MINISTRY OF HEALTH
AND SANITATION
THE REPUBLIC OF SIERRA LEONE

National Guideline for Healthcare for Ebola Virus Disease Survivors

THE PRESIDENT'S RECOVERY PRIORITIES
Comprehensive Program for Ebola Survivors
UKaid
USAID

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Acknowledgements

This clinical guideline is the product of a collaboration between personnel of the Ministry of Health and Sanitation (MOHS), Ministry of Social Welfare, Gender and Children's Affairs, World Health Organization, United States Centers for Disease Control and Prevention, United Nations Children's Fund, Partners in Health, International Medical Corps, Medicos Del Mundo, GOAL, Save the Children, World Hope International, and JSI Research & Training Institute, Inc., with funding provided by the United Kingdom Department for International Development and United States Agency for International Development.

The team is particularly grateful to the members and executives of the Sierra Leone Association of Ebola Survivors whose help on this guideline was of tremendous value. This work is a testament to all the men, women and children who survived Ebola outbreak that shaped the principles outlined in this guideline by telling their stories. Your country thanks you!

We would be remiss if we didn't mention the names of Drs. Ian Crozier and Steven Yeh from the Emory team, Dr. Florence Baingana, Dr. Mathew Vandy, Dr. John Mattia, Dr. Peter George, Dr. Faiqa Ebrahim, Dr. Mauricio Calderon, Dr. Charles Douglas, Sarah Cundy, Dr. Karim Kabineh, Else Kirk, Katie Bolbach, Jennifer Gottesfeld, Dr. Sorie Conteh, Dr. Charles Alpren, Carrie Jo Cain, Kings Sierra Leone Partnership, Welbodi Partnership, Dr. Marta Lado, Dr. Juan Cruz Diez Beltran, Dr. Helen Thompson, Dr. Anna Walder, and Rebecca Best, some of the many people who contributed to the drafting and validation of the guidelines.

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Foreword

The Ebola virus disease (EVD) outbreak of 2014-2016 left the largest cohort of survivors the world has ever known in the three worst affected countries, with Sierra Leone having the largest number of EVD Survivors.

As part of the Presidential Mandate of His Excellency the President Dr. Ernest Bai Koroma, to provide free healthcare services to survivors and to cater for their livelihoods, the Ministry of Health and Sanitation (MoHS) and the Ministry of Social Welfare Gender and Children's Affair's established a national programme for EVD survivors known as the Comprehensive Program for Ebola Survivors supported by the World Health Organization (WHO), UKAID through a partner-led consortium and USAID through John Snow Incorporated.

In a bid to strengthen and build the capacity of health-workers to be able to provide the basic and required healthcare for EVD survivors in the country, the MoHS in collaboration with the WHO country office brought together a multi-disciplinary team to develop clinical guidelines that will be used by health-workers for the assessment and treatment EVD survivors across Sierra Leone. The clinical guidelines have been developed in compliance with the WHO interim guidelines for Ebola survivors, adapted to the Sierra Leonean context by medical practitioners working with EVD survivors in-country. This effort of the MoHS and its partners is geared towards ensuring that survivors are well taken care of throughout the country by all stakeholders including private practitioners.

The Ministry wish to inform all that the treatment regimen in the guidelines are based on current scientific data and as new evidence becomes apparent the clinical guidelines will be revised to reflect up-to-date recommendations and policy.

Dr. Brima Kargbo (GOOR)
Chief Medical Officer

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Acronyms

CPES	Comprehensive Programme for EVD Survivors
CSF	Cerebrospinal Fluid
DFID	United Kingdom Department for International Development
EVD	Ebola Virus Disease
ESCC	Ebola Survivors Care Consortium
ETC	Ebola Treatment Center
ETU	Ebola Treatment Unit
EVD	Ebola Virus Disease
GERD	Gastro-Esophageal Reflux Disease
IBS	Irritable Bowel Syndrome
IgG – IgM	Immunoglobulin G - Immunoglobulin M
JSI	JSI Research & Training Institute, Inc.
IMC	International Medical Corps
IPC	Infection Prevention and Control
KSLP	King's Sierra Leone Partnership
MDM	Medicos Del Mundo
MOHS	Ministry of Health and Sanitation
MOSWGCA	Ministry of Social Welfare Gender and Children Affairs
MOC	Model of Care
NSAID	Non-Steroidal Anti-Inflammatory Drug
PHU	Peripheral Health Unit
PID	Pelvic Inflammatory Disease
PIH	Partners in Health
PIU	Program Implementation Unit
PPE	Personal Protective Equipment
PTSD	Post-Traumatic Stress Disorder
PUD	Peptic Ulcer Disease

RDT	Rapid Diagnostic Test
RT-PCR	Reverse Transcriptase-Polymerase Chain Reaction
SC	Save the Children
SL	Sierra Leone
STI	Sexually Transmitted Infection
STWG	Survivor Technical Working Group
TB	Tuberculosis
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
UTI	Urinary Tract Infection
WHI	World Hope International
WHO	World Health Organization


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Paula Nersesian

1. Introduction

Background

His Excellency President Ernest Bai Koroma has made a strong commitment to ensuring the well-being of all Ebola virus disease (EVD) survivors. The Ministry of Health and Sanitation (MOHS) and the Ministry of Social Welfare, Gender and Children's Affairs (MSWGCA) have accepted responsibility for EVD survivors and meeting their needs in a comprehensive manner. These ministries have been working with the survivor technical working group (STWG) and steering committee to define the Comprehensive Program for EVD Survivors (CPES) as a key component of the national EVD Survivor Policy in Sierra Leone. CPES has the following core objectives:

1. Support EVD survivors in the recovery of functional capacity through effective delivery of health care and psychosocial services.[1]

2. Support recovery of survivor livelihoods.

3. Support survivor re-integration into communities.

4. Address the risk of resurgence associated with possible extended EBO viral persistence in survivors.

The CPES program implementation unit (PIU) is tasked with executing the CPES objectives and will be held responsible for the operational success of CPES. The PIU is overseen by program director DCMO Dr. Sarian Kamara, and is led by two program managers, one each from the Ministry of Health and Sanitation and Ministry of Social Welfare, Gender and Childrens´ Affairs, who oversee day-to-day operations in their respective program areas and advisor the Ministries on matters of survivor health and social welfare respectively. Additional PIU staff provide administrative and operational support to program managers to monitor program rollout and implementation. The PIU is responsible for the regular convening of the STWG, which is meant to serve as a regular information sharing and discussion forum for all stakeholders involved in survivor care in Sierra Leone. TWG sub-groups are responsible for regular review of implementation progress and technical challenges arising in their respective area. Each sub-group should meet once per month, and will have two co-leads, ideally one from government and one from an implementing or technical partner. Proposed sub-groups include:

1. Community-based case management: review and advise survivor advocates, community-based case management, social mobilization and any other community-based components of CPES program. It will collaborate with MOHS Primary Care Directorate in mapping approach to longer-term integration of survivor services into national CHW program.

2. Facility-based survivor care: advise on primary, secondary, and tertiary care provided to survivors in government health facilities. This will include regular review of evolving specific medical complaints and clinical needs of survivors, consideration and advising on new clinical

services, including specialty care initiatives, for survivors.

3. Referrals: track and review implementation of referral systems from Peripheral Health Unit (PHU) to district hospital to referral facility, from initiation of care through discharge and counter-referral. Sub-group will track the activities of the referral coordinators and provide guidance on coverage for other free health care target populations over time.

4. Supply chain: track and review implementation of supply chain support components of CPES. Group will offer program realignments and adjustments advice based on learnings from early implementation.

5. Monitoring and evaluation (M&E): support and advise PIU M&E coordinator on the CPES log frame, M&E framework, reporting tools, and execution.

6. Risk mitigation: review implementation progress, advise planning, and overcome challenges to risk-mitigation programs and national semen testing program [including Project Shield activities].

The Department for International Development (DFID) is supporting CPES implementation by funding the Ebola Survivor Care Consortium (ESCC). ESCC comprises eight nongovernmental partners: GOAL, International Medical Corps (IMC), King's Sierra Leone Partnership (KSLP), Medicos Del Mundo (MDM), Partners in Health (PIH), Save the Children (SC), Welbodi Partnership, and World Hope International (WHI). DFID/ESCC partners are collaborating with other stakeholders to support the Government of Sierra Leone in the delivery of services and improved outcomes for Ebola survivors across Sierra Leone. ESCC has a coordinating unit [CU], led and staffed by GOAL, who as the lead agency is responsible for fiscal and compliance oversight of grant-funded partner activities.

The United States Agency for International Development (USAID) is supporting CPES implementation through the Advancing Partners & Communities project, led by JSI Research &Training Institute, Inc. (JSI). JSI provides training, technical assistance, and other operational support for CPES implementation by mobilizing a range of local and international organizations, including the Sierra Leone Association for Ebola Survivors.

Target audience

The primary audience for this clinical guidance includes health care professionals providing health care to people who have recovered from EVD. Specifically:

- Clinical staff from MOHS facilities, both primary health care facilities and hospitals.
- Community health nurses and other community health workers.
- Clinicians and program managers from CPES implementing partners.

Some parts of this guidance could be used by families and community members who support and care for EVD survivors, as well as planners of health care services and policy makers. However, the contents of the tool might be too technical and the vocabulary too specialized, which might confuse

Further Reading

"...Long-term sequelae persist for more than 2 years after Ebola virus disease. Definition of health consequences related to Ebola virus disease could improve patient care for survivors and contribute to understanding of disease pathogenesis..."

Clark DV, Kibuuka H, Millard M, Wakabi S, Lukwago L, Taylor A, et al. Long-term sequelae after Ebola virus disease in Bundibugyo, Uganda: a retrospective cohort study. The Lancet Infectious Diseases. 2015;Apr 21:pii: S1473-3099(15)70152-0

readers who do not have a formal clinical background. We recommend that clinicians photocopy and share with indirect beneficiaries only specific sections as appropriate and in conjunction with background information and context.

Guidance development methods

These guidelines have been developed by MOHS Sierra Leone Ministry of Defence Military 34 hospital, in collaboration with PIH, KSLP, GOAL, Medecins Sans Frontieres Belgium, and guidance of the WHO Geneva. It benefited from input and feedback from stakeholders such as Ministries of Health in Guinea, Liberia, and Sierra Leone, members of the UN Global Ebola Response Coalition, WHO country offices, research and non-governmental health organizations with recognized expertise and interest in the care of EVD survivors, including the U.S. Centers for Disease Control and Prevention (CDC), the U.S. National Institutes of Health, IMC, MDM, and Save the Children.

Due to the severe limitations of the existing scientific evidence base on clinical care for EVD survivors and the urgent need for guidance on this topic, the recommendations in this document have been developed by consensus of stakeholders consulted. Although this severely limits the scientific robustness of the guidance, the document represents best available practice and will be reviewed as new evidence emerges.

The unprecedented scale of the EVD outbreak that began in West Africa in 2013 has resulted in many more survivors than any other EVD outbreak[2], and thus more opportunities to vastly enhance clinical observations and understanding EVD survivor health challenges. New findings also come from clinical observations made on the 27 patients with EVD seen in high-resource settings in Spain, Italy, UK, Germany, Switzerland, and the U.S., where available medical technology allowed more detailed and comprehensive investigation. New presentations and complications of EVD are discovered on almost a weekly basis and new findings continue to be anticipated as capacity to care for EVD survivors in West Africa grows.

WHO will follow up on the research developments in the area of EVD and health outcomes for survivors, particularly those related to areas where new recommendations or a change in this guidance may be warranted.

Updating the guidance

This guidance will be updated six months after publication, unless significant new evidence that necessitates earlier revision emerges. Comments or suggestions regarding additional issues for inclusion in the updated guidance are welcomed.

An EVD survivor is an individual who has been lab-confirmed RT-PCR-positive, treated at an Ebola treatment center, and plasma tested PCR-negative and discharged from that center.

Definition of an EVD survivor

The following is the definition of an EVD survivor, as adopted by the SL STWG on 6th July 2015 with addendums and revisions on the 26th of November 2015 and February 18th 2016.

Addendums:

- **Undiagnosed EVD survivors:** Individuals who contracted EVD infec-

tion, suffered acute severe Ebola, but went through disease without being diagnosed or treated at an Ebola treatment center (ETC), and was later confirmed to be Ebola antibody positive (IgG – IgM) by serological testing and has not been vaccinated against Ebola virus.

- **Survivors of subclinical Ebola infection:** Individuals who do not refer a history of acute severe EVD, in spite of typically having had a high risk of exposure to the EBV (for example: inhabiting a "hot spot" or being a "high-risk contact") and who later are found to be IgG – IgM by serological testing and have not been vaccinated against Ebola virus.

These definitions identify the different types of persons who might present requesting health services included by the Government of SL within CPES.

The definition may be changed during an epidemic to correspond to the local situation. In most cases, government or laboratory-issued EVD survivor certificates have been issued and should serve as the basis for verification of survivor status. However, cross-checking with ETU records and other databases and, in some cases, antibody testing may be required.

Principles of the model of care (MOC)

CPES uses a pro-active model of care through which survivors are contacted on a regular basis to quickly identify existing and new health conditions. This is recommended for any future outbreak, to minimize the impact of sequelae from early stages, as well as to address aspects of psychosocial care that require attention. To achieve this, CPES MOC relies on:

- Active follow up of EVD survivor by survivor advocates.
- Continuous training for health care providers involved in survivor care.
- Prevention of recrudescence.
- Early identification of recrudescence.
- Reducing risk of transmission via contact with semen or other infective bodily fluids.

Principle of integrated care

An intensive, integrated program is necessary to meet the medical and psychosocial needs of EVD survivors and to reduce the risk of virus reintroduction. Medical services for EVD survivors should be integrated into existing routine health services and facilities. However, in areas where the necessary services do not exist or are inaccessible to EVD survivors, establishment of EVD survivor-specific services may be necessary. Regardless of the short-term approach to providing urgent care to EVD survivors, the medium- and long-term goals must be to strengthen health systems for all persons and for all health problems.

2. Planning follow-up of the EVD survivor

Prior to discharge from the ETU

In times of active EVD cases:

When an EVD patient's condition has stabilized but prior to being discharged from the ETU, s/he should receive education and counseling on the possible sequelae[3] and psychosocial challenges likely to be seen during convalescence. With the patient's permission, include a session/consultation with his/her close family members, explaining in simple terms the common sequelae and what is known about how Ebola virus can and cannot be transmitted during convalescence (see below under Monitoring for persistent Ebola virus infection in survivors: Guidelines for testing and counseling). Relatives should be informed of measures to avoid virus transmission (see below under Infection prevention and control considerations in EVD survivors). EVD survivors should be given a follow-up appointment to see a care provider within two weeks after discharge and specific instructions about who to contact if they encounter health problems or have questions.

Discuss issues such as confidentiality, avoiding stigmatization, and cost of follow-up care. In cases when significant mental health problems are noted before discharge or anticipated afterward, it may be appropriate to refer patients directly to a mental health care provider. At discharge, EVD survivors should be provided with documents containing their unique patient ID, name, age, symptoms at presentation, and any convalescent symptoms at discharge, a brief record of their test results and treatment in the ETU, and their government or laboratory-issued EVD survivor certificate. This will serve as 'transfer of care' information for outpatient management. Instruct survivors to bring these documents, as well as documents recording past vaccination, to all future clinic or hospital visits.

Offer sexual health education and counseling to all EVD survivors, both male and female, at discharge and at follow-up visits. The potential for Ebola virus persistence in the semen and the measures to prevent transmission should be explained to male EVD survivors as well as their partners (see below under *Semen testing and counseling for male EVD survivors*). Counsel pregnant survivors on the risks of Ebola virus-associated maternal and fetal complications as well as virus persistence and transmission (see below under *Considerations for special populations: pregnant women*).

Survivors of the 2014/15 outbreak did not receive this immediate care, but with the introduction of CPES in 2016 they will be followed up, receive psychosocial support, and referral to health and social services as required.

First visit after ETU discharge

The following should be performed at the first follow-up visit after discharge from the ETU (see detailed guidance by type of possible sequelae below).

- General medical history and physical examination, including vital signs (temperature, blood pressure, heart rate, respiratory rate), and nutritional evaluation
- Musculoskeletal evaluation

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- Ocular evaluation
- Auditory evaluation
- Abdominal evaluation
- Neurological evaluation
- Mental health evaluation
- Sexual health evaluation
- Consultation with social worker to address:
  - Stigma
  - Economic status and employment
  - Shelter and food security
  - Dependents
  - Social support (family, friends, religious community)
  - Potential substance misuse or dependency (alcohol, marijuana, cocaine, heroin, tobacco)
  - Identification of vulnerable individuals (children, disability, domestic abuse, etc.) for follow up/notification
- Routine laboratory tests:
  - Complete blood count
  - Creatinine
- Optional tests as indicated:
  - Ebola reverse transcriptase-polymerase chain reaction (RT-PCR) or IgG or IgM antibody
  - Hepatic transaminases (alanine aminotransferase and aspartate aminotransferase) and amylase
  - Thyroid function
  - Erythrocyte sedimentation rate or C reactive protein
  - Pregnancy
  - Malaria rapid diagnostic test (RDT)
  - Stool examination for ova, cysts, and parasites
  - Urinalysis (hematuria, protein, casts, and color of urine)
  - Syphilis (according to national guidelines)
  - HIV (according to national guidelines)

Note: Due to anecdotal reports of EVD recrudescence in HIV-positive survivors, some care providers recommend routine HIV testing with pre- and post-test counseling of all EVD survivors

In regions with a prevalence of onchocerca volvulus microfilaria infection >5%, ensure that patients are linked with the neglected tropical disease eradication program for mass drug administration of ivermectin

- All clinic visits made by EVD survivors and other relevant health information should be carefully charted and the records securely stored. Data collection forms specifically designed for follow-up of EVD survivors are available at: https://www.iddo.org/tools-and-resources

Subsequent visits

Because some EVD sequelae may appear weeks or months after resolution of acute disease and persist for years, regular follow-up of survivors is recommended for at least one year, regardless of presence or absence of symptoms at discharge or initial outpatient evaluation.

One suggested schedule for follow-up evaluation and care is as follows:

- Discharge from ETU
- Initial outpatient evaluation within 2 weeks, then
- Monthly follow-up for 6 months, then
- Follow-up every 3 months to complete one year
- Continued follow-up as needed and agreed upon by patient and care provider

The patient and provider may wish to adjust this schedule based on the patient's particular condition and needs. Detailed evaluation similar to that described for the first visit post-ETU discharge should be performed at a minimum every three months for the first year. For males, follow-up visits should be coordinated with visits for semen testing (see below under *Semen testing and counseling for male EVD survivors*).

Further Reading

Background: The limited data available for long-term Ebola virus disease health outcomes suggest that sequelae persist for longer than 1 year after infection. The magnitude of the present outbreak in west Africa necessitates a more complete understanding of the health effects and future medical needs of these patients. Methods: We invited adult survivors of the 2007 Bundibugyo Ebola virus outbreak in Uganda and their contacts to take part in an observational study roughly 29 months after the outbreak. We collected information about health status, functional limitations, and demographics. We collected blood samples for clinical chemistry, haematology, and filovirus antibodies using ELISA. Analyses were restricted to probable and confirmed survivors and their seronegative contacts. Findings: We recruited 70 survivors of the 2007 Bundibugyo Ebola virus and 223 contacts. We did analyses for 49 probable and confirmed survivors and 157 seronegative contacts. Survivors of the Bundibugyo Ebola virus were at significantly increased risk of ocular deficits (retro-orbital pain and blurred vision), hearing loss, difficulty swallowing, difficulty sleeping, arthralgias, and various constitutional symptoms controlling for age and sex. Chronic health problems and limitations due to memory loss or confusion were also reported more frequently by survivors of Bundibugyo Ebola virus. Interpretation: Long-term sequelae persist for more than 2 years after Ebola virus disease. Definition of health consequences related to Ebola virus disease could improve patient care for survivors and contribute to understanding of disease pathogenesis. Clark DV, Kibuuka H, Millard M, Wakabi S, Lukwago L, Taylor A, et al. Long-term sequelae after Ebola virus disease in Bundibugyo, Uganda: a retrospective cohort study. The Lancet Infectious Diseases. 2015;Apr 21:pii: S1473-3099(15)70152-0. Accessible at: http://www.sciencedirect.com/science/article/pii/S1473309915701520

Kendra Helmer/USAID

3. Common sequelae of EVD and recommended evaluation and clinical management

Musculoskeletal

Musculoskeletal pain, especially arthralgia (joint pain or ache without swelling or evidence of an effusion on examination), is one of the most commonly reported sequelae, noted in 50–75% of survivors.[4, 5, 6] Bwaka et al described this symptom in 7 of 19 survivors they followed for two months during an EVD outbreak in Democratic Republic of Congo in 1995.[7] A study conducted on 81 survivors from Kenema showed that all experienced health complications—arthralgia being among the most common—following recovery. A similar study conducted among 105 EVD survivors post-discharge from an ETC in Guinea concluded that arthralgia/myalgia is frequently reported, with 86.7% of participants experiencing joint pain, 26.7% muscle pain, and 45.7% back pain.[8]

The arthralgia is generally symmetrical and polyarticular, usually bilaterally distributed and worse in the morning and after exercise.[9] Large joints are the most frequently affected, although any joint may be involved. Periarticular tenosynovitis (enthesitis) frequently affects the shoulders and hips and is consistent with a spondyloarthritis, especially when there is concomitant inflammatory eye disease (see below). Physical examination does not typically reveal abnormalities, although signs of inflammatory arthritis with swelling and tenderness are occasionally seen. Costochondritis (chest or rib pain) is also commonly noted.

Guidelines for clinical evaluation

- Be sure to distinguish between non-inflammatory arthralgia (joint pain without other obvious abnormalities on physical exam) and inflammatory arthritis (joint pain with point tenderness, erythema, warmth, swelling, effusion, and/or limited range of motion).
- Radiographs are usually not indicated unless new deformities are noted.

Differential diagnosis of arthralgia/tenosynovitis

- Degenerative joint disease, autoimmune disease (such as rheumatoid arthritis or systemic lupus erythematosus).

Differential diagnosis of muscle pain

- Polymyositis, dermatomyositis, inclusion body myositis, rabdomyolysis.

Differential diagnosis of arthritis

- Septic joint (bacterial, such as staphylococci or gonococci, or TB), gout, pseudo-gout.

Treatment of arthralgia/ tenosynovitis and muscle pain

- Warm compresses
- Exercise can be beneficial and should be prescribed with caution on a case-by-case basis. Check Ian's tool (gentle exercise focusing on ROM and flexibility).
- Address possible psychosocial issues that may be contributing
- First-line therapy: paracetamol
  - Adults: 1 gram orally up to 3 times daily (Note: It is recommended to limit paracetamol to 3 grams daily due to the possibility that EVD survivors incurred liver damage during their acute disease)
  - Children: 15 mg/kg orally up to 3 times daily
- Second-line therapy (if inadequate response to paracetamol after 7–10 days): non-steroidal anti-inflammatory drugs (NSAIDs)
  - Adults: Ibuprofen 200–400 mg orally up to 3 times daily
  - Other acceptable NSAID regimens include diclofenac 50 mg orally 2 or 3 times daily or naproxen 250–500 mg orally twice daily

- Once-daily NSAIDs such as meloxicam, piroxicam, celecoxib, and etodolac XL may also be substituted if available, although there is no evidence that they have greater efficacy than ibuprofen

- Indomethacin should generally be avoided given the higher propensity for gastric complications

- Children: Ibuprofen 10 mg/kg orally up to 3 times daily

Considerations:

- For severe and acute arthralgia an initial treatment with a parenteral drug could be beneficial before switching to an oral drug

- NSAIDs may cause stomach upset and gastrointestinal bleeding and thus should be taken with food

- If patient > 60 years old and/or has a history of peptic ulcer disease (PUD) or gastro-esophageal reflux disease (GERD), consider prescribing an H2-blocker (e.g., ranitidine 150 mg orally twice daily) or a proton-pump inhibitor (e.g., omeprazole 20 mg orally daily for adults and as below for children):

  - <10 Kg: 1-2mg/Kg orally once a day

  - 10-20 Kg: 10mg orally once a day

  - >20 Kg: 20mg orally once a day

- If patient ≥ 40 years old and/or hypertensive (BP > 140/90), check blood, creatinine (also if NSAIDs given for more than 2 weeks) and potassium before starting NSAIDs and reduce dose if evidence of renal insufficiency. In such cases, consider relying on paracetamol if possible.

Treatment of arthritis

- Arthritis without systemic illness (i.e., no fever or malaise): Warm or cold compresses, optional exercise, and NSAID therapy as described above

- If significant symptoms persist after 7–10 days of NSAID treatment and no other treatable cause is identified, stop NSAIDs and consider corticosteroids for adults and methotrexate for children

  Dosing:

  - **Adults:** Prednisone 20 mg orally daily for 7 days, reducing dose progressively before stopping: 10 mg during 3 days, later 5 mg during 3 days and suspend

  - **Children:** Refer to a specialist to consider treatment with methotrexate

Considerations for use of corticosteroids (adults)

- Provide education about potential adverse effects, including mood changes, weight gain, hyperglycemia, high blood pressure, and sleep disturbances

- Consider and check for other underlying conditions and infections that could be exacerbated or reactivate with systemic corticosteroids, including diabetes, TB, and HIV. Newly diagnosed HIV patients should be started on antiretroviral treatment concomitantly with initiation of oral steroids. More details can be found at: www.who.int/hiv/topics/treatment

- Since corticosteroid use can result in overwhelming infection with the helminth Strongyloides stercoralis, before starting prednisone empirically treat possible underlying S. stercoralis infection with one dose of ivermectin 200 micrograms/Kg orally, taken with water on an empty stomach. Note that ivermectin is considered contra-indicated in pregnant and lactating women

- Ask women of child bearing age about pregnancy, last menstrual period, and lactation status and, if in doubt, conduct a pregnancy test. Corticosteroid use in pregnant women is associated with an increased risk of birth defects, such as cleft palate, in the newborn[9, 10]

- If the patient has a history of PUD or GERD, consider prescribing an H2-blocker (e.g., ranitidine 150 mg orally twice daily) or a proton-pump inhibitor (e.g., omeprazole 20 mg orally daily) for the duration of the steroid treatment

Follow patient after one week to **monitor response to treatment and for adverse effects** from oral corticosteroids, including:

- Ocular side effects, such as worsening vision, increased intraocular pressure and cataract development

- Hyperglycemia, with urine or blood glucose monitoring as necessary

Note that any effect of corticosteroid use on possible reactivation of Ebola virus persisting in immunologically privileged sites is unknown (see below under *Relapse due to persistent virus and evaluation of new onset fever*).

Indications for referral to specialist

- Recurrent or persistent arthralgia that significantly impedes daily activities and quality of life and is refractory to at least three weeks of NSAID therapy and one course of prednisone therapy
- Spondyloarthropathy (i.e., spine and sacroiliac joint involvement)
- Referral to a rehabilitation specialist may be required for survivors with prolonged musculoskeletal pain and fatigue. Referrals could be made to special pain control centers
- Arthritis with systemic illness or if suspicion of septic joint requiring aspiration joint fluid, laboratory testing of aspirate/sample and possible intravenous antibiotics

Further Reading

"...A cohort of convalescent Ebola hemorrhagic fever (EHF) patients and their household contacts (HHCs) were studied prospectively to determine if convalescent body fluids contain Ebola virus and if secondary transmission occurs during convalescence. Twenty-nine EHF convalescents and 152 HHCs were monitored for up to 21 months. Blood specimens were obtained and symptom information was collected from convalescents and their HHCs; other body fluid specimens were also obtained from convalescents. Arthralgias and myalgia were reported significantly more often by convalescents than HHCs. Evidence of Ebola virus was detected by reverse transcription–polymerase chain reaction in semen specimens up to 91 days after disease onset; however, these and all other non-blood body fluids tested negative by virus isolation. Among 81 initially antibody negative HHCs, none became antibody positive. Blood specimens of 5 HHCs not identified as EHF patients were initially antibody positive. No direct evidence of convalescent-to-HHC transmission of EHF was found, although the semen of convalescents may be infectious. The existence of initially antibody-positive HHCs suggests that mild cases of Ebola virus infection occurred and that the full extent of the EHF epidemic was probably underestimated...". Rowe AK, Bertolli J, Khan AS, Mukunu R, Muyembe-Tamfum JJ, Bressler D, et al. Clinical, virologic, and immunologic follow-up of convalescent Ebola hemorrhagic fever patients and their household contacts, Kikwit, Democratic Republic of the Congo. Commission de Lutte contre les Epidemies a Kikwit. J Infect Dis. 1999;179 Suppl 1:S28-35. Full article accesible for free on: http://jid.oxfordjournals.org/content/179/Supplement_1/S28.short

"...There is a paucity of data regarding health consequences of Ebola virus disease among survivors. Methods: we surveyed 105 Ebola virus disease survivors postdischarge from an Ebola treatment unit in Guinea using a standard data collection form. Patients rated recovery as the percentage of improvement in functional status, where 0% represents "unable to perform" and 100% represents "able to perform at prior level." Results: the mean ± standard deviation time interval between hospital discharge and administration of questionnaire was 103.5 ± 47.9 days in 105 survivors. Anorexia was reported by 103 patients, with varying severity levels: mild (n = 33), moderate (n = 65), or severe (n = 5). Reported pain according to site was chest (30.7%), joint (86.7%), muscle (26.7%), and back (45.7%), among others. Recovery in functional status was graded as mild (10%–30%) (n = 2 [1.9%]), moderate (40%–70%) (n = 52 [50.0%]), and excellent (80%–100%) (n = 50 [48.1%]). Severity of arthralgia (R2 = 0.09; P = .008) was directly associated with lower recovery in functional status in multivariate analysis. Conclusions: ebola virus disease survivors frequently reported anorexia and arthralgia. Severity of arthralgia was related to lower functional recovery. There may be a role for focused screening and intervention for symptoms identified in this study of survivors...", Qureshi AI, Chughtai M, Loua TO, Pe Kolie J, Camara HF, Ishfaq MF, et al. Study of Ebola Virus Disease Survivors in Guinea. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2015. Article accessible on: http://cid.oxfordjournals.org/content/61/7/1035.short

Background: Corticosteroids are first-line drugs for the treatment of a variety of conditions in women of childbearing age. Information regarding human pregnancy outcome with corticosteroids is limited. Methods: We collected prospectively and followed up 184 women exposed to prednisone in pregnancy and 188 pregnant women who were counseled by Motherisk for nonteratogenic exposure. The primary outcome was the rate of major birth defects. A meta-analysis of all epidemiological studies was conducted. The Mantel-Haenszel summary odds ratio was calculated for the pooled studies with 95% confidence intervals. A cumulative summary odds ratio was also calculated by combining studies in chronological order. Chi-squared for homogeneity was determined to establish the comparability of the studies. Results: In our prospective study, there was no statistical difference in the rate of major anomalies between the corticosteroid-exposed and control groups. In the meta-analysis, the Mantel-Haenszel summary odds ratio for major malformations with all cohort studies was 1.45 [95% CI 0.80, 2.60] and 3.03 [95% CI 1.08, 8.54] when Heinonen et al. ('77) was removed. This suggests a marginally increased risk of major malformations after first-trimester exposure to corticosteroids. In addition, summary odds ratio for case-control studies examining oral clefts was significant (3.35 [95% CI 1.97, 5.69]). Conclusions: Although prednisone does not represent a major teratogenic risk in humans at therapeutic doses, it does increase by an order of 3.4-fold the risk of oral cleft, which is consistent with the existing animal studies. Park-Wyllie L, Mazzotta P, Pastuszak A, Moretti ME, Beique L, Hunnisett L, et al. Birth defects after maternal exposure to corticosteroids: prospective cohort study and meta-analysis of epidemiological studies. Teratology. 2000;62(6):385-92. Accessible for free on: http://onlinelibrary.wiley.com/wol1/doi/10.1002/1096-9926(200012)62:6%3C385::AID-TERA5%3E3.0.CO;2-Z/abstract

Considerations for aspiration

- Joint aspiration should be performed using infection prevention and control (IPC) precautions for EVD as described under Infection prevention and control considerations in EVD survivors (see below) and the aspirate sent for RT-PCR test for Ebola
- It is advised that aspiration of the joint be done in a laboratory/medical ward/isolation unit at a district or tertiary hospital observing full SOP in the IPC guideline. Aspiration should not be done at the PHU
- If the articular fluid is negative for Ebola, perform white blood cell count, gram and acid fast bacilli stains, polarized light microscopy, and cultures for bacteria and TB as indicated and available

Ocular

Eye pain and redness, dry eyes, sensitivity to light, and blurry vision are common complaints among EVD survivors.[11,12,13,14,15] Ocular sequelae, which include uveitis, cataracts, retinal and optic nerve disease, may appear during acute EVD or present at variable times after ETU discharge. Patients with uveitis have reported ocular symptoms up to 17 weeks after ETU discharge.[16] Ocular clinical manifestations could be, as previously reported, due to the persistence of the virus in Aqueous fluid in the anterior chamber of the eye.[17] Ocular disease in EVD survivors can be sight-threatening and treatment outcomes may be time sensitive. Therefore, when ocular complaints arise, early treatment is essential. Early referral to an eye specialist should be considered where services are available.

Guidelines for clinical evaluation

- Evaluate for eye pain, irritation, or redness, increased tearing or dry eye, light sensitivity, and decreased visual acuity
- Test of visual acuity using Snellen or Tumbling E charts: check unilateral and bilateral at presentation and with best correction
- Pupillary exam, specifically testing for relative afferent pupillary defect
- Since preliminary evidence suggests that presence or absence of symptoms only moderately cor-

relates with clinical disease, within the first month after ETU discharge, when possible all patients should be referred to an eye specialist for a full examination, including:

- Dilated fundoscopic exam
- Slit lamp examination
- Measurement of intraocular pressure

See Appendix 1 for a Red Eye Diagnostic Chart

Differential diagnosis of eye pain/redness/irritation

Bacterial, viral, or allergic conjunctivitis; dry eye syndrome; ocular surface disease from sunlight exposure; corneal ulcer; acute angle closure glaucoma; scleritis; trauma; uveitis due to other viruses (herpes simplex, herpes zoster, and cytomegalovirus); parasites (*Toxoplasma gondii*); or bacteria (*Treponema pallidum*).

Differential diagnosis of decreased visual acuity

Cataract; refractive error (presbyopia, myopia, hyperopia, and/or astigmatism); retinal scars from other pathogens (such as Toxoplasma gondii, Treponema pallidum [i.e., syphilis], Onchocerca volvulus, and measles virus); post-traumatic pathology (e.g., corneal scars, optic nerve damage, congenital disease, vitamin A deficiency); glaucoma; retinal detachment.

Treatment of eye pain/redness/irritation

- When possible, exclude other infectious etiologies such as syphilis and HIV through serologic testing of the blood
- If ocular surface disease suspected, treat with artificial tears for topical lubrication
- If uveitis suspected, immediate treatment is required, with immediate referral to an ophthalmologist or other eye care specialist where available. Treatment of uveitis is not recommended at the PHU or district hospital if there no specialist is available.
- While referral is being arranged, the following treatment should be implemented:
  - prednisone 1% eye drops every 1–2 hours (reduce with improvement), and cyclopentolate 1% eye drops, 1 drop four times a day. It is expected that with this initial treatment the patient would then be under specialist care wherein the following treatment regimen is followed.
  - If no resolution after 7 days of topical prednisone and cyclopentolate, or if predominantly posterior/intermediate, or if panuveitis is suspected, consider adding systemic corticosteroids (adults) or methotrexate (children), following dosages and considerations as described under Treatment of arthritis above. Before prescribing, weigh benefits of using methotrexate in children against its side effects.

Treatment of refractive error

Prescribe and provide corrective lenses

Indications for referral to specialist

- Uveitis, especially suspected intermediate, posterior, or pan-uveitis and all cases of uveitis that do not respond to 7 days of topical therapy as described above. These are medical emergencies for which oral corticosteroids (adults) or methotrexate (children) may be required
- All children <10 years of age (since it may be difficult to ascertain a history of ocular symptoms in this group)
- Decreased vision or vision loss of any cause following EVD
- Pupillary abnormalities or optic nerve dysfunction (i.e., optic disc edema/swelling, optic nerve pallor)

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- Referral to a rehabilitation specialist may be required for people with permanent or severe vision loss

Auditory

Tinnitus and hearing loss have been reported in more than a quarter of EVD survivors, although the causal link between these findings and EVD has yet to be determined[18, 19, 20]

Guidelines for clinical evaluation

- Evaluate for hearing loss, tinnitus, aural fullness, and vertigo
- Otoscopic examination of ear canal and tympanic membrane
- Whispered voice screening test
- Tuning fork tests (Weber and Rinne testing): 256 Hz and 512 Hz
- Audiometry testing (if available)

Note: Children <10 years may not be able to report auditory sequelae and thus hearing tests, including audiometry if available, should be conducted in this group at each clinic visit.

Differential diagnosis of tinnitus and/or hearing loss

- Pre-EVD hearing loss due to diseas-

Further Reading

"...Three (15%) of 20 survivors of the 1995 Ebola outbreak in the Democratic Republic of the Congo enrolled in a follow-up study and 1 other survivor developed ocular manifestations after being asymptomatic for 1 month. Patients complained of ocular pain, photophobia, hyperlacrimation, and loss of visual acuity. Ocular examination revealed uveitis in all 4 patients. All patients improved with a topical treatment of 1% atropine and steroids..." Kibadi K, Mupapa K, Kuvula K, Massamba M, Ndaberey D, Muyembe-Tamfum JJ, et al. Late ophthalmologic manifestations in survivors of the 1995 Ebola virus epidemic in Kikwit, Democratic Republic of the Congo. J Infect Dis. 1999;179 Suppl 1:S13-4 Full article accessible for free on http://jid.oxfordjournals.org/content/179/Supplement_1/S13.full.pdf+html

Background: Limited data are available on the prevalence and predictors of clinical sequelae in survivors of Ebola virus disease (EVD). The EVD Survivor Clinic in Port Loko, Sierra Leone, has provided clinical care for 603 of 661 survivors living in the district. We did a cross-sectional study to describe the prevalence, nature, and predictors of three key EVD sequelae (ocular, auditory, and articular) in this cohort of EVD survivors. Methods; We reviewed available clinical and laboratory records of consecutive patients assessed in the clinic between March 7, 2015, and April 24, 2015. We used univariate and multiple logistic regression to examine clinical and laboratory features of acute EVD with the following outcomes in convalescence: new ocular symptoms, uveitis, auditory symptoms, and arthralgias. Findings: Among 277 survivors (59% female), median age was 29 years (IQR 20–36) and median time from discharge from an EVD treatment facility to first survivor clinic visit was 121 days (82–151). Clinical sequelae were common, including arthralgias (n=210, 76%), new ocular symptoms (n=167, 60%), uveitis (n=50, 18%), and auditory symptoms (n=67, 24%). Higher Ebola viral load at acute EVD presentation (as shown by lower cycle thresholds on real-time RT-PCR testing) was independently associated with uveitis (adjusted odds ratio [aOR] 3•33, 95% CI 1•87–5•91, for every five-point decrease in cycle threshold) and with new ocular symptoms or ocular diagnoses (aOR 3•04, 95% CI 1•87–4•94). Interpretation: Clinical sequelae during early EVD convalescence are common and sometimes sight threatening. These findings underscore the need for early clinical follow-up of survivors of EVD and urgent provision of ocular care as part of health systems strengthening in EVD-affected west African countries. John G Mattia MJV, Joyce C Chang, Devin E Platt, Kerry Dierberg, Daniel G Bausch, Tim Brooks, Sampha Conteh, Ian Crozier, Robert A Fowler, Amadu P Kamara, Cindy Kang, Srividya Mahadevan, Yealie Mansaray, Lauren Marcell, Gillian McKay, Tim O'Dempsey, Victoria Parris, Ruxandra Pinto, Audrey Rangel, Alex P Salam, Jessica Shantha, Vanessa Wolfman, Steven Yeh, Adrienne K Chan, Sharmistha Mishra Early clinical sequelae of Ebola virus disease in Sierra Leone: a cross-sectional study. Lancet Infectious Diseases. 2015. Accessible on: http://www.sciencedirect.com/science/article/pii/S1473309915004892

es such as Lassa fever or auditory trauma

- Cerumen accumulation (i.e., "ear wax").
- Acute viral labyrinthitis. The diagnosis is based on the acute development (< 10 days duration) of tinnitus, vertigo, and hearing loss (ideally documented by audiometry, but manual evaluation with tuning forks or based on symptomatology may suffice).
- Otitis media (if accompanied by ear pain).

Treatment of acute labyrinthitis

Note: Treatment of acute labyrinthitis is most efficacious when administered within 10 days (and ideally 72 hours) after symptom onset. Patients should therefore be educated upon ETU discharge to seek immediate medical attention if auditory symptoms develop.

- Acute labyrinthitis will often resolve on its own. The vestibular sedative prochlorperazine may be given to reduce vertigo while awaiting resolution:
  - Adults: 5–10 mg orally 3–4 times daily
  - Children, dose based on weight:
    - Under 10 kg: not recommended
    - 10–13 kg: 2.5 mg orally 1 or 2 times daily (do not exceed 7.5 mg per day)
    - 13–18 kg: 2.5 mg orally 2 or 3 times a daily (do not exceed 10 mg per day)
    - 18–39 kg: 2.5 mg orally 3 times daily or 5 mg 2 times daily (do not exceed 15 mg per day)
- Oral corticosteroids are sometimes prescribed for acute labyrinthitis, although their efficacy is unclear.
- Decisions to use corticosteroids for this condition should be left to otorhinolaryngology specialists.

Treatment of otitis media

- Amoxicillin:
  - Adults: 250 mg orally 3 times daily for 10 days
  - Children, dose based on weight:
    - 40–90 mg/kg orally in 2 or 3 divided doses daily for 10 days
    - If over 40 kg, use adult dose

Indications for referral to specialist

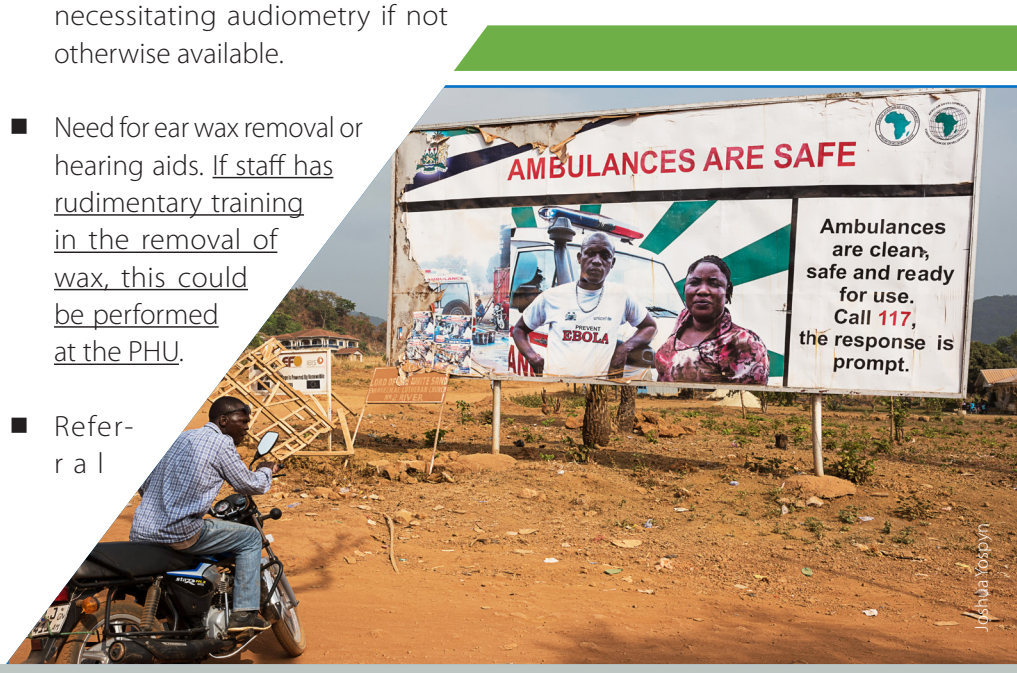
- Persistent hearing loss or tinnitus necessitating audiometry if not otherwise available.
- Need for ear wax removal or hearing aids. If staff has rudimentary training in the removal of wax, this could be performed at the PHU.
- Referral to a rehabilitation specialist may be required for people who have permanent or severe hearing loss, as well as training resources on primary ear and hearing care.

Abdominal

A number of health conditions can affect the gastrointestinal tract of EVD survivors. Most have no connection with the fact that they are survivors, but all must all be treated with caution due to the general health status of these patients which is in most cases, weaker than that of the general population. One of the most common complaints is abdominal pain. Its cause is generally unknown.

Guidelines for clinical evaluation

- Ask the client about the presence of abdominal pain:
  - severity/intensity
  - location
  - characteristics/type of pain (burning, cramp-like, other)

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- timing and relation with events such as eating or taking medication
- duration

- Ask about associated symptoms:
  - fever
  - nausea/vomiting
  - inability to eat
  - pain or difficulty swallowing
  - acid reflux
  - bowel movements: consistency, frequency, and presence of blood or mucus in stools, diarrhea
  - rapid weight gain or loss
  - recent intake of food, safety of the source, cooking techniques
  - any medication the client is taking
  - Record the client's weight and height
  - Measure vital signs (VS)
  - Look for yellowing of the eyes (scleral icterus) or palate, as well as paleness of mucous
  - Palpate the abdomen with the client in horizontal position. Try to assess for hepatomegaly, rebound or guarding (peritoneal signs), suprapubic tenderness, masses, swelling
  - Perform Murphy's maneuver. A positive result might indicate gallbladder disease
  - Auscultate the abdomen and look for decreased or hyper-active bowel sounds
  - Stool examination for ova, cysts, and parasites as clinically indicated
  - Abdominal imaging (Rx, ultrasound) as clinically indicated

Differential diagnosis

A detailed interrogatory, together with physical examination and some specific maneuvers will allow the clinician to make an accurate diagnosis. Below are some of the causes that can lead to abdominal pain in EVD survivors.

Gastritis

Symptoms include:

- nausea and vomiting
- feeling of fullness in epigastric, particularly after eating, sometimes hunger pain
- indigestion

With erosive gastritis, symptoms may include:

- black, tarry stool
- vomiting of blood or material that looks like coffee grounds

Gastroesophageal reflux disease (GERD)

Gastroesophageal reflux disease, commonly known as acid reflux, is when acid from the stomach moves backward into the esophagus. The lining of the esophagus is more delicate than the lining of the stomach. Therefore, acid in the esophagus causes a burning sensation in the chest, known as heartburn.

Symptoms include:

- heartburn

- feeling like stomach contents have come back up to the throat or mouth (regurgitation)
- chest pain
- dry cough
- asthma
- trouble swallowing

Peptic ulcer disease (PUD)

Peptic ulcers are sores that develop in the lining of the stomach, lower esophagus, or small intestine. The most common symptom of a peptic ulcer is burning abdominal pain that extends from the navel to the chest. Pain can range from mild to severe. In some cases, the pain may wake up the patient at night.

Other common signs of a peptic ulcer include:

- change in appetite
- nausea
- bloody or dark stools (melena)
- unexplained weight loss
- indigestion
- vomiting
- chest pain

Lower urinary tract infection (UTI)

Symptoms include:

- burning with urination
- increased frequency of urination
- scant amounts of urine passed per urination
- bloody or cloudy urine, or urine that looks like cola or tea
- strong odor to urine
- pelvic pain in women
- rectal pain in men

Murphy's Maneuver: a test for gallbladder disease in which the patient is asked to inhale while the examiner's fingers are hooked under the liver border at the bottom of the rib cage. The inspiration causes the gallbladder to descend onto the fingers, producing pain if the gallbladder is inflamed. Deep inspiration can be abruptly stopped due to inflammation related pain.

Upper UTI

Potentially life threatening if progresses to sepsis. Symptoms include:

- pain and tenderness in the upper back and sides
- chills and fever
- nausea and vomiting
- pain during fist percussion of the kidneys is a sign of alarm

Irritable bowel syndrome (IBS)

Irritable bowel syndrome is a common disorder affecting the large intestine and causing abdominal pain, constipation, or diarrhea. There is no cure for IBS. However, treatment is aimed at managing symptoms.

Symptoms vary, but the most common include:

- abdominal pain
- cramping
- bloating
- gas
- diarrhea
- constipation

Pelvic inflammatory disease (PID)

Pelvic inflammatory disease seems to be common in female EVD survivors. It is one of the most severe complications of sexually transmitted infections (STIs). It is advised that the syndromic treatment for PID be initiated after laboratory confirmation of the offending pathogen, most commonly gonorrhea or chlamydia.

The symptoms of PID can vary, but may include:

- Dull pain or tenderness in the stomach or lower abdominal area, or pain in the right upper abdomen
- Abnormal vaginal discharge that is yellow or green in color or that has an unusual odor
- Painful urination
- Chills or high fever
- Nausea and vomiting
- Pain during sex

Treatment

- Before installing any treatment, make sure that the patient does not meet criteria for urgent referral. Installing treatment too soon may mask symptoms and delay referral
- Rule out or treat more common etiologies not specific to EVD according to National Guidelines. Depending upon the symptoms and working diagnosis, initial treatment with H2 blockers or omeprazole may be considered
- Avoid NSAIDs like ibuprofen, diclofenac, or aspirin in patients with gastritis, GERD, and PUD as these drugs are these drugs cause further gastric irritation
- Consider de-worming

Non-pharmacological treatment

- Diet for acid-related abdominal pain limits foods that irritates the stomach
- Seasonings such as pepper increase stomach acid and irritate the stomach
- Chocolate, spices, and fatty foods irritate stomach
- Alcohol and caffeine may also cause symptoms
- Patients should reduce these as much as possible and increase intake of fiber-rich food

Indications for referral to specialist

- The "acute" or surgical abdomen is an emergency requiring urgent assessment and potential surgical intervention. Signs include:
  - absent or high-pitched bowel sounds
  - rebound tenderness
  - abdominal rigidity
  - guarding
  - tenderness severe enough that the patient is unwilling to be examined
- Severe or sudden pain; patient unable to tolerate oral intake of fluids or medication
- Fever in tandem with abdominal pain may represent intra-abdominal infection that may require hospital admission, surgical evaluation, and intravenous fluids and antibiotics.
- Yellowing of the eyes or palate may indicate severe liver disease, severe infection, or hemolysis and should be referred for specialist evaluation and care.
- Increased abdominal girth may represent fluid in the abdomen (ascites) and liver disease or a bowel obstruction. Either clinical presentation requires referral for specialist evaluation.

H2 blockers: a group of medicines that reduce the amount of acid produced by the stomach, and include cimetidine and ranitidine.

Follow up

- Refer persistent abdominal pain despite all attempts at diagnosis and treatment as described above.
- Refer worsening of symptoms or nonresponse to treatment cases.

Neurological

Headache, memory impairment, cognitive disturbances, altered sensation, dizziness, peripheral neuropathy and tremor appear to be common after EVD recovery.[21, 22] Less common neurologic sequelae include focal or generalized weakness, myopathy, seizures, Parkinsonism, or meningitis/encephalopathy. The causal link of these conditions with EVD has yet to be determined.

The acute manifestations in the central nervous system may be related to the posterior sequelae after recovery. Biological factors as well as stress, depression, and other psychosocial mediators may be implicated. Mental health sequelae are discussed in the section below.

Guidelines for clinical evaluation

- The neurologic examination should include general physical examination, evaluations of frontal release signs (glabellar, palmomental, and snout), eye pursuits, cranial nerves, motor strength and tone, sensory signs (especially of the distal extremities), reflexes, sensitive levels, coordination, and gait. It is important to account for possible contributions of psychiatric trauma and eye disorders when performing the evaluation

Differential diagnosis of headache

- Migraine, tensional headache. or cluster headache, idiopathic intracranial hypertension, chronic meningitis, TB meningitis, headache related to other infections (sinusitis, influenza, etc.), acute meningitis/meningoencephalitis, intracranial tumor, hydrocephalus, subarachnoid hemorrhage, temporal arteritis.

Differential diagnosis of peripheral neuropathy

- Nutritional deficiencies (B12 and other B vitamins), infections (HIV, syphilis, cytomegalovirus), endocrine abnormalities (diabetes mellitus, hypothyroidism, arteriosclerosis), exposure (heavy metals and toxins), compression neuropathies (carpal tunnel syndrome), autoimmune, paraproteinemia.

Differential diagnosis of tremor

- Parkinson's disease, liver dysfunction, metabolic dysfunction (hyperthyroidism), enhanced physiologic tremor, benign essential tremor, alcohol withdrawal, intoxication/exposure (heavy metals such as manganese).

Differential diagnosis of seizures

- Idiopathic seizure, seizure related to metabolic derangement (hypoglycemia, uremia, hypocalcaemia, etc.), alcohol withdrawal, stroke-related, post-traumatic, infection-related (meningitis, encephalitis), intoxication/medication-related.

Treatment of headache— abortive

- For infrequent (less than once a week) or less severe headaches, paracetamol (first line); ibuprofen or other NSAID (second line). See dosing and other considerations above under Treatment of arthralgia/tenosynovitis and muscle pain.

Considerations

These drugs should be used sparingly since analgesic rebound headaches may develop. Anti-emetics (promethazine 12.5–25mg orally every 4–6 hours as needed or metoclopramide 10 mg orally every 8 hours as needed) may be used for headache associated with nausea, as well as for more moderate to severe headache, in combination with NSAIDs.

Treatment of headache— preventive

If headaches occur more than once a week or are very severe:

- Propranolol 40mg orally twice daily, increasing to 80mg twice daily after 1–2 weeks if headaches persist and there are no symptoms of hypotension or bradycardia.

- Monitor heart rate and blood pressure. Avoid if heart rate <60 bpm, or history of asthma or depression.

- Amitriptyline 10–25mg orally each night, increasing monthly as needed up to 100 mg nightly. This therapy may be helpful in patients with comorbid depression and/or sleep difficulties. Amitriptyline is contraindicated in pregnancy.

Treatment of peripheral neuropathy

- Amitriptyline, as described above

Treatment of tremor

Postural/action tremor similar to benign essential tremor that interferes with activities of daily living:

propranolol as described above, titrating up to 120–320mg total daily as needed.

Treatment of seizures

- Check for hypoglycemia. If present, treat patient with dextrose 50% at start, and 5% for maintenance. If glycemia test is not available, treat empirically with dextrose 50%.
- For an acute seizure lasting more than 2 minutes:
  - Option 1: 10 mg rectal diazepam.
  - Option 2: 10 mg diazepam slow IV, diluted in 8 ml saline administered at 2 ml/min until seizure subsides.

Preventive therapy:

- First line: phenytoin 100 mg orally nightly, increasing up to 400 mg daily as needed.
- Second line: carbamazepine 200 mg orally twice a day, increasing as needed by 200mg/day at weekly intervals to a maximum of 1600 mg/day.

Considerations

- These drugs may cause severe rash, blood dyscrasia, or hepatotoxicity.
- Long-term use of phenytoin can lead to osteopenia.
- Complete blood count and liver function should be monitored after initiation of either drug.
- Both drugs are contraindicated in pregnancy. In females of childbearing potential, consider supplementation with folic acid.
- If seizures are untreated or refractory to medication, patients should not drive or operate heavy machinery, and should participate in certain activities (such as swimming) without supervision.

Indications for referral to specialist

- Refractory or worsening headaches.
- Headache with:
  - focal deficits or weakness
  - papilledema on exam, visual loss, or double vision
  - deafness, tinnitus, or full ears
  - confusion, depression, or psychosis
- Headache accompanied by meningeal signs, including fever, neck stiffness, or altered consciousness (this is a medical emergency).
- Refractory neuropathic pain or muscle weakness.
- Seizure lasting more than 10 minutes (this is a medical emergency) or episodes of altered consciousness, confusion, or jerking of limbs that may be indicative of seizures.
- Suspicion of Parkinson's disease.

Mental health

EVD survivors have experienced a life-threatening acute illness in an ETU, cared for by people they do not know and whose faces cannot be seen. Many survivors have witnessed deaths of family members and have not been able to

properly grieve.[23] The experience is particularly daunting for children, who are often alone and may have lost parents/caregivers during the outbreak.[24] Many survivors experience stigma and isolation, sometimes even from family and community members. As health care workers it's important not to further stigmatize survivors when providing care. The physical sequelae of EVD may impede resumption of work, with significant psychosocial impacts.[25] Following experiences such as these, many people may experience episodes of grief, stress, or difficulty sleeping. The majority will recover but some may need more specialized care.[26] Some mental disorders such as depression, anxiety, alcohol, and drug use may be present in a smaller population; these will require referral to a specialist.

Guidelines for clinical evaluation

- Always check for physical conditions that may cause mental health problems, such as anemia, vitamin deficiencies, infections, or chronic illness such as TB, HIV, and diabetes.
- Ask and look for symptoms and signs of emotional distress using symptoms checklist and duration (refer to MH triage tool).
- Ask about impairment in daily functioning, e.g., is the person able to conduct activities of daily living such as bathing, cooking, eating, dressing, caring for her/himself/child/elderly family member?
- Ask whether s/he has persistent thoughts of death or doesn't want to go on living, e.g., not wanting to wake up in the morning, thinking s/he has no future, feels hopeless. If yes, ask if s/he has made plans to end his/her life.
- Ask about social support from family and community members.
- In some settings, a home visit may be an opportunity to better assess psychosocial issues, especially for children who have lost their primary caregiver.

Further Reading

"...Most of the survivors in our sample had cared for a sick family member before becoming ill themselves, and most had never heard of Ebola before they developed symptoms and therefore did not suspect that they were infected by the virus. Fear, denial, and shame were their principal initial feelings. After release from hospital, survivors were abandoned by family or friends more often than they expected. Belief in god was an important aid to all of them. Their most negative experiences were witnessing other people dying in the isolation ward of the Kikwit General Hospital, and the reluctance of hospital personnel to treat them. During Ebola outbreaks more attention should be given to the psychosocial implications of such an epidemic. Information campaigns should include antidiscrimination messages and more psychosocial support should be given to patients and their families...", De Roo A, Ado B, Rose B, Guimard Y, Fonck K, Colebunders R. Survey among survivors of the 1995 Ebola epidemic in Kikwit, Democratic Republic of Congo: their feelings and experiences. Trop Med Int Health. 1998;3(11):883-5. Full article accessible for free on: http://onlinelibrary.wiley.com/doi/10.1046/j.1365-3156.1998.00322.x/full

"...By September 2014, an outbreak of EVD in West African countries of Guinea, Liberia, Sierra Leone, Senegal and Nigeria, had recorded over 4,500 and 2,200 probable or confirmed cases and deaths respectively. EVD, an emerging infectious disease, can create fear and panic among patients, contacts and relatives, which could be a risk factor for psychological distress. Psychological distress among this subgroup could have public health implication for control of EVD, because of potential effects on patient management and contact tracing. We determined the Prevalence, pattern and factors associated with psychological distress among survivors and contacts of EVD and their relatives. Results: most frequently occurring psychological distress were inability to concentrate (37.6%) and loss of sleep over worry (33.3 %). Losing a relative to EVD outbreak was significantly associated with feeling unhappy or depressed while being a health worker was protective. Conclusions: survivors and contacts of EVD and their relations develop psychological distress. Development of psychological distress could be predicted by loss of family member. It is recommended that psychiatrists and other mental health specialists be part of case management

teams. The clinical teams managing EVD patients should be trained on recognition of common psychological distress among patients. A mental health specialist should review contacts being monitored for EVD for psychological distress or disorders....", Mohammed A, Sheikh TL, Gidado S, Poggensee G, Nguku P, Olayinka A, et al. An evaluation of psychological distress and social support of survivors and contacts of Ebola virus disease infection and their relatives in Lagos, Nigeria: a cross sectional study - 2014. BMC Public Health. 2015;15:824. Full article accessible for free at:

Adults and children affected by emergencies experience a substantial and diverse range of mental, substance use, and neurological problems. The mhGAP Humanitarian Intervention Guide contains first-line management recommendations for mental, neurological and substance use conditions for non-specialist health-care providers in humanitarian emergencies where access to specialists and treatment options is limited. It is a simple, practical tool that aims to support general health facilities in areas affected by humanitarian emergencies in assessing and managing acute stress, grief, depression, post-traumatic stress disorder, psychosis, epilepsy, intellectual disability, harmful substance use and risk of suicide. This new tool is an adaptation of WHO's mhGAP Intervention Guide, a widely-used evidence-based manual for the management of these conditions in non-specialized health settings. Tool accessible for free on: http://www.who.int/mental_health/publications/mhgap_hig/en/

- For more information, refer to WHO mhGAP Humanitarian Intervention Guide for Mental, Neurological and Substance use Disorders in Non-specialized Health Settings.[27]
- A toolkit to assist social mobilizers and communicators in confronting stigma associated with EVD is also available online.[28]
- Some of the conditions survivors may present with are described below, with a brief management guide (for further information for those who have been trained, please refer to mhGAP).
- Normal reactions to extreme stress (acute stress, grief): May present with non-specific psychological and physical symptoms. Assess for comorbid physical or mental health conditions and refer as necessary.

Treatment

- Provide basic psychosocial support
- Listen, do not force people to talk
- Ask about basic needs and concerns and link them to services/ psychosocial support officers

Depression

This may affect people who have not had any exposure to a particular psychosocial stressor, though experiencing traumatic events puts people at higher risk. When first assessing the patient take a full history and rule out any physical comorbidities and drug or alcohol use.

Symptoms must be present for >2 weeks. Typical symptoms are:

- sadness or low mood
- difficulty sleeping
- lack of energy
- not enjoying activities they used to
- change in appetite
- isolating themselves
- unable to conduct tasks as normal
- patients may describe feeling hopeless, worthless or guilty

Always ask if the patient has any thoughts of harming him/herself, whether s/he doesn't want to go on living and have made plans to end his/her life. If yes, you must make sure the person is safe and has someone looking after him/her, and refer to the district mental health nurse.

Treatment

Provide psychoeducation and support. Explain it is a common condition and

can be treated, offer to discuss with family/social support. Encourage patient to participate in enjoyable activities as possible, keep regular sleeping patterns, exercise, and spend time with trusted friends.

Try to identify any psychosocial stressors such as family difficulties. For further assessment, or if considering antidepressant medication, refer to the mhGAP Intervention Guide or the district mental health nurses.

Acute psychotic episode

This condition affects a person's thinking, behavior, and feelings. S/he experiences or believes things that aren't real, is often unaware that s/he has a mental disorder, and his/her ability to function as normal is dramatically curtailed. When assessing a patient, take a full history, rule out any physical comorbidities, drug, or alcohol use. Typical symptoms:

- Behaving strangely (odd appearance, wandering in the street, self-neglect, laughing, or talking to self).
- Strange beliefs (people want to hurt him/her, s/he has been cursed, s/he has special powers); may hear or see things that aren't there.
- Patient may isolate his/herself from/be scared/suspicious of other people.

Treatment

- Provide psychoeducation and support.
- Ensure person is safe and has a trusted family member or friend to look after him/her if necessary.
- Refer to the district mental health nurse for further assessment and management.
- If mental health nurse is unavailable and provider is trained in mhGAP Humanitarian Intervention Guide (HIG), refer to it for management options.

Harmful use of drugs or alcohol

Use of alcohol, psychotropic substances (e.g., marijuana, amphetamines, cocaine, heroin, prescribed drugs such as benzodiazepines, tramadol) can lead to psychological and physical problems; these include withdrawal (physical and psychological symptoms that happen when people cut down or stop their usual intake); harmful use (that leads to negative physical and psychological effects); dependence (physical or psychological addiction).

NB: Alcohol withdrawal can present as a medical emergency and should be managed with a reducing regime of diazepam. A standard initiation dose is 10–20 mg up to 4 times daily, but dose depends on the patient's tolerance, the severity of the physical symptoms, and any medical comorbidities. Titrate carefully and monitor patient closely. Ask about the use of each drug separately, clarify current use, initiation, progression, onset of problem use, dependence symptoms and harm to themselves or others. Assess the patient's desire to stop or cut down use.

Treatment

Manage physical effects of the substance where necessary. If the patient wants to cut down, advise him/her to reduce the amount they use slowly; warn about withdrawal symptoms and cravings; determine whether s/he has support from a trusted family member or friend; and ensure s/he comes for follow up.

All mental disorders require regular follow up to monitor progress and ensure social support in place where possible. Treatment options can be found in the WHO mhGAP HIG: Clinical management of mental, neurological, and substance use conditions in humanitarian emergencies http://www.who.int/mental_health/publications/mhgap_hig/en/

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Sexual health

Sexual health complications are frequently reported by both men and women survivors, although the causal link of these conditions with EVD remains to be determined. Complications for men include testicular pain and erectile dysfunction, which is a particularly frequent complaint. Biological factors as well as psychosocial mediators may be implicated. It is important to be aware that erectile dysfunction leads to higher rates of unprotected sex, and counseling should be provided (see Section 5: Semen testing and counseling for male EVD survivors). Complications for women include dyspareunia, pelvic pain, menorrhagia/metorrhagia, and amenorrhea. Depending upon the specific complaint, patients should be evaluated for STIs as well as possible underlying causes and contributors, including hypertension, diabetes, menstrual abnormalities, and psychosocial factors. Consider referring patients to a reproductive health specialist and/or for psychosocial support services as needed.

Relapse due to persistent virus and evaluation of new onset fever

EVD survivors readily clear Ebola virus from the blood as the acute symptoms resolve, but the virus may persist for months, and in some cases perhaps up to a year or more, in body sites that are harder for the immune system to reach. These "immunologically privileged sites" include the inside of the eye, the central nervous system (brain and spinal cord), and the testicles. In women who have been infected while pregnant, the virus may persist in the fetus, amniotic fluid, placenta, and breast milk. Virus may also persist in the breast milk of women who were infected while breastfeeding. Although arthralgia is common in EVD survivors, it is unknown whether Ebola virus persists in the joints. There is presently no evidence that women who become pregnant after they have recovered from EVD run the risk of persistent Ebola virus infection in the developing pregnancy (fetus, amniotic fluid, or placenta).

Although considered rare, relapse due to EVD has been reported. In one case, a survivor developed meningitis nine months after recovery from acute EVD. Ebola virus was detected by polymerase chain reaction in the cerebrospinal fluid (CSF) and at a lower lever in the blood, which was thought to represent "leakage" from the active replication in the central nervous system.

Guidelines for clinical evaluation

- In most cases, a RDT for malaria is indicated.
- Clinicians should follow the standard operating procedures in the IPC guideline when examining EVD survivors with acute febrile illnesses or other clinical manifestations suspected to reflect potential EVD relapse, and when possible, exposure to blood (other) bodily fluid or tissue of an EVD survivor who is again ill is expected.
- Clinicians should consider more common causes of fever in the region, such as malaria and typhoid fever, as well as relapse due to persistent Ebola virus in survivors who present with new onset fever.
- Uveitis and meningitis (if the patient presents with neurological symptoms, including fever, headache, neck stiffness, photophobia, altered mental status, and/or seizures) may

be particularly suggestive of EVD relapse.

- In EVD survivors with new onset fever, test blood for Ebola by RT-PCR.
- If meningitis is suspected, a lumbar puncture should be performed and the cerebrospinal fluid (CSF) tested for Ebola by RT-PCR. This should be done even if the patient's blood has previously tested negative.
- RT-PCR testing of other body fluids related to observed focal symptoms, such as joint fluid in patients with inflammatory arthritis or aqueous humor of the eye in patients with uveitis, may be indicated.

Differential diagnosis

- Malaria
- Typhoid fever
- Rickettsial infection
- Bacterial, TB, or other viral (i.e., non-EVD) meningitis

Treatment

- Malaria treatment if confirmed by RDT or highly suspected
- Antibiotics for suspected typhoid fever or bacterial meningitis
- Anti-TB drugs if confirmed or suspected TB (note that, when possible, the Xpert MTB/RIF rapid test on CSF is preferred over conventional microscopy and culture in persons with suspected TB meningitis: http://www.who.int/tb/publications/xpert_policyupdate/en/)
- Doxycycline for suspected Rickettsial infection

Indications for referral to specialist

- Persons confirmed or highly suspected to have relapsed EVD should be immediately referred to an ETU.
- Persons with unprotected direct exposure to potentially infected body fluids and tissues of EVD survivors who have relapsed should be considered potential contacts and monitored for 21 days after exposure.

4. Considerations for special populations

Children (≤ 15 years old)

Few data are available on EVD sequelae in children, although the physical, psychological, and social effects of the disease on this vulnerable group are thought to be significant.

Guidelines for clinical evaluation

Evaluate nutritional status through the measurement of height, weight, head circumference (children < 1 year old), and middle upper arm circumference (children > 6 months–5 years old) and plot on a UNICEF country-specific growth chart at each clinic visit.

Refer to WHO child growth standards for the identification of severe acute malnutrition in infants and children: www.who.int/nutrition/publications/severemalnutrition/9789241598163/en/

- Evaluate neurological development through assessment of neurodevelopment milestones (gross motor, fine motor, speech and hearing, social and behavioral).
- Evaluate social/family situation and general psychological condition: determine primary care-giver (parents, extended family, foster care, orphanage, (other) vulnerable children), and look for signs of abuse or neglect, food insecurity, child labor, and truancy from school.
- Perform RDT for malaria if persistent fever or anemia.

Differential diagnosis of suspected malnutrition, faltering growth, or neuro-developmental delay

- Malnutrition (e.g., iron, folic acid, vitamin A and B12, or other vitamin deficiencies).
- Faltering growth (consider testing for other acute and chronic infections such as malaria, TB, HIV, gastrointestinal helminthic and parasitic infections, and thyroid abnormalities).
- Neuro-developmental delay due to previous EVD and/or seizure disorder-related brain injury.
- Underlying co-morbidity due to malignancy, diabetes mellitus, or immunocompromised state.

Treatment

- Malnutrition/faltering growth: Dietary advice and supplemental feedings according to integrated management of childhood illness guidelines (see the WHO Handbook on Integrated Management of Childhood Diseases: http://apps.who.int/iris/bitstream/10665/42939/1/9241546441.pdf according to specific deficiency if known, and general treatment guidelines if unknown.
- Check that vaccinations are up to date, including any that the child may have missed during the EVD epidemic. Vaccinations should be given per routine schedule (www.who.int/immunization/policy/immunization_tables/en/), remembering that children with evidence of immunosuppression or severe acute malnutrition who have active TB or HIV infection should not receive live organism vaccines until their disease is under control.
- Ensure all children are up to date with any mass drug administration program for eradication of neglected tropical diseases and vitamin A supplementation.

Indications for referral

- Faltering growth: Refer for thorough evaluation of malnutrition, coexisting metabolic or inherited diseases, and chronic infections such as TB and HIV, gastrointestinal helminthic, and parasitic.
- Suspicion of neurodevelopmental delay.

- Refer any child with mental health disorder to a child mental health specialist.

- Refer to social services: orphans, signs of abuse or neglect, forced labor, or other vulnerability.

Pregnant women

Women infected while pregnant

EVD in pregnancy is associated with a high rate of obstetric complications and poor maternal and perinatal outcomes, with neonatal mortality approaching 100%. One newborn survived after receiving experimental therapy. Accumulating evidence demonstrates that pregnant women may occasionally survive EVD without loss of the fetus and may transmit the virus during delivery and/or management of obstetric complications through contact with infectious intrauterine contents, such as amniotic fluid, placenta, and fetus.

Pregnant women should receive counseling at ETU discharge with subsequent close clinical follow-up, including antenatal and nutritional care. Arrangements should be made for immediate transfer from home or regular hospital to a setting where full EVD IPC precautions can be taken when labor or obstetric complications occur (see below under EVD IPC precautions and PPE when handling potentially infectious specimens). If chorioamnionitis is suspected, proceed with labor induction regardless of gestational age. At all deliveries of women who survived EVD while pregnant, cord blood and swabs of the products of conception (neonate, placenta, and amniotic fluid) should be tested for Ebola virus by RT-PCR. The newborn should also be managed using Ebola IPC precautions for 21 days following birth, regardless of laboratory results or presence or absence of symptoms, since EVD in neonates may be atypical or not evident early in infection.

Women who become pregnant after recovery

There is no evidence that women who become pregnant after they have recovered from EVD are at risk of persistent Ebola virus infection in the developing pregnancy (fetus, amniotic fluid, or placenta). Monitor and follow pregnancy, childbirth, and postnatal care. Provide care services according to WHO and national recommendations and follow standard obstetric IPC precautions.

As described above under Relapse due to persistent virus and evaluation of new onset fever, risks and benefits of epidural and spinal analgesia/anesthesia should include consideration of potential viral persistence in the CSF. Numerous anecdotal reports of stillbirths in women who have conceived after recovering from EVD exist but it is still uncertain whether the rate of stillbirth in EVD survivors is higher than that of the general population. Until more evidence is available, pregnancy in EVD survivors should be considered at-risk for fetal complications and providers should consider performing intermittent assessments of fetal well-being via exam or ultrasound when available.

More information on EVD in pregnancy is available at:

www.who.int/maternal_child_adolescent/documents/preconception_care_policy_brief.pdf?ua=1

www.who.int/csr/resources/publications/ebola/pregnancy-guidance/en/

5. Monitoring for persistent Ebola virus infection in survivors: guidelines for testing and counseling

Semen testing and counseling for male EVD survivors

Recent data suggest that Ebola virus can persist in the semen of male survivors for a year or more after acute infection, although it is not clear for how long the virus is still infectious.[29] Although thought to be rare, sexual transmission of Ebola virus has been reported.[30] Consequently, all EVD survivors and their sexual partners should receive counselling to ensure they adhere to safer sex practices until semen has been determined to be free of Ebola virus.

The semen of EVD survivors should be assumed to contain Ebola virus for the first three months after disease onset. RT-PCR testing of the semen should then be performed monthly until semen test results are *undetected for Ebola virus* two consecutive times, with an interval of at least one month between tests. Pre- and post-test counseling should be performed by experts in sexual transmission counseling.

Until a male EVD survivor's semen can be determined to be Ebola virus-free through the testing described above, survivors and their sexual partners should either abstain from all types of sex or observe safer sex through correct and consistent condom use.[31] Although condom use is thought to be protective and should be encouraged, no data exist on their efficacy in preventing sexual transmission of Ebola virus. Provide survivors with condoms and instructions for safe disposal to prevent contact with seminal fluids (see below under *Infection prevention and control considerations in EVD survivors*). Survivors should also practice good hand and personal hygiene by immediately and thoroughly washing with soap and water after any physical contact with semen, including masturbation. Having tested twice undetected for virus, condom use is still recommended for possible intermittent shedding of viral fragments, protection against STIs such as HIV, and unwanted pregnancy. If an Ebola survivor's semen has not been tested, he should continue to practice safer sex for a minimum of 12 months after the onset of symptoms; this interval may be adjusted as additional information becomes available on the duration of Ebola virus in the semen of survivors.

Vaginal fluids testing and counseling for female EVD survivors

Ebola virus ribonucleic acid (RNA) has been detected by RT-PCR in a woman's vaginal fluid 33 days after symptom onset. However, live virus has never been isolated from vaginal fluids and no suspected cases of female-to-male sexual transmission have been reported. Therefore, routine testing of vaginal fluids is not recommended currently. Additional information and guidance may be available after more research is performed.

Breast milk testing, breastfeeding, and counseling for female EVD survivors

Recent evidence suggests that breast milk can remain positive for Ebola virus for up to two months after symptom onset in survivors who were pregnant or lactating when infected. Furthermore, two cases of survivors who recovered prior to becoming pregnant had EVD-positive breastmilk in the first hours following birth, with samples becoming negative the next week. Spontaneous galactorrhea has also been reported in female survivors; one survivor's breast milk tested positive for Ebola by PCR nine months after onset of symptoms. More evidence on the precise duration of Ebola virus persistence in breast milk and risk of transmission is needed.

High levels of maternal IgG have been found in the babies of survivors at birth, disappearing by six months of age. This is of uncertain significance but potentially protects the baby from the risk of transmission through breastmilk of survivors who become pregnant after

recovery. In view of this and taking into account the known high-risk of replacement feeding, survivors who become pregnant after recovery should breastfeed, unless breastmilk testing is available.

If a pregnant woman contracts EVD or a woman who contracts EVD is breastfeeding a baby who is also EVD-positive, breastfeeding should continue or be initiated at birth.[1]

In cases where a lactating woman is EVD-positive and the baby is uninfected, the breast milk should be tested by RT-PCR immediately upon discharge. If the breastmilk tests positive for fragments of the virus, infants should be safely formula-fed to lessen the risk of transmission. A breast pump may be used to relieve breast engorgement symptoms and maintain lactation following EVD IPC guidelines to reduce risk of virus transmission (see below under *Infection prevention and control considerations in EVD survivors*). Breastfeeding may resume once the breastmilk tests negative twice, one week apart.

1 Recommendations for Breastfeeding/Infant Feeding in the Context of Ebola Virus Disease http://www.cdc.gov/vhf/ebola/hcp/recommendations-breastfeeding-infant-feeding-ebola.html and infant feeding in the context of Ebola at http://www.ennonline.net /infant-feedinginthecontextofebola2014).

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Further Reading

"...On March 20, 2015, 30 days after the most recent confirmed Ebola virus disease (Ebola) patient in Liberia was isolated, Ebola was laboratory confirmed in a woman in Monrovia. The investigation identified only one epidemiologic link to Ebola: unprotected vaginal intercourse with a survivor. Published reports from previous outbreaks have demonstrated Ebola survivors can continue to harbor virus in immunologically privileged sites for a period of time after convalescence. Ebola virus has been isolated from semen as long as 82 days after symptom onset and viral RNA has been detected in semen up to 101 days after symptom onset. One instance of possible sexual transmission of Ebola has been reported, although the accompanying evidence was inconclusive. In addition, possible sexual transmission of Marburg virus, a filovirus related to Ebola, was documented in 1968. This report describes the investigation by the Government of Liberia and international response partners of the source of Liberia's latest Ebola case and discusses the public health implications of possible sexual transmission of Ebola virus. Based on information gathered in this investigation, CDC now recommends that contact with semen from male Ebola survivors be avoided until more information regarding the duration and infectiousness of viral shedding in body fluids is known. If male survivors have sex (oral, vaginal, or anal), a condom should be used correctly and consistently every time...", Christie A, Davies-Wayne GJ, Cordier-Lasalle T, Blackley DJ, Laney AS, Williams DE, et al. Possible sexual transmission of Ebola virus - Liberia, 2015. MMWR Morb Mortal Wkly Rep. 2015;64(17):479-81. Article accessible on: http://europepmc.org/abstract/med/25950255

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More information on sexual transmission of Ebola virus is available at: http://www.who.int/reproductivehealth/topics/rtis/ebola-virus-semen/en/

6. Infection prevention and control considerations in EVD survivors

Standard IPC precautions for routine clinic visits

Maintain standard IPC precautions[32] at all routine (i.e., the survivor does not complain of acute febrile disease or other manifestations suggesting potential relapse) clinic visits, with appropriate use of personal protective equipment (PPE) and application of the *My Five Moments for Hand Hygiene* approach.[33] Wear full PPE when handling potentially infectious substances.

Disposing infectious waste

All waste potentially infected with Ebola virus should be collected in designated containers and two leak- proof bags and stored in a safe place away from children and animals until it can be collected and incinerated, preferably on site, according to waste management recommendations for EVD care. If waste is moved offsite, it is critical to ascertain where and how it will be treated and destroyed. If incineration is not possible, then burning and/or burying, followed by covering with soil, is recommended.[34]

At-home IPC guidance

Ebola virus may persist in the semen from male EVD survivors for many months. Men whose semen are PCR-tested positive or who have not been tested should practice good hand and personal hygiene by immediately and thoroughly washing with soap and water after any contact with these body fluids.

Any other potentially contaminated objects or surfaces should be washed with water and soap and then decontaminated by soaking them in a 0.5% chlorine solution for 15 minutes. Contaminated bed sheets or clothing should be disposed of and incinerated safely. All potentially contaminated materials should be collected in designated containers and safely disposed of as described in the section on Disposing of infectious waste above. If this is not possible, launder these materials with detergent and water, then rinse and soak in 0.05% chlorine solution for 15 minutes. Inform survivors that this handling may damage the materials.

Elective surgery and management of penetrating traumatic injury

Although more evidence is needed, available data indicate that Ebola virus may persist for a year or more in certain immunologically privileged body sites. Elective surgery on any of these sites in EVD survivors should thus be performed only after careful consideration of the risk-benefit to the patient and the surgical team and supporting health workers. In most cases, it is advisable to delay elective surgery until at least one year after resolution of acute EVD. In cases where it is deemed essential to proceed with surgery involving a known immunologically privileged body site for Ebola virus, the procedure should be done under full EVD IPC precautions. In addition, to assess and manage post-op risk, swabs of the implicated body site or fluid should be taken and tested for Ebola by RT-PCR. The same approach should be taken when attending to penetrating trauma to the immunologically privileged body sites in EVD survivors.

7. Risk communication considerations

How risk communication affects clinical care

Risk communication is the exchange of information between the expert (the health care team) and the person at risk (the Ebola survivor). It is a dynamic process and must be part of the clinical care provided to survivors. A key challenge of risk communication is that experts and those affected do not necessarily assess risk in the same way. Many subjective factors (e.g., familiarity of a hazard, magnitude of a hazard, previous experience, traditional beliefs, fear, and controllability) affect risk perception. This makes the work of clinical teams challenging because survivors do not always follow expert advice.

The second challenge in risk communication is that trust must be present for people to take expert advice. Trust can be eroded if those delivering health care are not credible, are not perceived to have expertise, do not show empathy, or do not keep their promises. Therefore all risk communication must aim to strengthen trust in the clinical care teams and services.

Effective risk communication improves use of health services, increases compliance with treatment and care, and builds trust and confidence in health professionals. Ultimately, it contributes to better outcomes in survivors and can help prevent further transmission.

Risk communication considerations

Ebola survivors and their families have all inevitably undergone great suffering and challenges. They have survived, but have many fears, concerns, and questions. Their understanding of Ebola and what it means to be a survivor are influenced by their previous experience and their social and cultural contexts. Therefore it is important that health care providers, health facility personnel, those providing community and family level care, and health policy and planning officers use good risk communication practice.

When people are consumed by worries, they cannot listen to or take advice, however reasonable. It is important to listen and acknowledge people's fears, concerns, or anger offering providing advice. In risk communication, misperceptions, misinformation, and rumors arise and must be identified and dispelled quickly and empathetically.

Good practice

Tips for effective risk communication in the clinical management of survivors include:

- Understand how the Ebola survivor and his/her family perceive his/her health status and identify their main concerns (stigma, inability to find employment, worries about transmitting the disease through sexual contact or from mother to baby).
- Discuss the survivors concerns before giving advice or instructions. Provide opportunities, prompted or spontaneous, for the patient to ask questions.
- Use language that is appropriate for the educational level of the survivor. Explain scientific terms and avoid jargon. Use the language of the survivor and her/his community.
- Use pictures and posters to reinforce provide another way to convey messages and advice.
- Work with community-level health workers, volunteers, and other groups and adapt information accordingly (e.g., content, language, mode of delivery).
- Engage community leaders, religious figures, and other trusted persons to convey messages across and reinforce advice given by clinical care personnel.
- Solicit and incorporate feedback from survivors and their families about risk communication.

- Work closely with risk communications experts to overcome challenges such as resistance and rumors. If possible, hire these experts to train clinical teams on risk communication.

- **Pre-clinical stage:** Good risk communication encourages and motivates survivors to seek clinical care and support.

- **First visit to a care facility or service:** Good risk communication by all personnel (i.e., doctors, nurses, receptionists, gatekeepers, cleaners) influences the perception that the survivor will develop about receiving health care and following advice and treatment.

- **Subsequent visits or interactions:** Good risk communication during subsequent visits can strengthen the trust and confidence the survivor develops about the services provided, and provides opportunities for the clinical care team to mollify persisting and new concerns. If the experience is positive, the survivor may become a champion and encourage others to seek care.

8. Additional reading

1. "...In November 1976 an investigator at the Microbiological Research Establishment accidentally inoculated himself while processing material from patients in Africa who had been suffering from a hemorrhagic fever of unknown cause. He developed an illness closely resembling Marburg disease, and a virus was isolated from his blood that resembled Marburg virus but was distinct serologically. The course of the illness was mild and may have been modified by treatment with human interferon and convalescent serum. Convalescence was protracted; there was evidence of bone-marrow depression and virus was excreted in low titre for some weeks. Recovery was complete. Infection was contained by barrier-nursing techniques using a negative-pressure plastic isolator and infection did not spread to attendant staff or to the community...". Emond RT, Evans B, Bowen ET, Lloyd G. A case of *Ebola virus infection. Br Med J. 1977;2(6086):541–4.* Full article accessible for free on http://www.bmj.com/content/2/6086/541.short

2. "...In November 1994 after 15 years of epidemiologic silence, Ebola virus re-emerged in Africa and, for the first time, in West Africa. In Cote d'Ivoire, a 34-year-old female ethologist was infected while conducting a necropsy on a wild chimpanzee. Eight days later, the patient developed a syndrome that did not respond to antimalarial drugs and was characterized by high fever, headache, chills, myalgia, and cough. The patient had abdominal pain, diarrhea, vomiting, and a macular rash, and was repatriated to Switzerland. The patient suffered from prostration and weight loss but recovered without sequelae. Laboratory findings included aspartate aminotransferase and alanine aminotransferase activity highly elevated, thrombocytopenia, lymphopenia, and, subsequently, neutrophilia. A new subtype of Ebola was isolated from the patient's blood on days 4 and 8. No serologic conversion was detected among contact persons in Cote d'Ivoire (n 22) or Switzerland (n 52), suggesting that infection-control precautions were satisfactory...". *Formenty P, Hatz C, Le Guenno B, Stoll A, Rogenmoser P, Widmer A. Human infection due to Ebola virus, subtype Cote d'Ivoire: clinical and biologic presentation. J Infect Dis. 1999;179 Suppl 1:S48–53.* Full article accessible for free on http://jid.oxfordjournals.org/content/179/Supplement_1/S48.short

3. "...**Background:** In the current epidemic of Ebola virus disease, healthcare workers have been transferred to Europe and the USA for optimised supportive care and experimental treatments. We describe the clinical course of the first case of Ebola virus disease contracted outside of Africa, in Madrid, Spain.

Methods: Herein we report clinical, laboratory, and virological findings of the treatment of a female nurse assistant aged 44 years who was infected with Ebola virus around Sept 25–26, 2014, while caring for a Spanish missionary with confirmed Ebola virus disease who had been medically evacuated from Sierra Leone to La Paz-Carlos III University Hospital, Madrid. We also describe the use of experimental treatments for Ebola virus disease in this patient.

Findings: The patient was symptomatic for 1 week before first hospital admission on Oct 6, 2014. We used supportive treatment with intravenous fluids, broad-spectrum antibiotics, and experimental treatments with convalescent plasma from two survivors of Ebola virus disease and high-dose favipiravir. On day 10 of illness, she had acute respiratory distress syndrome, possibly caused by transfusion-related acute lung injury, which was managed without mechanical ventilation. Discharge was delayed because of the detection of viral RNA in several bodily fluids despite clearance of viraemia. The patient was discharged on day 34 of illness. At the time of discharge, the patient had possible subacute post-viral thyroiditis. None of the people who had contact with the patient before and after admission became infected with Ebola virus.

Interpretation: This report emphasizes the uncertainties about the efficacy of experimental treatments for Ebola virus disease. Clinicians should be aware of the possibility of transfusion-related acute lung injury when using convales-

cent plasma for the treatment of Ebola virus disease...", *Mora-Rillo M, Arsuaga M, Ramirez-Olivencia G, de la Calle F, Borobia AM, Sanchez-Seco P, et al. Acute respiratory distress syndrome after convalescent plasma use: treatment of a patient with Ebola virus disease contracted in Madrid, Spain. Lancet Respir Med. 2015.* Full article accessible on: http://www.sciencedirect.com/science/article/pii/S2213260015001800

4. "...**Background:** More than 26,000 cases of Ebola virus disease have been reported in western Africa, with high mortality. Several patients have been medically evacuated to hospitals in the United States and Europe. Detailed clinical data are limited on the clinical course and management of patients with EVD outside western Africa.

Objective: To describe the clinical characteristics and management of a cluster of patients with EVD, including the first cases of Ebola virus infection acquired in the United States.

Design: Retrospective clinical case series.

Setting: Three U.S. hospitals in September and October 2014.

Patients: First imported EVD case identified in the United States and 2 secondary EVD cases acquired in the United States in critical care nurses who cared for the index case patient.

Measurements: Clinical recovery, EBOV RNA level, resolution of Ebola viremia, survival with discharge from hospital, or death.

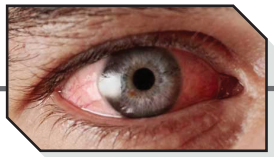
Results: The index patient had high EBOV RNA levels, developed respiratory and renal failure requiring critical care support, and died. Both patients with secondary EBOV infection had nonspecific signs and symptoms and developed moderate illness; EBOV RNA levels were moderate, and both patients recovered.

Limitation: Both surviving patients received uncontrolled treatment with multiple investigational agents, including convalescent plasma, which limits generalizability of the results.

Conclusion: Early diagnosis, prompt initiation of supportive medical care, and moderate clinical illness likely contributed to successful outcomes in both survivors. The inability to determine the potential benefit of investigational therapies and the effect of patient-specific factors that may have contributed to less severe illness highlight the need for controlled clinical studies of these interventions, especially in the setting of a high level of supportive medical care...", Liddell AM, Davey RT, Jr., Mehta AK, Varkey JB, Kraft CS, Tseggay GK, et al. Characteristics and Clinical Management of a Cluster of 3 Patients With Ebola Virus Disease, Including the First Domestically Acquired Cases in the United States. Annals of Internal Medicine. 2015. Full article accessible for free on: http://annals.org/article.aspx?articleid=2292050

Appendix I. Red Eye Diagnostic Chart

**By Mr Ian Gillespie, Consultant Ophthalmologist,
Royal Eye Unit, Kingston Hospital.**



NO STAIN

STAIN[1]

NO PATHOLOGY EVIDENT

INTERNAL PATHOLOGY EVIDENT

discomfort and' discharge

no discharge

semidilated pupil corneal oedema; HM[2] refraction

constricted pupil, ciliary congestion KP[3]

+ white corneal infiltrates

mucopurulent

walering follicles

pain and livid congestion

mild discomfort

Bacterial conjunctivitis

Viral conjunctivitis

Scleritis

Episcleritis

Acute angle closure glaucoma

Acute anterior uveitis

Marginal ulcer

Bacterial leratitis

Abrasion; foreign body

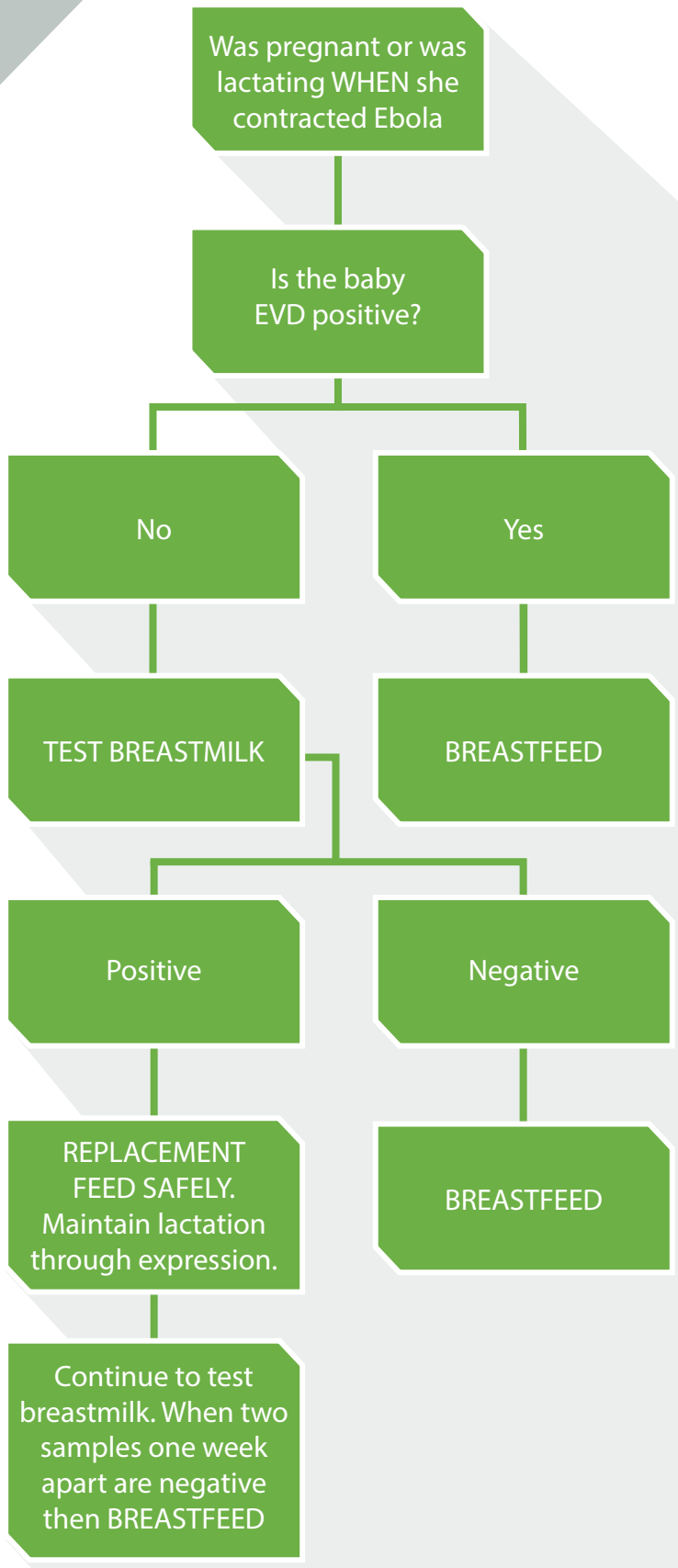
Dendritic ulcer

1. stain cornea with Fluoresein Minims (© Chauvin Pharmaceuticals)
2. HM = hypermetropia, or long sight (+ ve lenses, which magnify when you look through them)
3. KP= keratic precipitates (white cells & other inflammatory debris on post. corneal surface)

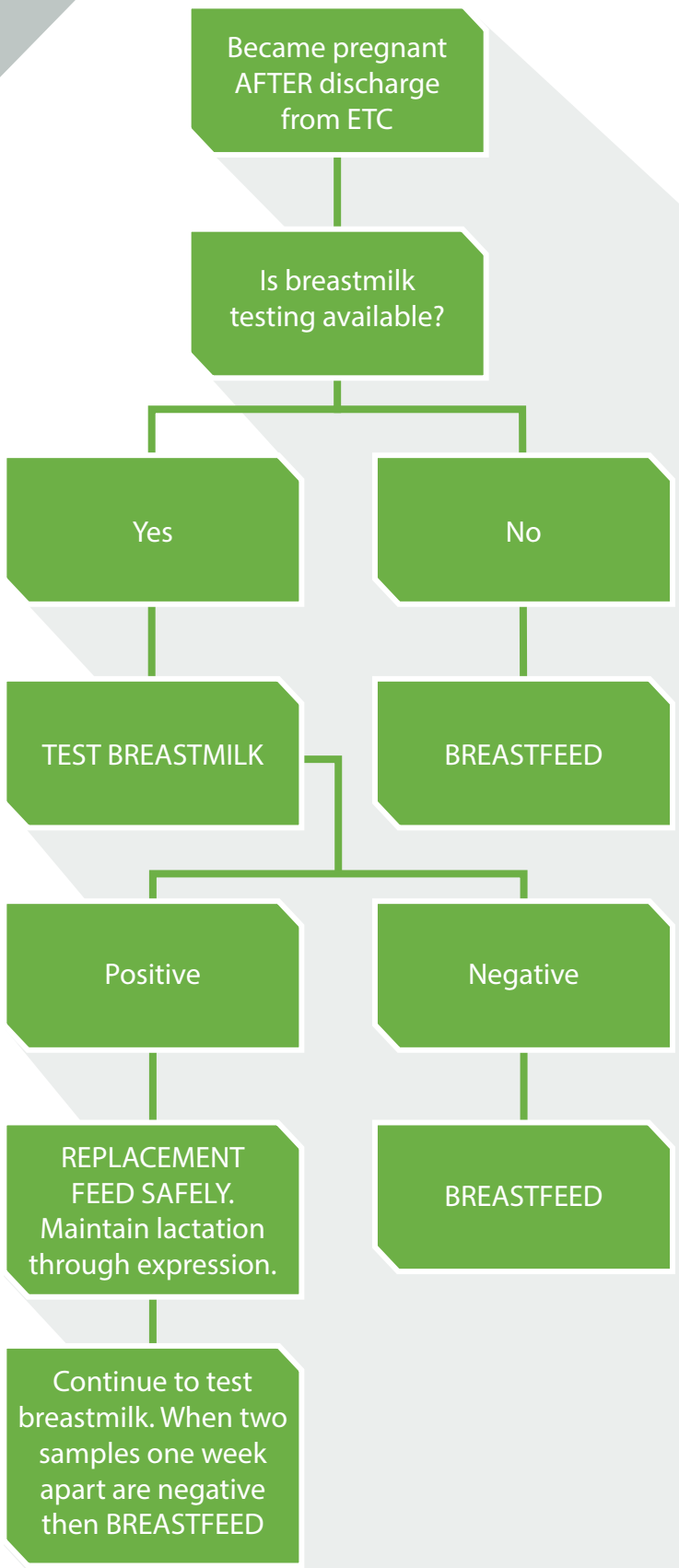
Appendix II. Patient Health Questionnaire for Depression

Patient Health Questionnaire - 9 (PHQ-9)				
Over the last 2 weeks, how often have you been bothered by any of the following problem (tick to indicate your answer)	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
1. Little interest or pleasure in doing things				
2. Feeling down, depressed, hopeless				
3. Trouble falling asleep, or sleeping too much				
4. Feeling tired or having little energy				
5. Poor appetite or overeating				
6. Feeling bad about yourself/or that you are a failure or have let yourself or your family down				
7. Trouble concentrating on thing, such as reading the newspaper or watching television				
8. Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual				
9. Thoughts that you would be better off dead or hurting yourself in some way				
			FOR OFFICE CODING _____ + _____ + ____ + ____ = Total score: _____	
If you checked off any problems, how difficult have these problems made it for you to you work, take care of things a home, or get along with other people?				
Not difficult at all ☐	Somewhat difficult ☐	Very difficult ☐	Extremely difficult ☐	

Appendix III. Breastfeeding EVD Flowchart



Appendix III. Breastfeeding EVD Flowchart (cont.)



Appendix IV. Essential Medications, Diagnostic Tests, and Equipment List for the Care of EVD Survivors

The following list is for guidance and should be adapted to context and level of care.

Medications

- Analgesics/anti-inflammatories
  - Paracetamol
  - Ibuprofen
  - Prednisone (oral and IV)
  - Methotrexate
- Antacids
  - Ranitidine
  - Omeprazole
- Antibiotics
  - Amoxicillin
- Antihelmenthics/antiparasitics
  - Ivermectin
- Antimalarial drug as per the current national treatment policy
- Antidepressants/anxiolytics/antipsychotics
  - Fluoxetine
  - Diazepam
  - Haloperidol
  - Amitriptyline
- Eye care
  - Prednisolone acetate drops 1%
  - Atropine drops 1%
  - Cyclopentolate 1%
  - Timolol drops 0.5%
  - Tetracycline ointment
  - Artificial tears

Diagnostic assays

- Molecular-based assays for Ebola virus RNA (i.e. RT-PCR)
- Malaria rapid tests
- Urine pregnancy tests
- HIV tests

Equipment

- Slit lamps
- Tonometers to measure intraocular pressure
- Ophthalmoscopes
- Audiometers
- Tuning forks
- UNICEF country-specific growth charts
- Mean upper arm circumference tapes

Endnotes:

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