blood sample: Whole Blood/Serum/Plasma, Urine, Saliva
- (CCHF is also detectable in nasal, conjunctival, rectal and vaginal swabs in more severe cases)

Postmortem

- Tissue sample:
 - (liver, spleen, bone marrow, kidney, Lung and brain)
- Bodily fluids including semen

Samples should be collected with all biosafety precautions including PPE and should be accompanied with detailed history of patient on the proforma which can be obtained from the testing laboratory.

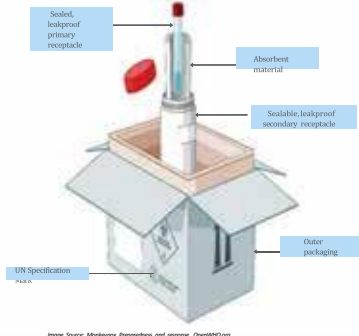
CCHF virus is classified as risk group 4 virus and hence the clinical samples should be handled in specially-equipped, high biosafety level laboratories (BSL 3 plus or 4)

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Notes

Triple packaging system



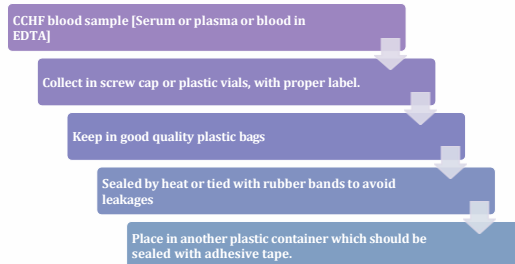
The packaging consists of three layers as follows -

- **Primary receptacle:** A labelled primary watertight, leak-proof receptacle containing the specimen. The receptacle is wrapped in enough absorbent material to absorb all fluid in case of breakage.
- **Secondary receptacle:** A second durable, watertight, leak-proof receptacle to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be used to cushion multiple primary receptacles.
- **Outer shipping package:** The secondary receptacle is placed in an outer shipping package which protects it and its content from outside influences such as physical damage and water while in transit

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Procedure of transportation (in absence of triple layer packaging)



Source: NCDC Manual on Zoonotic Diseases of Public Health Importance

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Transportation of the sample to the reference laboratory

- Always use a triple-layer packaging and transport within 48 hours of collection
- Maintain cold chain (using dry ice or at least with cooling gels).
- The original samples should be packed, labelled, and marked.
- Always include the filled out
 - clinical and epidemiological record



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Storage of Specimens

The samples, after collection, should be sent immediately to the laboratory for testing.

Keep serum of human cases refrigerated (2-8 °C) if it is to be processed (or sent to a reference laboratory) within 8 hours.

Keep frozen (-20 °C to -10 °C), if it is to be processed after one week. The sample can be preserved for extended periods



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NOTE TO FACILITATORS

This guide has been meticulously designed to enhance the understanding and expertise doctors, veterinarians, paramedical staff, and laboratory personnel in dealing with CCHF cases. Your role is crucial in ensuring the success of this training, so please follow these instructions carefully:

Familiarize Yourself with the Content

Thoroughly review all the materials provided in the CCHF training guide. This includes presentations, handouts, case studies and assessment tools.

Tailor the Training to Your Audience

Understand the professional backgrounds of your participants (doctors, veterinarians, paramedics, and lab personnel). Tailor your examples and discussions to make the training relevant to their specific roles.

Set Clear Objectives

Begin each session by clearly stating the objectives participants are expected to achieve by the end. This will give them a sense of direction and purpose throughout the training.

Create an Interactive Learning Environment

Encourage active participation and open discussions. Use real-world scenarios to prompt critical thinking and problem-solving.

Use Multimodal Techniques

Utilize a mix of teaching methods, such as presentations, group discussions and case-based learning. This will cater to different learning styles and keep participants engaged.

Encourage Questions

Welcome questions and create a safe environment for participants to seek clarifications. This fosters deeper understanding and engagement.

Provide Regular Feedback

Throughout the training, provide constructive feedback on participants' performance. This will help them identify areas for improvement and enhance their skills.

Summarize and Review

At the end of each module, summarize key points and takeaways. Conduct a brief review to reinforce learning before moving on to the next topic.

Assessment and Certification

Develop an assessment mechanism, such as quizzes, practical assessments, or case presentations. Issue certificates of completion to participants who meet the training requirements.

Adapt to Participants' Pace

Gauge the participants' pace of learning. Adjust the training speed, accordingly, ensuring that everyone can follow and grasp the content.

Facilitate Networking

Create opportunities for participants to interact and network with each other. This can lead to valuable knowledge exchange and collaboration.

Remember, your role as a trainer or facilitator is to guide participants through this comprehensive CCHF training with expertise, enthusiasm, and a dedication to enhancing their professional skills. Your efforts will contribute to building a more capable and knowledgeable medical workforce prepared to handle CCHF cases effectively.

Course Outline

It is imperative to underscore that the course outline harmonizes with the course schedule. Consequently, any modifications or adaptations made to the course schedule should be duly reflected in this course outline. This synergy between the schedule and the outline ensures consistency and alignment between training plans and their actual implementation.

Note: Make copies of the schedule, one for each participant and include in the training material bag.

TIME	TOPICS/ACTIVITIES	TRAINING/LEARNING METHODS	RESOURCES/MATERIALS
20 min	Welcome participants Facilitate introductions of participants Explore participants' expectations for the course	Open course with a word of welcome by organizers, lead trainers, etc. Facilitate the introductions of all participants and trainers. Explore participants' expectations for the course. Allow participants to freely explore their expectations. In the next session on review of the course objectives, address which expectations can be met and which cannot be met.	Prepare welcome sign, Name badges
20 min	Review course objectives and schedule. Review components of the training guide	Review the course goals and objectives; the course design and expected outcomes; Review the course schedule, including starting and ending times and times for breaks and lunch; Review the materials to be used in the course and ensure that participants understand the use of course materials.	Copies of course schedule, one for each participant from Facilitators' Guide (FG). Full set of the training guide: Facilitator's Guide Questionnaire
20 min	Assess participants' pre-course knowledge	Distribute the Pre-course Knowledge Assessment sheet to each participant. Ask them to answer each question. Allow 15 minutes for assessment. Immediately review the correct responses—Have participants grade the papers while the trainer reviews the correct answers with them and collect the papers after reviewing all the answers.	Pre-Training Quiz Sheet for each participant

TIME	TOPICS/ACTIVITIES	TRAINING/LEARNING METHODS	RESOURCES/MATERIALS
4-5 hours	Presentation/ Discussion	Use the PowerPoint slides to present information	Power Point slides on the sessions planned as per agenda
20 min	Assess participants' post training knowledge	Distribute the Post Training Knowledge Assessment sheet to each participant. Ask them to answer each question. Allow 15 minutes for the Post Training Knowledge Assessment.	Copies of Post Training Knowledge Assessment Sheets (one for each participant)
15 min	Course Evaluation	Ask questions of the participants and engage them in the presentation of the information.	
15 min	Closing	Closing remarks by training organizers. Distribute certificates to participants.	Certificate for each participant

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PRE-TEST/ POST TEST

Trainee Name:

Date: _____

Designation:

Test taken before the training (yes/no):

Test taken after the training (yes/no):

Instructions for the trainee:

- The test quiz carries 25 questions.
 - Attempt all the questions.
 - Put a tick mark on the correct option or fill the blanks with True/ False
 - Please check whether all questions are answered before submitting.
1. Which region(s) is the Crimean-Congo hemorrhagic fever (CCHF) widely distributed in?
 - A. Africa
 - B. Middle East
 - C. Southeast Asia
 - D. All of the above
 2. In which year was the acute febrile illness with symptoms like shock and bleeding first reported in the Crimean Peninsula?
 - A. 1944
 - B. 1956
 - C. 1969
 - D. 2018
 3. Which event led to the disease being named Crimean-Congo Hemorrhagic fever?
 - A. The first outbreak in the Crimean Peninsula
 - B. The discovery of an identical agent in Belgian Congo
 - C. The identification of acute febrile illness in Soviet troops
 - D. The endemic status of Iran, Iraq, Pakistan, and Turkey
 4. Which family does the Crimean-Congo hemorrhagic fever belong to?
 - A. Flaviviridae
 - B. Bunyaviridae
 - C. Retroviridae
 - D. Orthomyxoviridae

5. Which factor(s) contribute to increased human contact with domestic and wild animals, potentially affecting the transmission of Crimean-Congo hemorrhagic fever (CCHF)?
 - A. Deforestation and agricultural activity
 - B. Migratory bird population
 - C. Changing human-animal interaction
 - D. All of the above
6. What is the primary mode of transmission of Crimean-Congo hemorrhagic fever (CCHF) from ticks to humans?
 - A. Direct contact with infected tick saliva
 - B. Ingestion of infected tick larvae
 - C. Tick bite or handling adult infected ticks
 - D. Inhalation of airborne tick particles
7. How can humans primarily become infected with Crimean-Congo hemorrhagic fever (CCHF) in healthcare settings?
 - A. Contact with contaminated medical equipment
 - B. Inhalation of aerosols containing infected blood
 - C. Direct contact with infected patients' blood or body fluids
 - D. Ingestion of contaminated food or water
8. Which of the following clinical manifestations is a hallmark feature of Crimean-Congo hemorrhagic fever (CCHF) in humans?
 - A. Skin rash and itching
 - B. Muscle weakness and fatigue
 - C. Jaundice and liver dysfunction
 - D. Rapid onset of high fever
9. Which body system is primarily affected by Crimean-Congo hemorrhagic fever (CCHF) in humans?
 - A. Respiratory system
 - B. Digestive system
 - C. Nervous system
 - D. Hematological system

10. Which of the following diseases should be considered in the differential diagnosis of Crimean- Congo hemorrhagic fever (CCHF) due to similar clinical manifestations?
- A. Dengue fever
 - B. Leptospirosis
 - C. Malaria
 - D. All of the above
11. Which of the following criteria is required for a confirmed case of Crimean-Congo hemorrhagic fever (CCHF)?
- A. Abrupt onset of high fever and severe headache
 - B. Thrombocytopenia and two or more hemorrhagic manifestations
 - C. History of tick bite or contact with infected animal fluids, and specific laboratory confirmation
 - D. Detection of specific IgM antibodies by ELISA or IFA
12. Which of the following samples is commonly used for the ante-mortem diagnosis of Crimean- Congo hemorrhagic fever (CCHF)?
- A. Whole Blood
 - B. Saliva
 - C. Urine
 - D. All of the above
13. At which biosafety level should clinical samples of Crimean-Congo hemorrhagic fever (CCHF) be handled?
- A. BSL-1
 - B. BSL-2
 - C. BSL-3
 - D. BSL-4
14. Which of the following measures is recommended for the transportation of clinical samples of Crimean-Congo hemorrhagic fever (CCHF) to the reference laboratory?
- A. Single-layer packaging within 72 hours of collection
 - B. Transporting at room temperature
 - C. Using cooling gels for cold chain maintenance
 - D. Excluding the clinical and epidemiological record

15. Which of the following institutions are mentioned as diagnostic laboratories where samples for Crimean-Congo hemorrhagic fever (CCHF) can be sent?
- A. National Centre for Disease Control (NCDC), Delhi
 - B. National Institute of Virology (NIV), Pune
 - C. National Institute of High-Security Animal Diseases (Formerly HSADL), Bhopal
 - D. All of the above
16. Which type of enzyme-linked immunoassay (ELISA) is commonly used to detect IgM antibodies in livestock such as sheep, goat, and cattle for Crimean-Congo hemorrhagic fever (CCHF)?
- A. IgM-capture ELISA
 - B. IgG-sandwich ELISA
 - C. Competition ELIS
 - D. Indirect ELISA
17. Which type of antibodies remains detectable for up to four months after Crimean-Congo hemorrhagic fever (CCHF) infection?
- A. IgM antibodies
 - B. IgG antibodies
 - C. IgA antibodies
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18. Which laboratory testing method is considered the test of choice for detecting Crimean-Congo hemorrhagic fever (CCHF) infection within the first 10 to 12 days after symptom onset?
- A. Enzyme-Linked Immunosorbent Assay (ELISA)
 - B. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)
 - C. Immunofluorescence Assay (IFA)
 - D. Serological testing for antibody detection
19. Which of the following cell lines is commonly used for viral culture to isolate Crimean-Congo hemorrhagic fever (CCHF) ?
- A. HEK-293
 - B. BHK-21
 - C. CHO
 - D. Jurkat

20. Which antiviral agent is recommended for the treatment of Crimean-Congo hemorrhagic fever (CCHF)?
- A. Ribavirin
 - B. Oseltamivir
 - C. Acyclovir
 - D. Remdesivir
21. Which group of patients is ribavirin contraindicated for in the treatment of Crimean-Congo hemorrhagic fever (CCHF)?
- A. Elderly patients
 - B. Pediatric patients
 - C. Pregnant women
 - D. Immunocompromised patients
22. Which of the following measures is recommended for the prevention of CCHF transmission to humans?
- A. Use of personal protective equipment (PPE) during contact with animals and their tissues/fluids
 - B. Implementation of tick control measures
 - C. Avoidance of consumption of raw or undercooked animal products
 - D. All of the above
23. What is an effective measure to reduce the risk of CCHF infection to people?
- A. Vaccination against CCHF
 - B. Strict quarantine measures for infected individuals
 - C. Promoting awareness about tick-bite prevention
 - D. Restricting travel to endemic regions
24. Which initiative was jointly undertaken by the Indian Council of Medical Research (ICMR) and the Indian Council of Agricultural Research (ICAR) to conduct a survey related to Crimean- Congo hemorrhagic fever (CCHF)?
- A. Tick-borne Disease Surveillance Program
 - B. National Tick Control Program
 - C. CCHF Prevention and Control Initiative
 - D. CCHF IgG Antibody Serosurvey

25. What is an important measure in the management of CCHF outbreaks to prevent nosocomial infections?
- A. Early diagnosis and isolation of suspected or confirmed cases
 - B. Implementation of vector control measures
 - C. Vaccination of healthcare workers
 - D. Public awareness campaigns

ANSWER KEY

1. Which region(s) is the Crimean-Congo hemorrhagic fever (CCHF) widely distributed in?
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