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Editor's Note



Dr Ann Mathews

This edition of the *Communiqué*, our last for 2020, includes reports on rabies, tick bite fever, malaria, and articles on international outbreaks of significance beyond our borders.

There is also a description of the emergence of a new SARS-CoV-2 lineage in South Africa, as well as the resurgence of COVID-19 cases in the Western Cape Province. The Western Cape Province reported its first

case of COVID-19 on 9 March 2020, and it was the first province to reach a peak during the first wave. In the first wave, the highest incidence risk was reported in Overberg, followed by City of Cape Town Metropolitan, Garden Route and then Cape Winelands districts. Although not yet peaked, three districts are contributing to the current resurgence in cases; namely, Garden Route, followed by Central Karoo, and to a lesser extent the City of Cape Town Metropolitan, with incidence risk of cases exceeding those reported during the first wave in some districts. The incidence risk of hospitalisation in the Garden Route and Central Karoo districts is reported to be much higher during the current resurgence of cases than compared to the first wave. In addition, compared to the first wave, in-hospital deaths reported during the current resurgence is higher in the Garden Route and Overberg districts. This article highlights the importance of resurgence of COVID-19 cases in the Western Cape Province, as well as nationally in all nine provinces in the country. We would like to remind our readers not to be complacent, and to continue to be responsible during this festive season – keep a physical distance from others, wear your mask and wash or sanitise your hands regularly.

We wish our readership safe, communicable-disease-free festive season. See you again in 2021.

ZOONOTIC AND VECTOR-BORNE DISEASES

An update on rabies in South Africa

No new cases of human rabies have been reported in South Africa over the past month. In 2020, as of 15 December, rabies accounted for six laboratory-confirmed human deaths in the country, reported from KwaZulu-Natal (n=5) and Limpopo (n=1) provinces. In addition, three probable cases were also reported from KwaZulu-Natal (n=1), Limpopo (n=1) and the Eastern Cape (n=1) provinces. These cases fit with the case definition for probable rabies given the clinical and exposure histories; however, laboratory confirmation for rabies was not possible. The total number of cases in 2020 is lower compared to the previous year where 10 laboratory-confirmed and six probable cases were reported. It is unclear how the emergence of COVID-19 may have affected the recognition and reporting of human rabies cases in South Africa (Figure 1).

Despite being a vaccine-preventable disease, dog-mediated human rabies continues to be reported from low- and middle-income countries. A global initiative to achieve zero human fatalities from dog-mediated rabies by

2030 has been initiated by WHO and partners.¹ The primary tools for meeting this goal are: mass dog vaccination to disrupt transmission in domestic dog populations that maintain infection, adequate post-exposure prophylaxis (PEP) for rabies-exposed persons to prevent the fatal onset of disease, along with education to promote its successful uptake. Various preventive initiatives have been effective in preventing dog-mediated human rabies deaths, including dog population management, parental dog vaccination programmes, access to human rabies vaccinations, and a bite prevention and wound care education programme. It can be difficult to incorporate these strategies in resource-poor settings, and the greatest challenge is maintaining sufficient herd immunity in dog populations, especially when free-roaming.²

Please visit the NICD website for more information on rabies and disease prevention: <https://www.nicd.ac.za/diseases-a-z-index/rabies/>.

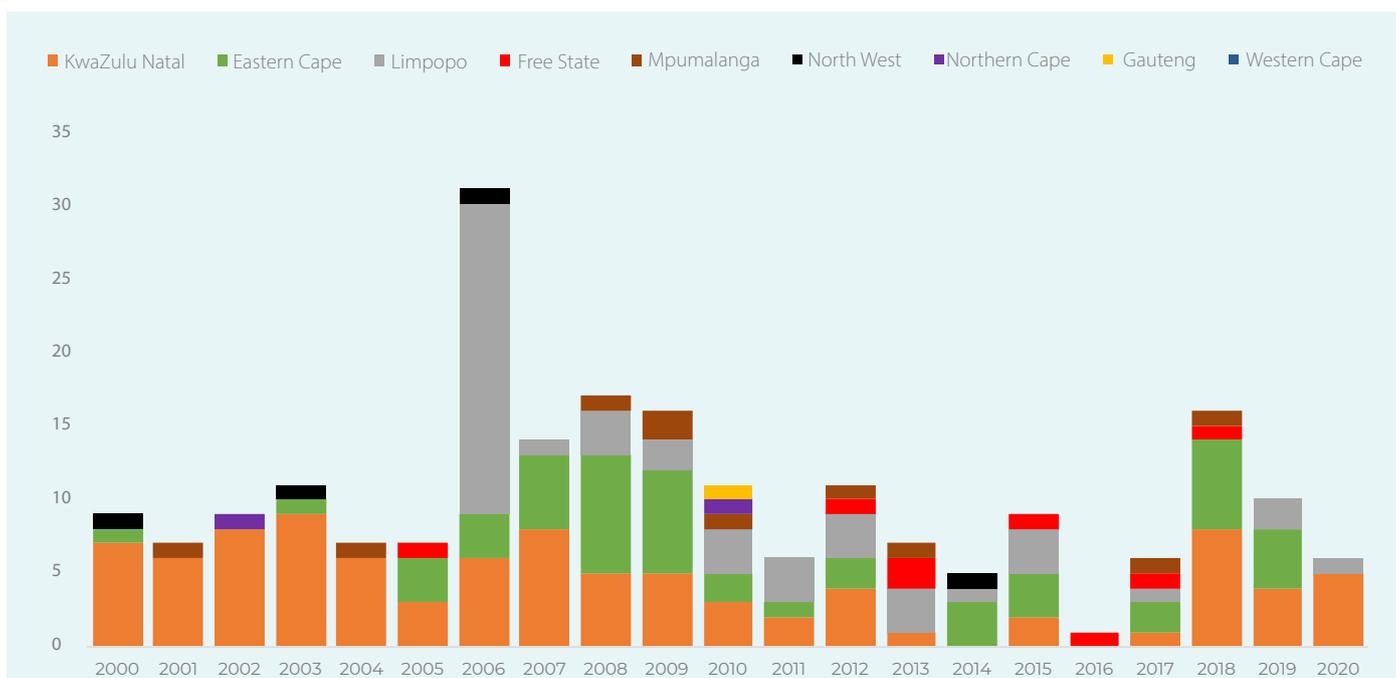


Figure 1. Laboratory-confirmed cases of human rabies in South Africa, 2000 - 2020.

1. WHO Rabies Modelling Consortium. Zero human deaths from dog-mediated rabies by 2030: perspectives from quantitative and mathematical modelling. *Gates Open Res.* 3, 1564 (2019).

2. Wallace, R. M. et al. Role of Oral Rabies Vaccines in the Elimination of Dog-Mediated Human Rabies Deaths. *Emerg. Infect. Dis.* 26, 1–9 (2020).

ZOONOTIC AND VECTOR-BORNE DISEASES

Severe tick bite fever

Tick bite fever must be considered as part of the differential diagnosis in patients with acute febrile illness, particularly when there is a supportive epidemiological history, negative laboratory tests for malaria, no response to the usual empiric antibiotics for 'septicaemia' and evidence of multisystem pathology, with or without bleeding. Two fatal cases of tick bite fever were recently referred to the NICD for consideration as possible Crimean-Congo haemorrhagic fever (CCHF).

The first patient was a 57-year-old male who lived on a smallholding (with no animals) in North West Province. Due to the COVID-19-related restriction on visitors, important history about possible tick exposures and a bite mark on the neck was not elicited. He was admitted to hospital with a history of a stiff neck for 10 days with headache, diarrhoea and a maculopapular rash. The patient appeared to have a thick neck and the tick bite was not noted. Encephalitis was considered due to the history, clinical findings of confusion and disorientation, and CSF findings (polymorphonuclear cells 3/mm³, lymphocytes 17/mm³, protein 655 mg/dL; culture negative; PCR for viral pathogens negative). He was treated with ceftriaxone and acyclovir, but his condition deteriorated rapidly and he required ventilator support and renal dialysis. Laboratory results: Hb 12.4 g/dL, WCC 7.07 x10⁹/L, neutrophils 88%, lymphocytes 6.2%, eosinophils 0%; platelets 52 x10⁹/L, CRP 201 mg/L, bilirubin 88 µmol/L, AST 210 U/L, ALT 124 U/L, creatinine 341 µmol/L, urea 13.6 mmol/L, SARS-CoV-2 negative by PCR. A history of tick exposures and bite on the back of the neck was obtained from family members later in the admission. Tick bite fever was considered but the patient demised despite the introduction of ciprofloxacin and doxycycline treatment. PCR for *R. conorii* on blood was positive.

The second patient was an adult male who lived in a Free State Province town and worked in recycling. A week before the onset of his illness, he underwent ablative treatment for refractory atrial fibrillation, complicated by a minor tear in the oesophagus. He was admitted to hospital with an acute febrile illness and multi-organ failure, and was intubated, ventilated and dialysed. A very astute physician noted a lesion highly suggestive of an eschar on the chest wall in between the multiple and extensive

ecchymotic lesions. Doxycycline and ciprofloxacin were started but his condition deteriorated and he demised.

While the majority of cases of tick bite fever (TBF) are mild and uncomplicated, a number of severe cases with multi-organ pathology have been referred previously. Severe tick bite fever may be misdiagnosed as bacterial sepsis and even Crimean-Congo haemorrhagic fever (CCHF). In very ill patients, especially those requiring admission to the intensive care unit, the history of a possible tick exposure may be missed and the finding of an eschar may be particularly difficult, given that ticks frequently attach in unusual places not easily visible in a critically-ill patient. Haematological abnormalities including low white cell and platelet counts, raised transaminases, and a rash that may be petechial or maculopapular, are often reported. *Rickettsia conorii* infections are more likely to evolve to serious and complicated disease, compared with *R. africae* infections.

Routine serological tests do not distinguish between the two rickettsial species, and antibodies are often undetectable at the onset of illness. In any case, the diagnosis of TBF is primarily clinical, based on presence of fever, intense headache and an eschar, often accompanied by tender local lymphadenopathy. PCR for rickettsiae in blood has low sensitivity; however, when applied to a dry cotton wool swab from an eschar, PCR can be a useful confirmatory investigation.

If TBF is considered based on the clinical findings or as part of the differential diagnosis of a patient with 'sepsis', particularly if tick exposure is likely as a result of occupation (e.g. farmers, vets), animal contact or geographic exposure, empiric treatment should be commenced with doxycycline, the treatment of choice. In patients unable to tolerate oral treatment, particularly those who are critically ill, intravenous ciprofloxacin should be used. Experience with tigecycline is very limited with only one clinical case report of its use in severe murine typhus, although in vitro and animal studies suggest it is likely to be effective in other rickettsial infections. CCHF must be considered in critically-ill patients with no obvious eschar, on the basis of clinical and epidemiological findings (tick exposure, occupational risk, incubation period).

INTERNATIONAL OUTBREAKS OF IMPORTANCE

An update on the coronavirus disease 2019 (COVID-19) outbreak, South Africa

Resurgence of COVID-19 cases in Western Cape Province, December 2020

The Western Cape Province, in South Africa, with an estimated population of 7 005 741 in 2020, reported its first case of COVID-19 on 9 March 2020 (epidemiologic week 11). From 3 March through 5 December (week 49), there were 140 257 cases of COVID-19 reported from the Western Cape Province, of which 128 385 (91.5%) had allocation by district. At the start of the pandemic, the weekly incidence risk of cases was 2.5 cases per 100 000 persons, this increased steadily to a smaller peak in

week 21 (114.7 cases per 100 000) where it stabilised until week 25, and increased to a higher peak in week 27 (week ending on 4 July 2020) (136.0 cases per 100 000 persons). From week 28 there was a steady decline in weekly incidence risk until week 40 (15.0 cases per 100 000 persons). There has been an ongoing resurgence of cases from week 41 to 49 (21.3 to 111.5 cases per 100 000 persons), with a steep increase reported from week 46 to week 49 (Figure 2).

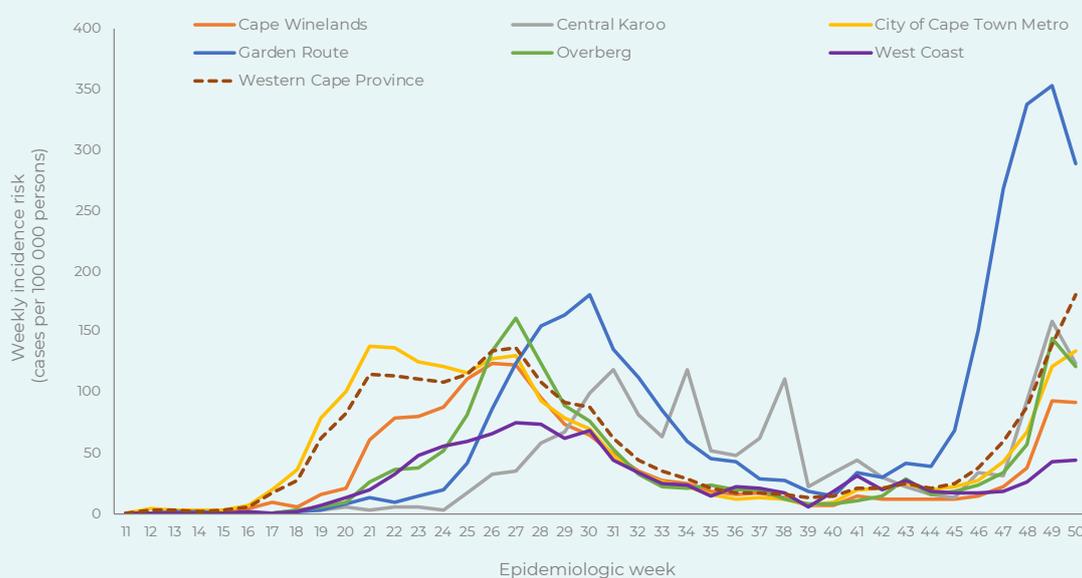


Figure 2. Weekly incidence risk of PCR-confirmed cases of COVID-19 by district and epidemiologic week, Western Cape Province, South Africa, 3 March-5 December 2020 (n=128 385, 11 872 missing district)

In week 49, Western Cape Province reported the second highest cumulative incidence risk of cases reported in South Africa to date (2 002.0 cases per 100 000 persons) and the highest weekly incidence risk (111.5 cases per 100 000 persons). Western Cape Province was the first province to reach a peak during the first wave. The first wave in the province peaked in week 27, incidence risk 136.0 cases per 100 000 persons with highest incidence risk reported in Overberg (160.4 cases per 100 000), followed by City of Cape Town (129.8 cases per 100 000), Garden Route (123.9 cases per 100 000) and Cape Winelands (121.8 cases per 100 000). Although not peaked yet, the overall highest weekly incidence risk of cases from the Western Cape in week 49 was lower (111.5 cases per 100 000) than the peak in week 27. However, the peak incidence risk reported in week 49 from two of the three districts contributing to the current resurgence in cases was higher than that reported during the first peak, Garden Route (299.4 vs 179.7 cases per 100 000) and

Central Karoo District (133.1 vs 118.5 cases per 100 000 persons). City of Cape Town District (98.6 cases per 100 000) contributed the third highest incidence risk in week 49 (Table 1).

The majority of cases in the first wave (week 11-40) were in the 20-39- (46 446/111 585, 41.6%) and 40-59-year (41 530/111 585, 37.2%) age groups. Similarly, during the resurgence in the past few weeks, majority of cases were in the 20-39- (12 005/28 672, 41.9%) and 40-59-year (10 000/28 672, 34.9%) age groups.

Hospital admissions for COVID-19 cases in the Western Cape Province peaked in week 26 (21.8 cases per 100 000 persons) and week 49 (17.6 cases per 100 000 persons) during the first and second waves respectively. City of Cape Town (14 403/18 665, 77.2%) followed by Cape Winelands District (1 916/18 665, 10.3%) contributed majority of hospital admissions during the first wave. During the second wave, City of Cape Town (2 437/4 046, 60.2%) and Garden Route (1 016/4 046, 25.1%)

INTERNATIONAL OUTBREAKS OF IMPORTANCE

districts contributed the majority of admissions. City of Cape Town reported the highest peak of weekly incidence risk for the first wave (27.0 admissions per 100 000 persons). In contrast, much higher incidence risk for admissions during the current resurgence than those reported during the first wave were reported by the Garden Route District (43.9 vs 9.8 cases per 100 000 persons) and Central Karoo District (30.6 vs. 1.3 cases per 100 000 persons).¹

The peak weekly incidence risk of deaths reported in Western Cape Province was in weeks 26 and 49 for the first and second wave, respectively. City of Cape Town District reported the majority of deaths during both peaks. Although the second wave has not yet peaked, the highest weekly incidence risk of deaths was higher during the second wave compared to the first wave, in Garden Route (10.3 vs 1.3 cases per 100 000) and Overberg (2.0 vs 1.0 cases per 100 000) districts, and was lower in City of Cape Town District (1.6 vs 5.2 cases per 100 000). Testing rates peaked to 530.5 tests per 100 000 in week 21 (first wave) and to 467.8 tests per 100 000 in week 46 (second wave).²

This summary highlights an increase in the burden of COVID-19 cases in the Western Cape Province currently, mainly driven by

Garden Route, Central Karoo and to a lesser extent the City of Cape Town Metropolitan districts, with incidence risk of cases exceeding those reported during the first wave in some districts. In addition, the incidence risk of hospitalisation in Garden Route and Central Karoo districts is much higher during the second wave. To date, in-hospital deaths reported during the second wave are higher in Garden Route and Overberg compared to the first wave; however, the trend in other districts may change due to a delay in deaths and a delay in reporting of deaths. With increasing numbers of cases, strengthening the capacity of facilities to cope with increasing demand for admissions is recommended.

References

- https://www.nicd.ac.za/wp-content/uploads/2020/12/NICD-COVID-19-Weekly-Sentinel-Hospital-Surveillance-update-Week-49-2020_.pdf
- <https://www.nicd.ac.za/wp-content/uploads/2020/12/COVID-19-Testing-Summary-Week-49-Dec-2020.pdf>

Table 1. Number and incidence risk (cumulative/weekly) of laboratory-confirmed cases of COVID-19, hospitalisations and deaths per 100 000 population during the first wave (week 11-40) and second wave (week 41-49) by district, Western Cape, South Africa, 3 March-5 December 2020 (n=128 385, 11 872 missing district)

District	Cumulative number of cases in Eastern Cape Province to date	Number of cases in weeks 11-40	Number of cases in weeks 41-49	Population mid-2020*	First wave peak weekly incidence risk of cases per 100,000 population (week 27)	Second wave peak weekly incidence risk of cases per 100 000 population (week 49)	First wave peak weekly incidence risk of admissions** per 100 000 population (week 26)	Second wave peak weekly incidence risk of admissions per 100 000 population (week 49)	First wave peak weekly incidence risk of deaths** per 100 000 population (week 25)	Second wave peak weekly incidence risk of deaths** per 100 000 population (week 49)
Cape Wine-lands	12 807	10 977	1 830	941 262	121.8	61.8	16.1	14.2	5.0	1.7
Central Karoo	1 098	786	312	75 113	34.6	133.1	1.3	30.6	0.0	0.0
City of Cape Town Metro	89 177	73 344	15 833	4 604 986	129.8	98.6	27.0	16.2	5.2	1.6
Garden Route	16 577	8 666	7 911	623 658	123.9	299.4	9.8	43.9	1.3	10.3
Overberg	4 045	3 166	879	299 908	160.4	92.7	9.0	13.0	1.0	2.0
West Coast	4 681	3 723	958	460 813	74.9	33.9	9.5	2.6	2.0	0.4
Unallocated	11 872	10 923	949							
Grand Total	140 257	111 585	28 672	7 005 741	136.0	111.5	21.8	17.5	4.4	2.3

*2020 Mid-year population Statistics South Africa;**Data on hospital admissions and deaths sourced from DATCOV report published in week 49, hospitalisations and deaths are expected to be delayed in relation to cases, in addition there may be delays in reporting.

INTERNATIONAL OUTBREAKS OF IMPORTANCE

Emergence of a new SARS-CoV-2 lineage in South Africa

The Network for Genomics Surveillance in South Africa (NGS-SA), which includes the NICD, UKZN, UCT, SUN and UFS, has been monitoring changes in SARS-CoV-2, the virus which causes COVID-19, since March 2020. While SARS-CoV-2, like all viruses, mutates with time, between March and September 2020, this virus mutated at a relatively slow rate, as evidenced by over 2 000 sequences from across eight of the nine provinces.

We have recently detected a new lineage, which is a group of mutated viruses of SARS-CoV-2 in the Eastern Cape, Western Cape and KwaZulu-Natal provinces. This lineage, named 501Y.V2, possesses between up to 20 mutations that were not previously seen in viruses from South Africa prior to September 2020. This lineage has been detected in 219 infections thus far from the three provinces mentioned previously. The spike region of this virus is under constant scrutiny, because it is used by the virus to infect human cells and is a target for neutralising antibodies. Figure 3 shows that between September and November 2020, eight lineage-defining mutations accumulated in the spike region of viral sequences in the Eastern Cape Province.

One of these spike mutations has been shown to increase binding to the human cell receptor, which could make it easier for the virus to cause infection. Two of these spike mutations reduce virus sensitivity to some antibodies, meaning that these

antibodies may not be as effective against this new mutated lineage compared to the previous lineage, which caused the initial wave of infections in South Africa. These mutations will not affect PCR testing sensitivity. The mutated lineage from the Eastern Cape Province has already been detected in 219 samples, using South Africa's current repertoire of real-time PCR tests. In addition, our tests typically detect at least two or three different SARS-CoV-2 gene targets, which serves as a backup in the case of a mutation arising in one.

Another lineage with a significant number of mutations across the genome and within the spike region has also been described in the United Kingdom (UK), and accounts for over 1 000 infections (Figure 3). The UK lineage, named 501Y.V1, is different from the South African lineage, with only one mutation, N501Y, common to both lineages.

We remain cautious about the implications of these mutations, until we perform the necessary experiments. However, we advise the public to remain vigilant and continue to follow COVID-19 protocol by wearing masks (which cover your nose, mouth and chin), washing or sanitising your hands and surfaces regularly, and keeping 1.5m distance from others as much as possible. These non-pharmaceutical interventions are still proven to prevent the spread of all SARS-CoV-2 viruses.



Figure 3. SARS-CoV-2 spike region highlighter plot. This highlighter plot displays mutations that were not present in South African sequences prior to September 2020. The horizontal axis displays each position in the sequence of the spike protein. Individual sequences are shown as a horizontal grey line with sequences from early September and those from after late September in grey and green respectively. Mutations are indicated as coloured vertical bars. Missing sequences are displayed as black bars. Three sequences from the United Kingdom 501Y.V1 lineage are included (blue).

Source: Centre for Respiratory Diseases and Meningitis, NICD-NHLS; cherylc@nicd.ac.za

SEASONAL DISEASES

Malaria

Missed malaria following COVID-19 diagnosis, with fatal outcome

A 19-year-old man in one of South Africa's malaria-endemic provinces tested positive for SARS-CoV-2 at a public clinic; the reason for testing is not known. Nine days later he presented to the clinic with headache and fever, and after two further days to a general practitioner with similar symptoms. At this stage confusion and jaundice were noted, and he was admitted to hospital. Initial assessment was of fulminant hepatitis. He was apyrexial, with low blood pressure and depressed level of consciousness. The platelet count was low; he had a raised total bilirubin level and was severely acidotic, with acute renal failure. A rapid malaria test was positive. Intravenous quinine was started, along with IV fluid resuscitation. A high parasitaemia of 11% was reported. The patient developed progressive respiratory distress requiring intubation; the clinical condition deteriorated and he demised within eight hours of admission.

This is one of several recent cases where the current focus on COVID-19 has obscured or diverted attention from a concurrent malaria infection, with tragic consequences. At this time of year when there are increases in both travel and malaria transmission, it is important to remember about the risk of malaria and the danger of missing the diagnosis. The early symptoms of both malaria and COVID-19 are similarly non-specific, namely fever,

headache, fatigue, and muscle and joint pains; more severe signs and symptoms can also be shared between these infections, e.g. respiratory difficulties (See Communiqué issue of September 2020: https://www.nicd.ac.za/wp-content/uploads/2020/09/NICD-Monthly-Communique%CC%81_Sep-2020.pdf). Unrecognised and untreated malaria can rapidly progress to severe illness with a high mortality, and we again remind readers that even non-malaria-endemic provinces (particularly Gauteng) receive imported malaria cases throughout the summer months. It is therefore mandatory that any persons presenting with fever and 'flu-like illness, if they are resident in, or have travelled within the last six weeks from, a malaria risk area, regardless of suspected COVID-19 condition and/or pending COVID-19 tests, be checked for malaria by rapid diagnostic test or blood smear microscopy, and the results obtained urgently. Finally, sometimes malaria vector mosquitoes are transported accidentally, and transmit malaria outside their normal habitats to persons with no travel history. This type of malaria should be considered in a patient with a progressively worsening febrile illness of unknown cause.

Information about malaria prevention and treatment is available at www.nicd.ac.za.

BEYOND OUR BORDERS

The 'Beyond our Borders' column focuses on selected and current international diseases that may affect South Africans travelling abroad. Numbers correspond to Figure 4 on page 9

Hepatitis E: Burkina Faso

Between 8 September and 24 November 2020, a cumulative total of 442 cases of febrile jaundice was reported in the North-Central region of Burkina Faso. A large majority of these were in the Barsalogo health district where 287 cases and 16 deaths have thus far been totalled. Of note, 15 of the 16 deaths in the district were reported in pregnant or postpartum women. The case fatality rate currently stands at 4.1%.

Testing began in early September when specimens were sent to the National Reference Laboratory for Viral Haemorrhagic Fever (NRL-VHF). Of the 14 specimens initially sent, one yielded a positive IgM result for yellow fever; nine were indeterminate and thus sent to Lapeyronie Hospital, Montpellier, France for hepatitis E testing. Here, eight of the nine samples were hepatitis E IgM positive. Hepatitis E has been confirmed in ten cases to date. This event has now been confirmed as a hepatitis E outbreak.

Case descriptions according to individual characteristics show that 67% of cases are younger than 30 years with nearly 5%

of cases being less than 5 years old. In addition, 54% were in female patients.

The public health response to this rise in hepatitis E cases has been hampered by the great social and economic strife currently facing Burkina Faso. There are many internally displaced persons in the region, most of whom are currently residing with host families and some are living in camps. Furthermore, the North-Central region is affected by the closure of health facilities due to insecurity raised from frequent attacks by unidentified armed men. The lack of essential water, hygiene, sanitation and health services only worsens the spread of this disease which is transmitted via the faecal-oral route.

Burkina Faso is also affected by the COVID-19 pandemic, and as of 6 December 2020, 3 156 COVID-19 cases and 68 deaths have been reported. The context of the COVID-19 pandemic further complicates the response to this hepatitis E outbreak.

Enterohaemorrhagic *Escherichia coli* (EHEC): Germany

Enterohaemorrhagic *Escherichia coli* (EHEC) is a human pathogen responsible for outbreaks of bloody diarrhoea and haemolytic uremic syndrome (HUS) worldwide. More than 25 cases of EHEC (also known as Shiga-toxin producing *E. coli*) are being investigated with outbreaks reported in four daycare centres in the Luetzow-Luebstorf District, Germany. Authorities warned that further testing is underway and numbers are expected to rise. Those affected currently include children, their relatives as well as a few daycare centre employees. Currently,

there have been no hospitalised cases with the majority having no to mild symptoms, and a few having severe diarrhoea.

Testing of products as well as the premises of the food processing company that supplies the daycare centres was negative. Despite multiple centres being affected, authorities believe that the pathogen entered the centres through means outside of their common food supply source. The investigation is still ongoing.

BEYOND OUR BORDERS

Malaria: Namibia

In 2020, 2 643 cases and six deaths related to malaria were recorded in the Zambezi region, Namibia. This is a dramatic rise from the 261 positive cases and one death that had been recorded at the same time last year. Regional health director Agnes Mwillima told reporters that the increase in malaria cases might be because the climate in the region is conducive for mosquitoes to breed throughout the year. She further urged the community to allow residual spraying teams access to their houses as well as to practice the standard behaviours that prevent mosquito bites, including use of mosquito repellents

and wearing clothes that covers skin.

The World Malaria Report released on 1 December stated that there were 229 million cases of malaria in 2019 compared to 228 million cases in 2018. The estimated number of malaria deaths in the world stood at 409 000 in 2019, compared with 405 000 in 2018. The World Health Organization African Region continues to carry the largest global burden of the disease, contributing 94% of the total number of malaria cases and deaths in 2019, highlighting once again the need for continued efforts to both prevent and manage the disease on this continent.



Source: Promed (www.promed.org), World Health Organization (www.who.int)

WHO AFRO UPDATE

WEEKLY BULLETIN ON OUTBREAKS AND OTHER EMERGENCIES

Week 48: 23 - 29 November 2020
Data as reported by: 17:00; 29 November 2020

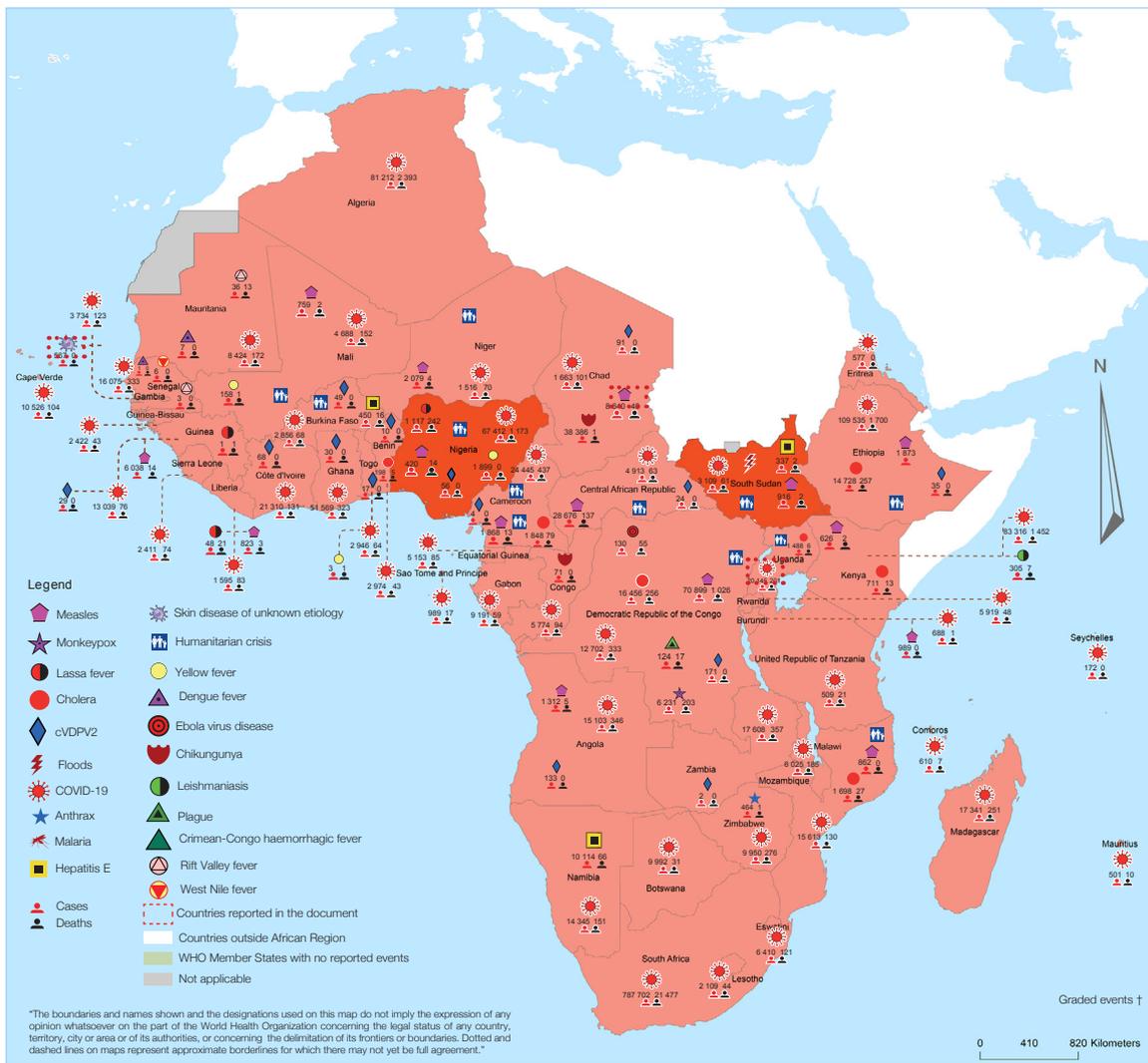


0 New event

117 Ongoing events

104 Outbreaks

13 Humanitarian crises



49 Grade 3 events	19 Grade 2 events	5 Grade 1 events	36 Ungraded events
2 Protracted 3 events	3 Protracted 2 events	3 Protracted 1 events	

Health Emergency Information and Risk Assessment

Figure 5. The Weekly WHO Outbreak and Emergencies Bulletin focuses on selected public health emergencies occurring in the WHO African Region. The African Region WHO Health Emergencies Programme is currently monitoring 117 events. For more information see link below:
<https://apps.who.int/iris/bitstream/handle/10665/337245/OEW48-2329112020.pdf>

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