

A database in ACCESS for assessing vaccine serious adverse events

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Purpose: To provide a free flexible database for use by any researcher for assessing reports of adverse events after vaccination.

Results: A database was developed in Microsoft ACCESS to assess reports of serious adverse events after yellow fever vaccination using Brighton Collaboration criteria. The database is partly automated (if data panels contain identical data fields the data are automatically also entered into those fields). The purpose is to provide the database free for developers to add additional panels to assess other vaccines.

Keywords: serious adverse events after vaccination, database, process to assess vaccine-associated events

Introduction

There are multiple databases worldwide used to assess reported adverse events and serious adverse events (SAEs) after vaccination. The US VAERS database¹ is open for data reports by members of the public and community health care workers. A database was designed in Microsoft ACCESS to permit independent assessment by two reviewers of all data in reports of SAEs following yellow fever vaccination. The official criteria for assessing SAEs after yellow fever vaccination are those of the Brighton Collaboration²⁻⁵ and these criteria are assessed in a series of panels. The ACCESS database uses panels to organize variables based on logic and entry workflows.

Summary of Figures

This panel is used to gather general demographic and admission data regarding a case, as well as references to the original publication (Figure 1). Fields in the Summary panel include: country, sex, age, vaccine, vaccine type, batch number, days until first symptoms, if admitted to hospital, days in hospital, if died, and publication details. Figures 2–4 assess yellow fever vaccine-associated neurological disease.

Figure 2 Encephalitis

Classified by Brighton Collaboration Levels 1, 2, and 3 of diagnostic certainty. Fields include central nervous system inflammation histopathology, if encephalopathy is present, temperature, cerebrospinal fluid (CSF) findings, electroencephalogram (EEG) or neuroimaging, and 13 clinical signs or symptoms (Figure 2).

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WHO CaseID Details

World Health Organization 2.61-M- Country: Belgium Save and New Close

Summary Encephalitis Myelitis ADEM Viscerotropic YEL-AVD Guillain-Barre Anaphylaxis Anaphylaxis Level Lab Diag of YF / Other Other Findings Decisions

Unique ID Assigned by WHO: 2 Entered By: Roger Thomas Status: Completed Created Date: 3/20/2010

Gender: Male Pregnant: ☐ Age at Vaccination: 61 Causative: ☐ Date of Birth: Village: District: Province: Country: Belgium get new

Date of Vaccination: Vaccine Type: 17D Batch Number: Days till First Symptoms: 5 Causative: 5 Minutes till First Symptoms: Date of First Symptoms: Died: ☐ Yes ☒ No ☐ No Data

Hospital Admission: ☒ Date of Death: Hospital Admit days after: Days till Death: Causative: ☐ Days spent in Hospital: 9

Publication/Document Details Original Case Number: BE-10-05

Original Data Source: Journal Year of Publication: 2008

Document Title: Immune response during adverse events after 17D-derived yellow fever vaccination

Journal Title: Journal of Infectious Diseases 2008; 197:1577-84. [also reported in Monath 2008 Tal]

Author(s): Bae H-G, Domingo C, Tenorio A, de Ory F, Munoz J, Weber P, et al.

Database designed by Professor Roger Thomas and Dave Jackson

Figure 1 Age, sex, country, time to symptoms and hospitalization, whether died, and publication details.

WHO CaseID Details

World Health Organization 1.47-M- Country: UK Save and New Close

Summary Encephalitis Myelitis ADEM Viscerotropic YEL-AVD Guillain-Barre Anaphylaxis Anaphylaxis Level Lab Diag of YF / Other Other Findings Decisions

Encephalitis: Level 1 of diagnostic certainty ☐ Yes ☒ No ☐ No Data

CHS Inflammation histopathology ☐ Yes ☒ No ☐ No Data

Encephalitis: Level 2 of diagnostic certainty ☐ Yes ☒ No ☐ No Data

Encephalopathy ☐ Yes ☒ No ☐ No Data

TWO OR MORE of

T3BC ☐ Yes ☒ No ☐ No Data CSF ☐ Yes ☒ No ☐ No Data

EEG or Neuroimaging encephalitis ☐ Yes ☒ No ☐ No Data

AND ONE OR MORE of

Response ☐ Yes ☒ No ☐ No Data Eye Contact ☐ Yes ☒ No ☐ No Data

External stimuli ☐ Yes ☒ No ☐ No Data Arousability ☐ Yes ☒ No ☐ No Data

Seizure ☐ Yes ☒ No ☐ No Data

OR ONE OR MORE of

Focal cortical signs ☐ Yes ☒ No ☐ No Data Cranial Nerve ☐ Yes ☒ No ☐ No Data

Visual Field ☐ Yes ☒ No ☐ No Data Primitive reflexes ☐ Yes ☒ No ☐ No Data

Motor weakness ☐ Yes ☒ No ☐ No Data DTRs ☐ Yes ☒ No ☐ No Data

Sensory abnormality ☐ Yes ☒ No ☐ No Data Cerebellar ☐ Yes ☒ No ☐ No Data

EXCLUDE IF

Other diagnosis for illness present ☐ Yes ☒ No ☐ No Data

Encephalitis: Level 3 of diagnostic certainty ☐ Yes ☒ No ☐ No Data

Encephalopathy ☐ Yes ☒ No ☐ No Data

AND ONE of

T3BC ☐ Yes ☒ No ☐ No Data CSF ☐ Yes ☒ No ☐ No Data

EEG or Neuroimaging encephalitis ☐ Yes ☒ No ☐ No Data

AND EITHER 1 or more of...

Response ☐ Yes ☒ No ☐ No Data Eye Contact ☐ Yes ☒ No ☐ No Data

External stimuli ☐ Yes ☒ No ☐ No Data Arousability ☐ Yes ☒ No ☐ No Data

Seizure ☐ Yes ☒ No ☐ No Data

OR one or more of...

Focal cortical signs ☐ Yes ☒ No ☐ No Data Cranial Nerve ☐ Yes ☒ No ☐ No Data

Visual Field ☐ Yes ☒ No ☐ No Data Primitive reflexes ☐ Yes ☒ No ☐ No Data

Motor weakness ☐ Yes ☒ No ☐ No Data DTRs ☐ Yes ☒ No ☐ No Data

Sensory abnormality ☐ Yes ☒ No ☐ No Data Cerebellar ☐ Yes ☒ No ☐ No Data

EXCLUDE IF

Other diagnosis for illness present ☐ Yes ☒ No ☐ No Data

Encephalitis: Level 3A of diagnostic certainty ☐ Yes ☒ No ☐ No Data

Insufficient information to distinguish between acute encephalitis or ADEM: case unable to be definitively classified

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Figure 2 Three levels of diagnostic certainty of encephalitis according to Brighton Collaboration criteria.

WHO CaseID Details

World Health Organization 2.61-M- Country: Belgium Save and New Close

Summary Encephalitis Myelitis ADEM Viscerotropic YEL-AVD Guillain-Barre Anaphylaxis Anaphylaxis Level Lab Diag of YF / Other Other Findings Decisions

Myelitis: Level 1 of diagnostic certainty ☐ Yes ☒ No ☐ No Data

Spinal cord inflammation histopathology ☐ Yes ☒ No ☐ No Data

Myelitis: Level 2 of diagnostic certainty ☐ Yes ☒ No ☐ No Data

Myelopathy ☐ Yes ☒ No ☐ No Data

AND TWO OR MORE of...

T3BC ☐ Yes ☒ No ☐ No Data CSF ☐ Yes ☒ No ☐ No Data

Neuroimaging acute inflammation (i.e. meningitis), or demyelination of spinal cord ☐ Yes ☒ No ☐ No Data

Myelitis: Level 3 of diagnostic certainty ☐ Yes ☒ No ☐ No Data

Myelopathy ☐ Yes ☒ No ☐ No Data

AND ONE of...

T3BC ☐ Yes ☒ No ☐ No Data CSF ☐ Yes ☒ No ☐ No Data

Neuroimaging acute inflammation (i.e. meningitis), or demyelination of spinal cord ☐ Yes ☒ No ☐ No Data

Encephalomyelitis: Meet criteria for both encephalitis and myelitis in any category ☐ Yes ☒ No ☐ No Data

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Figure 3 Three levels of diagnostic certainty for myelitis according to Brighton Collaboration criteria.

Figure 3 Myelitis

Classified by Brighton Collaboration Levels 1, 2, and 3 of diagnostic certainty. Fields include spinal cord inflammation histopathology, if myelopathy is present, temperature, CSF findings, and neuroimaging (Figure 3).

Figure 4 Acute disseminated encephalomyelitis (ADEM)

Classified by Brighton Collaboration Levels 1, 2, and 3 of diagnostic certainty. Fields include demyelination on histopathology, magnetic resonance imaging (MRI) white matter lesions, monophasic illness, and nine clinical signs or symptoms (Figure 4).

Figure 5 Viscerotropic disease

Viscerotropic disease is assessed in Figures 5 and 6. The case definition is classified by Brighton Collaboration Levels 1, 2, and 3 of diagnostic certainty and does not imply causality by yellow fever vaccine. Seven major and seven minor criteria are entered then the level is assessed (Figure 5).

Figure 6 Yellow fever vaccine-associated viscerotropic disease

A second level of classification assigns levels of possible causality into “confirmed”, “probable”, and “suspect” levels. This permits differentiation between cases caused

by wild yellow fever virus and by yellow fever vaccine. The case meets the suspect level if the individual had been in a yellow fever-endemic or -epidemic area within 10 days of onset of symptoms and yellow fever virus-specific antigen was detected in tissue demonstrated by immunohistochemistry or histopathology consistent with yellow fever. It meets the probable and definite levels if it meets the suspect level and yellow fever 17D virus is demonstrated within specific time periods or at specific concentrations (Figure 6).

Figure 7 Guillain–Barré syndrome

Cases are classified into levels 1, 2 or 3 of diagnostic certainty. Level 3 of diagnostic certainty requires three groups of clinical symptoms or signs and the absence of an alternative diagnosis. Level 2 requires level 3 plus CSF white blood cell <50 cells/microliter or, if no CSF was collected then electrophysiological findings consistent with Guillain–Barré syndrome. Level 1 requires level 3 plus electrophysiological findings consistent with Guillain–Barré syndrome and CSF cytoalbuminologic dissociation (Figure 7).

Figure 8 Anaphylaxis

Figures 8 and 9 are used to assess anaphylaxis. Three dermatological or mucosal, five cardiovascular, and eight respiratory symptoms are assessed (Figure 8).

The screenshot displays the 'WHO CaseID Details' form for 'ADEM' (Acute Disseminated Encephalomyelitis). The form is titled '1.47-M-' and includes a 'Country' dropdown set to 'UK'. The 'Summary' tab is selected, showing the following sections:

- ADEM: Level 1 of diagnostic certainty** (Yes/No):
 - Demyelination on histopathology: Yes/No/No Data
 - OR ONE or MORE of...:
 - Encephalopathy: Yes/No/No Data
 - Focal cortical signs: Yes/No/No Data
 - Primitive reflexes: Yes/No/No Data
 - Sensory abnormality: Yes/No/No Data
 - Cerebellar: Yes/No/No Data
 - AND:
 - MRI white matter lesions: Yes/No/No Data
 - AND:
 - Monophasic illness: Yes/No/No Data
- ADEM: Level 2 of diagnostic certainty** (Yes/No):
 - ONE or MORE of...:
 - Encephalopathy: Yes/No/No Data
 - Focal cortical signs: Yes/No/No Data
 - Primitive reflexes: Yes/No/No Data
 - Sensory abnormality: Yes/No/No Data
 - Cerebellar: Yes/No/No Data
 - AND:
 - MRI white matter lesions: Yes/No/No Data
 - AND:
 - Monophasic illness: Yes/No/No Data
- ADEM: Level 3A of diagnostic certainty** (Yes/No):
 - Insufficient information is available to distinguish case between acute encephalitis or ADEM; case unable to be definitively classified: Yes/No/No Data
- ADEM: Exclusion criteria for all levels of diagnostic certainty** (Yes/No/No Data):
 - Presence of a clear alternative acute infectious or other diagnosis for illness: Yes/No/No Data
 - Recurrence or relapse of illness at any point following a 3 month period of clinical improvement from symptomatic nadir: Yes/No/No Data
 - If known, MRI findings or histopathologic data inconsistent with the diagnosis of ADEM: Yes/No/No Data

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Figure 4 Three levels of diagnostic certainty for Acute Disseminated encephalomyelitis (ADEM).

Case Definition of Viscerotropic Disease

Level 1 of diagnostic certainty: ☐ Yes ☒ No ☐ Unclear (≥ 3 major criteria)

Level 2 of diagnostic certainty: ☐ Yes ☒ No ☐ Unclear (2 major criteria OR 1 major criterion AND ≥ 2 minor criteria)

Level 3 of diagnostic certainty: ☐ Yes ☒ No ☐ Unclear (≥ 3 Minor criteria OR 1 Major and 1 Minor criterion)

Minor Criteria

Hepatic jaundice: ☐ Yes ☒ No ☐ No Data

Renal: Urine output <500 ml urine/24 hours for adults; urine output children < 0.5 ml/kg/hour for children: ☐ Yes ☒ No ☐ No Data

Musculoskeletal: Positive urine dipstick for blood with a negative urine microscopic exam for RBCs: ☐ Yes ☒ No ☐ No Data

Respiratory: Increased respiratory rate for age*: ☐ Yes ☒ No ☐ No Data

Platelet disorder: Petechiae or purpura present: ☐ Yes ☒ No ☐ No Data

Hypotension: Systolic BP < 90 mmHg for adults; Systolic BP < 50th percentile for age in children < 16 years: ☐ Yes ☒ No ☐ No Data

Coagulopathy: Clinically evident hemorrhage consisting of at least one of: Epistaxis, Hematemesis, Melena, Hematochezia, Hematuria, Hemoptysis, Metrorrhagia or menorrhagia, Gingival hemorrhage: ☐ Yes ☒ No ☐ No Data

Major Criteria

Musculoskeletal: CPK ≥ 5X ULN: ☐ Yes ☒ No ☐ No Data

Hepatic: Total bilirubin ≥ 1.5 X ULN* (≥ 1.5X patient's baseline value if known) OR ALT or AST ≥ 3X ULN (≥ 3X patient's baseline value if known): ☐ Yes ☒ No ☐ No Data

Renal: Creatinine ≥ 1.5 ULN (≥ 1.5X patient's baseline value if known): ☐ Yes ☒ No ☐ No Data

Platelet disorder < 100,000/μL: ☐ Yes ☒ No ☐ No Data

Respiratory: Oxygen saturation ≤ 88% (by pulse oximetry) OR Requirement for mechanical ventilation: ☐ Yes ☒ No ☐ No Data

Coagulopathy: INR** ≥ 1.5 OR Prothrombin time: 1.5 ULN OR Activated partial thromboplastin time: 1.5 ULN OR elevated Fibrin degradation products (DNR = upper limits of normal): ☐ Yes ☒ No ☐ No Data

Hypotension: Requirement for vasopressor drugs to maintain systolic BP: ☐ Yes ☒ No ☐ No Data

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Figure 5 The Case definition of viscerotropic disease with minor and major criteria according to Brighton Collaboration criteria.

Definite yellow fever vaccine-associated causality ☐ Yes ☒ No ☐ Unclear One or more of the following are present:

Yellow fever 17D virus isolation from blood > 10 days post vaccination: ☐ Yes ☒ No ☐ Unclear

Yellow fever 17D virus concentration in blood ≥ 3 log10 pfu/mL on any day: ☐ Yes ☒ No ☐ Unclear

Yellow fever 17D virus RNA amplification from blood ≥ 34 days post vaccination: ☐ Yes ☒ No ☐ Unclear

Isolation of yellow fever 17D virus OR amplification of yellow fever 17D virus RNA from tissue AND histopathology consistent with yellow fever (e.g., liver midzonal necrosis, Councilman bodies): ☐ Yes ☒ No ☐ Unclear

IF virus-specific antigen in tissue with characteristic vaccine-associated distribution (intrahepatic or mesenchymal cell involvement) demonstrated by immunohistochemistry (IHC) AND histopathology consistent with yellow fever in e.g., liver midzonal necrosis, Councilman bodies AND no history of being in a yellow fever-endemic or epidemic area within 10 days of symptom onset: ☐ Yes ☒ No ☐ Unclear

Probable yellow fever vaccine-associated causality ☐ Yes ☒ No ☐ Unclear One or more of the following are present:

Yellow fever 17D virus isolation from blood 8-10 days post vaccination: ☐ Yes ☒ No ☐ Unclear

Yellow fever 17D virus concentration in blood ≥ 2 log10 pfu/mL but < 3 log10 pfu/mL on any day 1-10 days post vaccination: ☐ Yes ☒ No ☐ Unclear

Yellow fever 17D virus RNA amplification from blood ≥ 11 and < 14 days post vaccination: ☐ Yes ☒ No ☐ Unclear

Isolation of yellow fever 17D virus OR amplification of yellow fever 17D virus RNA from tissue: ☐ Yes ☒ No ☐ Unclear

Histopathology consistent with yellow fever (e.g., liver midzonal necrosis, Councilman bodies) AND no history of being in a yellow fever-endemic or epidemic area within 10 days of symptom onset: ☐ Yes ☒ No ☐ Unclear

Suspect yellow fever vaccine-associated causality ☐ Yes ☒ No ☐ Unclear One or more of the following are present:

Histopathology consistent with yellow fever (e.g., liver midzonal necrosis, Councilman bodies) AND history of being in a yellow fever-endemic or epidemic area within 10 days of symptom onset: ☐ Yes ☒ No ☐ Unclear

IF virus-specific antigen in tissue demonstrated by immunohistochemistry (IHC) AND history of being in a yellow fever-endemic or epidemic area within 10 days of symptom onset: ☐ Yes ☒ No ☐ Unclear

Insufficient data to determine yellow fever vaccine-associated causality ☒ Yes ☐ No ☐ Unclear

No yellow fever testing done OR Yellow fever testing done and test results do not meet any of the criteria for causality levels 1, 2, or 3 above: ☐ Yes ☒ No ☐ Unclear

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Figure 6 Three levels of diagnostic certainty for yellow fever vaccine-associated viscerotropic disease (YEL-AVD) according to Brighton Collaboration criteria.

Clinical Case Definitions: Guillain-Barre syndrome

Level 3 of diagnostic certainty: ☐ Yes ☒ No ☐ Unclear

Bilateral AND flaccid weakness of the limbs: ☐ Yes ☒ No ☐ Unclear

Decreased or absent deep tendon reflexes in weak limbs: ☐ Yes ☒ No ☐ Unclear

Monophasic illness pattern AND interval between onset and nadir of weakness between 12 h and 28 days AND subsequent clinical plateau: ☐ Yes ☒ No ☐ Unclear

Absence of an identified alternative diagnosis for weakness: ☐ Yes ☒ No ☐ Unclear

... Level 3 Diagnostic Certainty AND

Level 2 of diagnostic certainty: ☐ Yes ☒ No ☐ Unclear

CSF total white cell count <50 cells/microL with or without CSF protein elevation above laboratory normal value: ☐ Yes ☒ No ☐ Unclear

IF CSF not collected or results not available, electrophysiologic studies consistent with GB: ☐ Yes ☒ No ☐ Unclear

... Level 3 Diagnostic Certainty OR

Level 1 of diagnostic certainty: ☐ Yes ☒ No ☐ Unclear

Electrophysiologic findings consistent with GBs: ☐ Yes ☒ No ☐ Unclear

Cytoalbuminologic dissociation (i.e., elevation of CSF protein level above laboratory normal value AND CSF total white cell count <50 cells/microL): ☐ Yes ☒ No ☐ Unclear

... Level 3 Diagnostic Certainty AND

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Figure 7 Clinical case definition of Guillain-Barre syndrome according to Brighton Collaboration criteria.

WHO CaseID Details

World Health Organization 1.47-M-

Country: UK Save and New Close

Summary Encephalitis Myelitis ADEM Viscerotropic YEL-AVD Guillain-Barre Anaphylaxis Anaphylaxis Level Lab Diag of YF / Other Other Findings Decisions

Dermatologic or Mucosal

Generalized urticaria (hives) or generalized erythema ☐ Yes ☐ No ☒ No Data

Angioedema, localized or generalized ☐ Yes ☐ No ☒ No Data

Generalized pruritus with skin rash ☐ Yes ☐ No ☒ No Data

Cardiovascular

Tachycardia ☐ Yes ☐ No ☒ No Data

Measured Hypotension ☐ Yes ☐ No ☒ No Data

Capillary Refill time > 3s ☐ Yes ☐ No ☒ No Data

Reduced central pulse volume ☐ Yes ☐ No ☒ No Data

Decreased level of consciousness or loss of consciousness ☐ Yes ☐ No ☒ No Data

Respiratory

Bilateral wheeze (bronchospasm) ☐ Yes ☐ No ☒ No Data

Stridor ☐ Yes ☐ No ☒ No Data

Upper airway swelling (lip, tongue, throat, uvula, or larynx) ☐ Yes ☐ No ☒ No Data

Tachypnoea ☐ Yes ☐ No ☒ No Data

Increased use of accessory respiratory muscles (sternocleidomastoid, intercostals, etc.) ☐ Yes ☐ No ☒ No Data

Recession ☐ Yes ☐ No ☒ No Data

Cyanosis ☐ Yes ☐ No ☒ No Data

Grunting ☐ Yes ☐ No ☒ No Data

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Figure 8 Dermatologic or mucosal, cardiovascular and respiratory symptoms in the definition of anaphylaxis according to Brighton Collaboration criteria.

Figure 9 Anaphylaxis levels of diagnostic certainty

Anaphylaxis is then classified into Brighton Collaboration Levels 1, 2, and 3 of diagnostic certainty using the major criteria in Figure 8 and minor criteria in the case definition (Figure 9).³

The next two figures (Figures 10 Laboratory diagnosis, and Figure 11 Other findings) are used to capture additional information about the case helpful in making an informed classification. Data entry in these sections was

set up to be dynamic to reflect the wide variety of potential entry types.

Figure 10 Laboratory tests for the diagnosis of yellow fever and other infectious diseases

Laboratory diagnosis of yellow fever and other infections: fields include eleven yellow fever specific tests, 22 tests for other infectious diseases, and free entry of other laboratory tests with values and units (Figure 10).

WHO CaseID Details

World Health Organization 1.47-M-

Country: UK Save and New Close

Summary Encephalitis Myelitis ADEM Viscerotropic YEL-AVD Guillain-Barre Anaphylaxis Anaphylaxis Level Lab Diag of YF / Other Other Findings Decisions

Level 1 of Diagnostic Certainty

≥ 1 major dermatological ☐ Yes ☐ No ☒ No Data AND

≥ 1 major cardiovascular AND/OR ≥ 1 major respiratory criterion ☐ Yes ☐ No ☒ No Data

Level 2 of Diagnostic Certainty

≥ 1 major cardiovascular AND ≥ 1 respiratory criterion ☐ Yes ☐ No ☒ No Data OR

1 major cardiovascular OR respiratory criterion ☐ Yes ☐ No ☒ No Data AND

≥ 1 minor criterion involving ≥ 1 different systems (other than cardiovascular or respiratory systems) ☐ Yes ☐ No ☒ No Data OR

(≥ 1 major dermatologic) AND (≥ 1 minor cardiovascular AND/OR minor respiratory criterion) ☐ Yes ☐ No ☒ No Data

Level 3 of Diagnostic Certainty

≥ 1 minor cardiovascular OR respiratory criterion ☐ Yes ☐ No ☒ No Data AND

≥ 1 minor criterion from each of ≥ 2 different systems/categories ☐ Yes ☐ No ☒ No Data

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Figure 9 Three levels of diagnostic certainty for anaphylaxis according to Brighton Collaboration criteria .

WHO CaseID Details

World Health Organization 147-M-

Country: Save and New Close

Summary Encephalitis Myelitis ADEM Viscerotropic YEL-AVD Guillain-Barre Anapylaxis Anaphylaxis Level Lab Diag of YF / Other Other Findings Discussions

Lab Diagnosis of Yellow Fever

YF IgM	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	No Data
YF RT/PCR	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
YF IgG	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Anti-YFV IgM	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Anti-YFV IgG	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Viral load by real time PCR	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
RT/PCR for flavivirus RNA	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Neutralising Abs to YF by plaque reduction neutralisation PRNT	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	130
Viral RNA isolation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Cell culture for YF	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
YF virus isolation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data

Lab Diagnosis of Other Diseases

Enterovirus DNA	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
IgG Herpes Simplex	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
HSV	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Herpes Simplex Isolation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Epstein Barr	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Respiratory syncytial virus RSV	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Japanese Encephalitis	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Urine bacterial culture	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Influenza A	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Influenza B	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Blood bacterial culture	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Cytomegalovirus	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
IGM Herpes Simplex	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Dengue IgM	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Dengue virus isolation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Hepatitis A	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Hepatitis B	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Hepatitis C	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Adenovirus	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Parainfluenza	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Vaccinia	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Feces	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data
Other bacterial culture	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	No Data

Add Other Lab Values

Lab Test	Lab Test Value	Classification	Lab Test Unit
YF Immunofluorescence	1:5000 serum		
GPT	65 Liver		
GGT	322 Liver		
elevations in CRP, LDH and urea (data)	serum		
	4		

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Figure 10 Laboratory tests for the diagnosis of yellow fever and other infectious diseases.

[illegible]

Figure 11 Other Clinical Findings (Details of past medical history, vaccines and medications can be entered by opening categories).

[illegible]

Figure 12 The decision flow tree for Brighton Collaboration definitions of yellow fever-associated adverse events can be opened by tapping the space under “Decision by”.

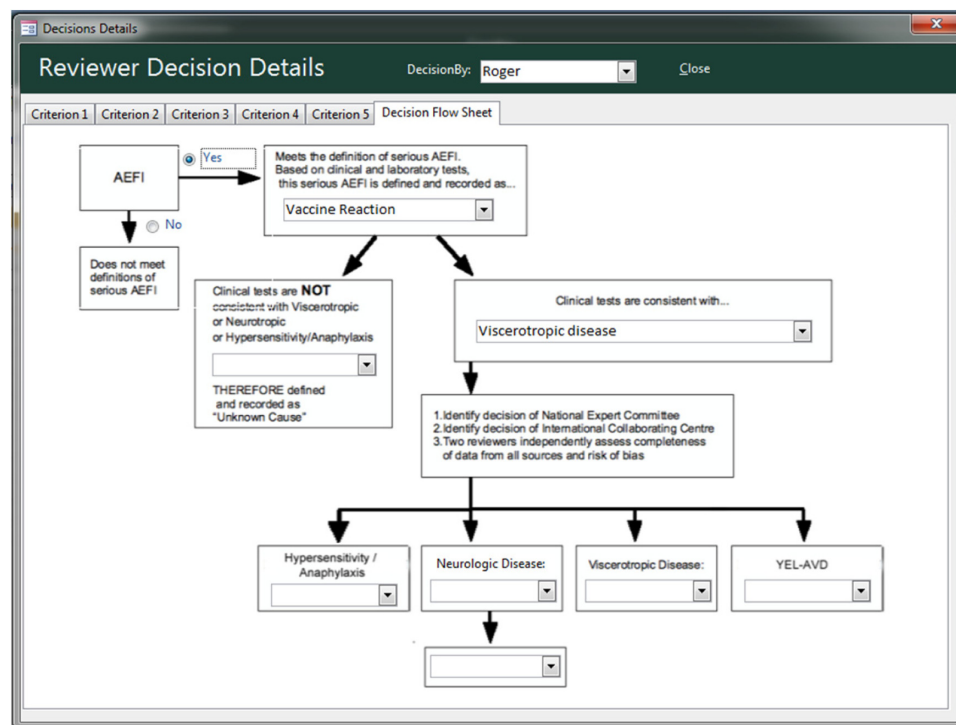


Figure 13 Decision flow tree for Brighton Collaboration yellow fever vaccine-associated severe adverse events.
Abbreviation: AEFI, adverse events following immunization.

Figure 11 Other findings

Fields include past medical history, other vaccines received, and current medications (Figure 11).

Figures 12 and 13 Decision flow tree for Brighton Collaboration yellow fever vaccine-associated decisions

Figure 12 shows how to open the Decision tree, and Figure 13 uses all the data captured in the previous eleven figures. The decisions section of the database allows for multiple reviewers to make an evaluation of the case. By tapping on the top leftmost area five criteria panels and a decision panel open up (Figure 12).

All evaluations are made using the logic: 1a) is the method by which the authors selected the case clearly described? b) Did the authors assess probable confounders in the past medical history? c) Did the authors address probable confounders from medications, vaccines or other interventions? 2) Is there complete clinical data for the case? 3) Is there complete detection of SAEs due to yellow fever vaccination with sensitive, specific, and valid outcome measures? 4) Is there complete assessment of probable confounders: other infections, illnesses? 5) Is the judgment on this case that it meets the Brighton Collaboration criteria and what level does it meet? 6) A decision flow sheet selecting the Brighton

Collaboration diagnosis and level of diagnostic certainty. (If a case met eg, both encephalitis 2 and ADEM 3 criteria, the principal classification was the higher one, ie, encephalitis 2 and the secondary classification was ADEM 3).

Conclusion

Researchers can modify the ACCESS database to assess other vaccines using Panel 1, modifying Panels 10–12, and adding panels for the criteria to assess other vaccines. The database is intended to be adapted by researchers either who wish to assess published cases of potential SAEs attributed to other vaccines, or are in the field and wish to assess reported SAEs during vaccination campaigns (they could modify or simplify the panels in this database). In the case of published cases data integrity should have been assured by the publishing editors. In the case of databases used during vaccine campaigns the researchers would need to code and encrypt the basic identifying data for cases.

Acknowledgments

In 2010 the Global Advisory Committee on Vaccine Safety (GACVS) requested that the World Health Organization (WHO) commission an independent systematic review of the safety of yellow fever vaccine. A systematic review was prepared for the WHO and GACVS by a research team at the University of Calgary headed by Roger E Thomas. The focal

contact person for the WHO was Dr Alejandro Costa with Dr Rosamund Lewis. There was extensive correspondence with the WHO focal person and Dr Rosamund Lewis, with additional correspondence with Dr Sergio Yactayo. The literature search for the current article is partly based on the literature search for the commissioned systematic review. The initial literature search and systematic review was funded by The Global Alliance for Vaccines and Immunization (GAVI).

Disclosure

The authors have no conflicts of interest to disclose.

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