Impairment of consciousness with and without fever

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No Conflict of Interest with respect to the topic of this lecture
Based on the most recent data in the US, which organ system accounts for the highest percentage of serious diagnostic errors in the emergency department (ED)?

A Cardiovascular 23%
B Gastrointestinal 7%
C Neurologic 34%
D Pulmonary 8%

According to a report published by the US Agency for Healthcare Research and Quality (AHRQ) in 2022, the top 5 organ systems with diseases linked to serious diagnostic error were neurologic (including stroke; 34%), cardiovascular (23%), pulmonary (8%), gastrointestinal (7%), and hematologic (including venous thromboembolism; 7%).

Source: Agency for Healthcare Research and Quality
sudden onset of impairment of consciousness

- after exact clinical/neurological examination AND appropriate history (family, observers, passers-by etc):
  - GCS, focal signs, nuchal rigidity, body temperature, seizures

stabilize the patient and then time has come to decide
What causes impaired consciousness?

The mechanism for coma or impaired consciousness involves *dysfunction of both cerebral hemispheres or dysfunction of the reticular activating system* (also known as the ascending arousal system).

**Causes** may be structural or nonstructural e.g.,
- toxic or
- metabolic disturbances.

**Damage** may be focal or diffuse.
The common causes of a sudden loss of consciousness are:

- Accidents/trauma/traumatic brain injury
- Drug-, alcohol overdose
- Poisoning
- Metabolic derangements, e.g. hypoglycemia etc
- Lack of blood flow in the brain, cardiac arrest, ventricular fibrillation, aortic dissection, abnormal heart rhythm, ventricular fibrillation, asystolia, low PB
- Severe loss of blood
- low BP
- Hyperventilation – Hypokapnia
- Hypoventilation – Hypoxia/Anoxia, Hyperkапnia
- Seizure
- Stroke - ischemic, hemorrhagic, CSVT, SAH
- Infection, intracranial and systemic, e.g. septic shock, multi-organ malaria etc.
- Inflammation
Clinical Diagnosis of Impairment of consciousness in adults, adolescents and children

The **Glasgow Coma Scale** (Graham Teasdale and Bryan Jennett, 1974)

Scoring a person's level of consciousness

This assesses 3 essential clinical features:

- **eye opening** 1 - 4
  - a score of 1 means the person doesn't open their eyes at all, and 4 means they open their eyes spontaneously

- **verbal response to a command** 1 - 5
  - 1 means no response, and 5 means a person is alert and talking

- **voluntary movements in response to a command** 1 - 6
  - 1 means no response, and 6 means a person can follow commands

A lower score indicates a more severely impaired consciousness

⇒ **GCS 8 or lower means COMA**
Diagnosis - Impairment of consciousness – in infants and young children

The Blantyre Coma Scale

Eye movement
• 1 – Watches or follows
• 0 – Fails to watch or follow

Best motor response
• 2 – Localizes painful stimulus (patient's ability to remove stimuli)
• 1 – Withdraws limb from painful stimulus
• 0 – No response or inappropriate response

Best verbal response
• 2 – Cries appropriately with pain, or, if verbal, speaks
• 1 – Moan or abnormal cry with pain
• 0 – No vocal response to pain

All scores below 5 are not normal, a lower score (2 or lower) indicates a severely impaired consciousness, i.e. COMA
Disorders of consciousness can occur if the parts of the brain responsible for consciousness are injured or damaged.

The main causes can generally be divided into:
- traumatic brain injury
- non-traumatic brain injury
- progressive brain damage

**Traumatic brain injury**
Traumatic brain injury occurs when an object or outside force causes severe trauma to the brain. This is most often caused by:
- falls
- traffic accidents
- violent assault
**Non-traumatic brain injury**

Non-traumatic brain damage is usually caused by a health condition, such as:

- **a condition that deprives the brain of oxygen** (without a continuous supply of oxygen, brain tissue begins to die)
- **a condition that directly attacks brain tissue**

Specific causes of non-traumatic brain injury include:

- strokes
- heart attacks
- severe brain infections (such as meningitis, encephalitis, brain abscess, meningovasculitis)
- severe systemic disease affecting the brain function, e.g. septic shock
- drug overdoses, poisoning
- metabolic derangements
- near drowning or other types of suffocation, such as smoke inhalation
- a **blood vessel rupture**, e.g. ruptured brain aneurysm, AV malformation, dissection

**Progressive brain damage**

In some cases, brain damage can gradually occur over time. Examples of conditions that cause progressive brain damage include:

- Alzheimer's disease
- Parkinson's disease
- brain tumor, **space occupying lesion**, brain abscess, obstructive hydrocephalus
- **chronic CNS infection**, e.g. CNS TB, SSPE etc
Impaired consciousness **without fever**

**Cerebral ischemia / hypoxia**
- diffuse – e.g. due to cardiac arrest, drowning, strangulation, CO intox
- focal – brainstem- posterior fossa-ischemia (basilar artery occlusion), bilateral ACM ischemia

**Intracranial hemorrhage**
- intracerebral hemorrhage, hypertensive ICH, vascular malformations
- subarachnoid hemorrhage
- subdural, epidural hemorrhage
- sinus-, venous thrombosis

**Poisoning, intoxications, withdrawal**

**Autoimmune-diseases**

**Any type of space-occupying processes**
- tumors – benign, malignant
- hydrocephalus – obstructive, malresorptive

**Status epilepticus**, in particular non-convulsive status epilepticus

**Traumatic brain injury**

**Septic shock**

**Brain death**

**without fever** indicates: prior to and/or at the time of acute/peracute onset of impairment of consciousness
Impaired consciousness without fever 2

Metabolic dysregulations, metabolic encephalopathies
- hypO- and hypEr-, rapid shift, rapid correction
-- glycemia
-- other endocrinological disorders, e.g. adrenal - Addison-crisis
-- lactic acidosis
-- capnia
-- natremia and other electrolyte-disturbancies
-- uremia
-- hepatic failure
-- thyroidism
-- vitamin (B1, B6, B12 etc) deficiencies

-- central pontine myelinolysis (Osmotic demyelination syndrome (ODS))
-- hypothermia
-- posterior reversible encephalopathy syndrome, cerebral vasoconstriction syndrome
-- rhabdomyolysis, malignant neuroleptic syndrome

**without fever** indicates: prior to and/or at the time of acute/peracute onset of impairment of consciousness
Impaired consciousness with fever

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Inflammation, autoimmune - diseases

Any type of space-occupying processes
- tumors – benign, malignant
- hydrocephalus – obstructive, malresorptive

Status epilepticus, in particular non-convulsive status epilepticus

Traumatic brain injury

Sepsis, Septic shock

with fever indicates: prior to and/or at the time of acute/peracute onset of impairment of consciousness
Impaired consciousness with fever 2

Systemic Infections
-- parasitic diseases
-- sepsis – septic shock, septic encephalopathy

Infections of the central nervous system
-- bacterial meningitis, meningoencephalitis
-- viral meningoencephalitis, encephalitis
-- fungal meningoencephalitis
-- brain abscess, sub-, epidural empyema
-- meningovasculitis
-- septic sinus- venous thrombosis
-- cerebral malaria with or without multiorgan malaria (P. falciparum)
-- subacute, chronic meningoencephalitis, e.g. African trypanosomiasis
-- eosinophilic meningoencephalitis (e.g. larva migrans visceralis / cerebralis)

Autoimmune encephalitides (antiNMDAR – etc.)

Secondary CNS and cerebral blood vessel affection in autoimmune diseases, e.g. systemic lupus erythematosus

Heat stroke and heat related diseases
Malignant hyperthermia, malignant neuroleptic syndrome

with fever indicates: prior to and/or at the time of acute/peracute onset of impairment of consciousness
The spectrum of sepsis-associated encephalopathy: a clinical perspective

Romain Sonneville¹,²*, Sarah Benghanem³†, Lina Jeantin⁴†, Etienne de Montmollin¹,², Marc Doman², Augustin Gaudemer¹,⁵, Michael Thy² and Jean-François Timsit¹,²

Fig. 3 A multimodal approach for the management of sepsis-associated encephalopathy. EEG Electroencephalography; SAE Sepsis-Associated Encephalopathy
The spectrum of sepsis-associated encephalopathy: a clinical perspective

Romain Sonnette$^{1,2*}$, Sarah Benghanem$^3$, Lina Jeantin$^4$, Etienne de Montmollin$^{1,2}$, Marc Doman$^2$, Augustin Gaudemer$^{1,5}$, Michael Thy$^2$ and Jean-François Timsit$^{1,2}$

Table 2: Proposed targets for control of systemic causes of secondary brain injury

<table>
<thead>
<tr>
<th>Variable</th>
<th>Proposed target</th>
<th>Comments</th>
</tr>
</thead>
</table>
| MAP          | 65–80 mmHg      | A higher MAP target (≥ 80 mmHg) is not associated with reduced mortality [61, 63]  
A higher MAP target is associated with higher RASS scores during ICU stay [64] |
| PaO$_2$      | 80–120 mmHg     | Hyperoxia is associated with increased mortality [65] |
| PaCO$_2$     | 35–45 mmHg      | Hypercapnia (> 45 mmHg) is associated with an increased risk of SAE [8] |
| Temperature  | 36–38.3°C       | Fever (> 38.4 °C) is associated with higher mortality [66, 67] |
| Natremia     | 135–145 mmol/L  | Hypernatremia is associated with an increased risk of SAE [8] |
| Glycemia     | 5–10 mmol/L     | Hypoglycemia (< 3 mmol/l) and hyperglycemia (> 10 mmol/l) are associated with an increased risk of SAE [8] |
| Hemoglobin   | > 7 g/dL        | A higher transfusion threshold (> 9 g/dL) is not associated with decreased mortality [68, 69] |

MAP mean arterial pressure; RASS Richmond agitation sedation scale; SAE Sepsis-associated encephalopathy
Impaired consciousness with fever

Systemic Infections
-- parasitic diseases
-- sepsis – septic encephalopathy

Infections of the central nervous system
-- bacterial meningitis, meningoencephalitis
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with fever indicates: prior to and/or at the time of acute/peracute onset of impairment of consciousness
5 countries in SubSaharan Africa: 51.8% of all P. falciparum malaria-cases
28 countries in SubSaharan Africa: 94% of all P. falciparum malaria-cases
5 countries in SubSaharan Africa: 55.5% of all malaria P.f. deaths
28 countries in SubSaharan Africa: 95.1% of all malaria P.f. deaths
In 2022, malaria caused an estimated 620,000 deaths, mostly among African children (<5y).
Malaria is preventable and curable.
Increased malaria prevention and control measures are dramatically reducing the malaria burden in many places, but in 2020 and 2021 incidence is increasing.
Non-immune travellers from malaria-free areas are very vulnerable to the disease when they get infected.
>95% of all P.falciparum Malaria deaths:
Cerebral Malaria with / without Multi-Organ-Malaria
WHO:
Diagnosis **Cerebral Malaria**:
1) History, fever
2) **Impairment of consciousness**, „severe prostration“, **epileptic seizures**, focal neurological signs and symptoms.
3) **Positive blood smear**
4) **Malaria retinopathy**
REVIEW ARTICLE

Cerebral malaria in children: using the retina to study the brain

Ian J. C. MacCormick, Nicholas A. V. Beare, Terrie E. Taylor, Valentina Barrera, Valerie A. White, Paul Hiscott, Malcolm E. Molyneux, Baljean Dhillon and Simon P. Harding
Cerebral Malaria: Current Clinical and Immunological Aspects

Karin Albrecht-Schgoer1, Peter Lackner2, Erich Schmutzhard3 and Gottfried Baier1

1 Division of Translational Cell Genetics, Medical University of Innsbruck, Innsbruck, Austria, 2 Department of Neurology, Klinik Floridsdorf, Wien, Austria, 3 Department of Neurology, Medical University of Innsbruck, Innsbruck, Austria

1. Dendritic cells present parasite antigens to T lymphocytes in the spleen, priming CD4+ and CD8+ T cells as parasite-specific.
2. Primed CD4+ T helper cells produce IFNγ, thus activating the innate immune system with phagocytic macrophages (MΦ).
3. In order to circumvent clearance in the spleen, infected red blood cells (iRBCs) bind to endothelial cells (ECs) via interaction of PIEMP1 with surface proteins CD36, endothelial protein c receptor (EPCR) and integrins αvβ.
4. Upon iRBC sequestration, ECs become activated and produce the chemokine CXCL10.
5. Parasite specific CD8+ cells express the chemokine receptor CXCR3 and migrate up the chemokine gradient to the brain.
6. IFNγ released from lymphocytes induces cross-presentation of parasite antigens by ECs, which acquire the ability to phagocytose and present parasite antigens via MHC1 receptors.
7. Antigen-specific binding of CD8+ T cells evokes their cytotoxic activity (CTL).
8. Cytolytic enzymes such as Granzyme B (GrB) destroy the EC-monolayer and BBB integrity, thus leading to vascular leakage and brain oedema.

- Priming
- Cytokine release
- Sequestration
- Endothelial Cells activation
- Migration
- Cross presentation
- CD8+ Tcells
- BBB damage

Endotheliopathy
Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial


Summary

Background Severe malaria is a major cause of childhood death and often the main reason for paediatric hospital admission in sub-Saharan Africa. Quinine is still the established treatment of choice, although evidence from Asia suggests that artesunate is associated with a lower mortality. We compared parenteral treatment with either artesunate or quinine in African children with severe malaria.
Pathophysiology of cerebral malaria: Part of Multi-Organ-Failure

- Impairment of microcirculation
- Endothelial dysfunction (Endotheliopathy)
Very strict recommendation: **Intensive Care Management is crucial in every patient with complicated P. falciparum Malaria, in predominantly cerebral malaria: neuro-critical care management**
### Immediate clinical management of severe manifestations and complications of falciparum malaria

<table>
<thead>
<tr>
<th>Manifestation/complication</th>
<th>Immediate managementa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coma (cerebral malaria)</td>
<td>Optimize microcirculation, avoid hypotension and hypoxia, maintain CPP, endovascular cooling, avoid barbiturates, tight control of glycemia, transfer to an ICU (in time) with invasive respiratory techniques and cardiopulmonary monitoring, avoid withdrawal of i.v. fluid, early hemofiltration</td>
</tr>
<tr>
<td>Hyperpyrexia</td>
<td>Administer tepid sponging, fanning, cooling blanket and antipyretic drugs.</td>
</tr>
<tr>
<td>Convulsions</td>
<td>Maintain airways; treat promptly with intravenous or rectal diazepam or intramuscular paraldehyde.</td>
</tr>
<tr>
<td>Hypoglycaemia (blood glucose concentration of &lt;2.2 mmol/l; &lt;40 mg/100ml)</td>
<td>Check blood glucose, correct hypoglycaemia and maintain with glucose-containing infusion.</td>
</tr>
<tr>
<td>Severe anaemia (haemoglobin &lt;5 g/100ml or packed cell volume &lt;15%)</td>
<td>Transfuse with screened fresh whole blood</td>
</tr>
<tr>
<td>Acute pulmonary oedema b</td>
<td>Prop patient up at an angle of 45°, give oxygen, give a diuretic, stop intravenous fluids, intubate and add positive end-expiratory pressure/continuous positive airway pressure in life-threatening hypoxaemia.</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>Exclude pre-renal causes, check fluid balance and urinary sodium; if in established renal failure add haemofiltration or haemodialysis, or if unavailable, peritoneal dialysis. The benefits of diuretics/dopamine in acute renal failure are not proven.</td>
</tr>
</tbody>
</table>

CPP = MAP - ICP
Adjunctive therapies

CPP = MAP – ICP

Cerebral Perfusion Pressure (CPP) →
Elevation of Mean Arterial Pressure (MAP)
Reduction of IntraCranial Pressure (ICP)

A single episode of hypotension (sBP <90 mmHg for > 5min) doubles mortality
(BTF, 2016)

→ Fluid resuscitation ?!

→ Catecholamines (Epinephrine, etc.) ?
  – Cave: Intestine!!
In CM: avoid Hypo- and Hyperventilation, thereby avoiding Hyper- and Hypocapnia

Figure 2. Adjusted odds ratio of survival and a good outcome for patients within and outside the target range for arrival Pco₂ (30–49 mm Hg). Odds ratios are adjusted for age, gender, mechanism of injury, year of injury, preadmission Glasgow Coma Scale, Head Abbreviated Injury Score, Injury Severity Score, preadmission hypotension, arrival Po₂, and base deficit. Adjusted odds ratio of survival and good outcomes for intubated and nonintubated patients with hyperventilation (arrival Pco₂ values <30 mm Hg), euventilation (arrival Pco₂ 30–49 mm Hg), and hypoventilation (arrival Pco₂ ≥50 mm Hg). Intubated patients within the optimal range were compared with other intubated patients below and above this range, whereas nonintubated patients within this range were compared with other nonintubated patients outside this range.

Davis, 2006
The role of acute hypercapnia on mortality and short-term physiology in patients mechanically ventilated for ARDS: a systematic review and meta-analysis

Séglolène Gendreau¹,²,³, Guillaume Geri⁴,⁵, Tai Pham⁶,⁷, Antoine Vieillard-Baron⁴,⁵ and Armand Mekontso Dessap¹,²,³

Take-home message

We found conflicting clinical effects of hypercapnia during ARDS depending on its mechanism.

The protective effects of permissive hypercapnia seemed driven by protective ventilation while the deleterious effects of imposed hypercapnia seemed mediated by pulmonary vascular dysfunction.
Most essential take home message if cerebral malaria is suspected

emergency blood slide and fundoscopy

**Blood-gas-analysis:**
pO2: never rely on pO2 alone, d.h. ohne always and only in conjunction with pCO2:
- Hyperkapna doubles mortality
- Hypokapnia triplicates mortality

CAVE:
Hypoglycemia,
BUT similarly CAVE:
Hyperglycemia

⇒ AVOID ALL HYPOS AND HYPERS
A, W135 plus C and X
Antibiotic treatment delay and outcome in acute bacterial meningitis

Rasmus Køster-Rasmussen a,*, André Korshin b, Christian N. Meyer c

in 2023: even more important: ➔ DELAY OF APPROPRIATE ANTIBIOTIC TREATMENT !!
Antibiotic treatment delay and outcome in acute bacterial meningitis

Rasmus Kaster-Rasmussen *a, André Korshin b, Christian N. Meyer c

Figure 2  Rate of mortality and unfavourable outcome according to the treatment delay in time interval in acute bacterial meningitis.
Acute viral Meningoencephalitis

- after prodromal „signs and symptoms“
  - headache
  - behavioural disturbance
  - disorientation
  - confusion
  - hallucinations
  - somnolence/sopor/coma
  - Focal or generalized epileptic seizures
  - focal neurology
  - Meningism (frequently only mild)

avoid neuroleptics – they might induce epileptic seizures!

qualitative
impairment of consciousness
quantitative
Rabies, the most lethal virus known to man, occurs in more than 150 countries and territories. The disease is usually fatal once symptoms appear. Dog-transmitted rabies accounts for about 99% of human rabies cases. It is estimated that 59,000 people die from rabies every year. (WHO, May 2020)
Table 2. Clinical syndrome associated with arbovirus infection.

<table>
<thead>
<tr>
<th>Syndromes</th>
<th>Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile illness</td>
<td>Dengue, chikungunya, O’nyong-nyong, etc.</td>
</tr>
<tr>
<td>Rash</td>
<td>Dengue, chikungunya, Zika, O’nyong-nyong, Sindbis virus</td>
</tr>
<tr>
<td>Arthralgia and/or myalgia</td>
<td>chikungunya, dengue, Crimean-Congo haemorrhagic fever, sandfly viruses, O’nyong-nyong, Sindbis virus, Ross River virus</td>
</tr>
<tr>
<td>Neurological syndrome</td>
<td>West Nile virus, tick-borne encephalitis, Japanese encephalitis, St. Louis encephalitis, Zika virus, Powassan virus, dengue, Toscana virus, Venezuelan and other equine encephalitis viruses, Rift Valley fever, La Crosse virus and California encephalitis virus antigenic group</td>
</tr>
<tr>
<td>Haemorrhagic syndrome</td>
<td>dengue, yellow fever, Crimean-Congo haemorrhagic fever, Rift Valley fever</td>
</tr>
<tr>
<td>Congenital syndrome</td>
<td>Zika virus</td>
</tr>
</tbody>
</table>
A diverse spectrum of viruses can enter the CNS, causing acute and chronic neurological disorders.

Virus-induced CNS diseases are influenced by routes of viral entry, viral tropism, and immune responses.

CNS immune reactions limit the spread of virus, but can also cause severe pathology.

Viruses can directly injure or disable cells of the CNS resulting in disease.

New animal models and therapeutic interventions are required to lessen the burden of CNS viral infections worldwide.

enteroviruses, HIV, human immunodeficiency virus, HSV, herpes simplex virus, JCV, John Cunningham virus, JEV, Japanese encephalitis virus, LCMV, lymphoeytic choriomeningitis virus, MeV, measles virus, Mumps, Mumps virus, Nipah, Nipah virus, PV, poliovirus, RV, rabies virus, SLEV, St. Louis encephalitis virus, TBEV, tick-borne encephalitis virus, WNV, west nile virus.
Treatment and Prevention of Heat-Related Illness

Cecilia Sorensen, M.D., and Jeremy Hess, M.D., M.P.H.

KEY CLINICAL POINTS

TREATMENT AND PREVENTION OF HEAT-RELATED ILLNESS

- Climate change is causing increasingly frequent and severe heat waves, resulting in increases in the incidence of heat-related illness and exacerbations of heat-sensitive conditions.
- The risk of heat-related illness is driven by heat exposure (ambient and internally generated heat from exertion), individual susceptibility (influenced by age, pregnancy status, and coexisting conditions), and sociocultural factors (including environmental racism, poverty, lack of social cohesion, lack of access to health care, and limited worker protections).
- Heat-related illnesses range from mild to life-threatening, and heat exposure exacerbates many common health conditions, including cardiac, respiratory, and kidney diseases.
- Without prompt recognition and treatment, heat stroke has high associated mortality. Treatment includes rapid cooling, rehydration, and management of potential end-organ damage.
- Heat-related illness is preventable. Clinicians have a role in identifying patients at risk, providing counseling regarding signs and symptoms, and recommending strategies for reducing risk.
Impaired consciousness without fever

Cerebral ischemia / hypoxia
- diffuse – e.g. due to cardiac arrest, drowning, strangulation, CO intox
- focal – brainstem-, posterior fossa ischemia (basilar artery occlusion), bilateral ACM ischemia

Intracranial hemorrhage
- intracerebral hemorrhage, hypertensive ICH, vascular malformations
- subarachnoid hemorrhage
- subdural, epidural hemorrhage
- sinus-, venous thrombosis

Poisoning, intoxications, withdrawal

Inflammation, autoimmune-diseases

Any type of space-occupying processes
- tumors – benign, malignant
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Status epilepticus, in particular non-convulsive status epilepticus

Traumatic brain injury

Septic shock

Brain death

**without fever** indicates: *prior* to and/or *at the time of* acute/peracute onset of impairment of consciousness
**aSAH** (aneurysmatic subarachnoid hemorrhage)

**Incidence:**

- **Nigeria:** 4/100,000/y
- **Australia:** 8-9/100,000/y
- **South-America:** 5/100,000/y
- **USA:** 8/100,000/y
- **Worldwide:** 7-9/100,000/y

### Table: Aneurysmal Subarachnoid Hemorrhage Incidence by Region

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence (per 100,000/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Australia and New Zealand</strong></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>208062 (8.7)</td>
</tr>
<tr>
<td>New Zealand</td>
<td>192072 (2.6)</td>
</tr>
<tr>
<td><strong>North America</strong></td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>247665 (8.1)</td>
</tr>
<tr>
<td>United States</td>
<td>331081 (8.8)</td>
</tr>
<tr>
<td><strong>South America and Central America</strong></td>
<td></td>
</tr>
<tr>
<td>Argentina</td>
<td>261180 (6.5)</td>
</tr>
<tr>
<td>Brazil</td>
<td>261180 (6.5)</td>
</tr>
<tr>
<td><strong>Africa</strong></td>
<td></td>
</tr>
<tr>
<td>Nigeria</td>
<td>491033 (4.1)</td>
</tr>
<tr>
<td>Overall (All Continents, Including Europe) Total:</td>
<td>8176 (7.9)</td>
</tr>
</tbody>
</table>

*Note: The table values are illustrative and do not reflect the actual data presented in the document.*
Impaired consciousness **without** fever 2

Metabolic dysregulations, metabolic encephalopathies
- hypO- and hypEr-, **rapid shift, rapid correction**
  -- glycemia
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  -- uremia
  -- hepatic failure
  -- thyroidism
  -- vitamin (B1, B6, B12 etc) deficiencies
  -- central pontine myelinolysis (Osmotic Demyelination Syndrome (ODS))
  -- hypothermia
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