PACIFIC JOURNAL OF MEDICAL SCIENCES

VOLUME 16, No. 1, May 2016

Section 1: Focus on Zika and Dengue

Section 2: Research papers

SPECIAL ANNOUNCEMENT

MANILA DECLARATION ON THE AVAILABILITY AND USE OF HEALTH RESEARCH INFORMATION IN AND FOR LOW- AND MIDDLE-INCOME COUNTRIES IN THE ASIA PACIFIC REGION

We, the participants in the Joint Meeting of the Asia Pacific Association of Medical Journal Editors (APAME), the Index Medicus of the South East Asia Region (IMSEAR), and the Western Pacific Region Index Medicus (WPRIM) held in Manila from 24 to 26 August 2015, in conjunction with the COHRED Global Forum on Research and Innovation for Health held in Manila from 24-27 August 2015, drawing on the Pre-Forum Discussions on HIFA from 20 July to 24 August 2015 *"Meeting the information needs of researchers and users of health research in low- and middle-income countries"* available at http://www.hifa2015.org/meeting-the-information-needs-of-researchers-and-users-of-health-research-2/ and the BMJ Blogs 20 July 2015 *"How can we improve the availability and use of health research in developing countries?"* available at http://blogs.bmj.com/bmj/2015/07/20/how-can-we-improve-the-availability-and-use-of-health-research-in-developing-countries/ :

CONSIDERING

That the WHO Constitution "enshrines the highest attainable standard of health as a fundamental right of every human being;" and that "The right to health includes access to timely, acceptable, and affordable healthcare of appropriate quality in tandem with "the underlying determinants of health," including" access to health-related education and information;"

That increasing the availability of quality health research information is fundamental to the successful attainment of global health and progressive realization of the right to health; and that all healthcare stakeholders (individuals, researchers, providers, professionals, leaders and policymakers) need seamless access to peer-reviewed research and information that are relevant to their respective contexts, and presented in a language they can understand;

That despite a growing momentum towards free and open access to research literature, and important initiatives, such as HINARI Access to Research In Health Programme and IRIS Institutional Repository for Information Sharing, that have helped to improve the availability of research in low- and middle-income countries, there continue to be many challenges, limitations and exclusions that prevent health research information from becoming freely and openly available to those who need it;

That the Global Health Library (GHL), Index Medicus of the South East Asia Region (IMSEAR), Western Pacific Region Index Medicus (WPRIM), and Asia Pacific Association of Medical Journal Editors (APAME)are important

collaborative initiatives that can promote and uphold the availability and use of health research information especially in and for low- and middle-income countries in the Asia Pacific Region;

CONFIRM

Our commitment to champion and advocate for the increased availability, accessibility and visibility of health research information from and to low- and middle-income developing countries through our Journals, our respective National Associations of Medical Editors, and APAME;

Our commitment to make research information freely and openly available in the right language to producers and users of health research in low- and middle-income countries through IMSEAR, WPRIM, the Asia Pacific Medical Journal Articles Central Archives (APAMED Central) and other platforms;

Our commitment to improve availability, accessibility and interoperability of the different formats of health information suitable to different users in their respective contexts including through both conventional and alternative channels of research dissemination such as new and social media, mobile and disruptive technologies, blogging and microblogging tools and communities, and communities of practice;

CALL ON

Member States of and governments in the South East Asia and Western Pacific Regions, in collaboration with stakeholders from the non-government and private sectors to formulate and implement policies and certification schemes such as the COHRED Fairness Index™ (CFI) that promote free and open availability of health research information for both its producers and users, especially in low- and middle-income countries;

Stakeholders from the public and private sectors, national and international organizations, universities and academic societies, and discussion groups such as Healthcare Information for All (HIFA2015) to support IMSEAR, WPRIM, the GHL, APAMED Central, and develop Integrated Scholarly Information Systems and similar initiatives, in order to ensure the free, open and global accessibility of health research done in the South East Asia and Western Pacific Regions;

The Eastern Mediterranean Association of Medical Editors (EMAME), the Forum for African Medical Editors (FAME), the European Association of Science Editors (EASE), the World Association of Medical Editors (WAME), the International Committee of Medical Journal Editors (ICMJE), the Committee on Publication Ethics (COPE) and other editors' and publishers' associations to support APAME in implementing various activities, guidelines and practices that would improve the quality, availability and accessibility of scientific writing and publications in

the Asia Pacific Region and the world;

Bibliographic, Citation and Full-Text Databases such as PubMed, Global Health Database (CAB Direct), the Directory of Open Access Journals (DOAJ), EMBASE, SciELO Citation Index, Scopus, and the Web of Science to review their policies and processes for indexing Journals from low- and middle-income countries, as well as making health research information freely and openly available to users in these countries who cannot afford to pay for it;

COMMIT

Ourselves and our Journals to publishing innovative and solution-focused research in all healthcare and related fields such as health promotion, public health, medicine, nursing, dentistry, pharmacy, other health professions, health services and health systems, particularly health research applicable to low- and middle-income countries;

Ourselves and our publishers to disseminating scientific, healthcare and medical knowledge fairly and impartially by developing and using Bibliographic Indices, Citation Databases, Full-Text Databases and Open Data Systems including, but not limited to, such Regional Indexes of the Global Health Library as IMSEAR, WPRIM and APAMED Central;

Our organization, APAME, to building collaborative networks, convening meaningful conferences, and organizing participative events to educate and empower editors, peer reviewers, authors, librarians and publishers to achieve real impact, and not just impact factor, as we advance free and open access to health information and publication that improves global health-related quality of life.

26 August 2015, Manila

apame@wpro.who.int

This declaration was launched at the 2015 Convention of the Asia Pacific Association of Medical Journal Editors (APAME) held in Manila from 24 to 26 August 2015. It is concurrently published by Journals linked to APAME and listed in the Index Medicus of the South East Asia Region (IMSEAR) and the Western Pacific Region Index Medicus (WPRIM).It is co-published with special permission in the Pacific Journal of Medical Sciences that was represented in the APAME2015 Convention and Joint Meeting with the Western Pacific Region Index Medicus Regional Journal Selection Committee Meeting.

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INFORMATION

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ZIKA VIRUS PREPAREDNESS AND RESPONSE: OPERATIONAL ISSUES, CHALLENGES, AND OPPORTUNITIES

[1]*John O. Davies-Cole, [1] Preetha J. Iyengar, [2] Andrew K. Hennenfent, [1] Sasha A. McGee, [3]Vito R. DelVento, [1] Fern M. Johnson-Clarke and [4] Anicet G. Dahourou

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ABSTRACT:
On February 1, 2016, the World Health Organization (WHO) declared that the Zika virus disease (ZVD) outbreak constituted a public health emergency of international concern. ZVD is usually mild with symptoms lasting for several days to a week after being bitten by an infected mosquito. However, there have been reports of increased microcephaly cases and Guillain-Barré syndrome associated with the infection. Due to the large number of international travelers visiting the Washington, District of Columbia (DC) metropolitan area, health care workers within the city were asked to screen all patients about their recent travel history outside the United States (US). In addition, Washington, DC has a large population of frequent travelers, since many residents work in governmental or international non-governmental organizations. Our challenge was to not only develop and optimize a DC Zika surveillance protocol, but also to develop a regional protocol in collaboration with the neighboring jurisdictions of Maryland and Virginia. This report discusses planning for ZVD surveillance and response, including some ongoing challenges and opportunities to build and strengthen public health capacity to respond to emerging infectious diseases.

Keywords: Zika virus, surveillance, *Aedes aegypti, Aedes albopictus*, Washington, DC
Submitted April 2016, Accepted May 2016

INTRODUCTION:

Zika virus is a flavivirus generally transmitted by mosquitos that have recently spread throughout Central and South America, the Caribbean, and Mexico. The lack of immunity to the virus and the presence of suitable and efficient vectors effectively spread the disease to vulnerable countries and regions. On February 1, 2016, the alarming threat from this disease caused the World Health Organization (WHO) to declare that "the recent cluster of neurological disorders and neonatal malformations reported in the Americas constituted a public health emergency of international concern" [1]. Although the disease was reported in Uganda in 1947, over the last few decades only occasional outbreaks have been reported in a few countries [2]. In contrast, the recent outbreak that started in Brazil in May 2015 has spread to several

surrounding countries. Since 2007, 55 countries in the Americas, Asia, Africa and Oceania have identified local transmission of the virus but not at the scale of the current epidemic that has affected almost 1.5 million people in Brazil [3].

Zika virus disease (ZVD) is usually mild with symptoms lasting for several days to a week after being bitten by an infected mosquito. Eighty percent (80%) of cases are asymptomatic [3]. Symptoms include acute onset of fever, rash, arthralgias, and conjunctivitis [4]. Although the symptoms of ZVD are mild, there have been reports of increased microcephaly cases and Guillain-Barré syndrome associated with this infection. In 2015, an increase in the number of cases of microcephaly was reported to the Ministry of Health of Brazil. By January 2016, a total of 3,530 suspected microcephaly cases had been reported, many of which occurred in infants born to women who lived in or had visited areas where ongoing Zika virus transmission was occurring [5]. By the end of 2015, 4,180 suspected cases of microcephaly had been reported [6]. More recently, instances of sexual transmission of the virus have been reported. The United States (US) Centers for Disease Control and Prevention (CDC) received reports of 14 cases of suspected sexual transmission of ZVD between February 6 and 22, 2016. This included two laboratory-confirmed cases and four probable cases of ZVD that were identified among women whose only known risk factor was unprotected sexual contact with a symptomatic male partner that recently travelled to an area with ongoing Zika virus transmission [7].

Health authorities in affected countries have to face the challenges of dealing with a new pathogen that they may know very little about [8]. Mounting an appropriate response is even more exigent in most tropical and subtropical countries where the mosquito vectors *Aedes aegypti* and *Aedes albopictus* are widely distributed and the introduction of the virus to these areas could readily result in endemic transmission of the disease [9]. The US Department of Health and Human Services decided that there was an urgent need for additional research to better characterize ZVD, focusing in particular on the mode of transmission and infection during pregnancy [10]. Even though, the US has been faced with several emerging and re-emerging infectious disease threats in the past, important gaps remain in core areas of public health system readiness. It is recognized that stable, sustained investments are required to establish a solid foundation for achieving necessary national public health emergency preparedness and response capacity [11]. This report describes planning for ZVD surveillance and control, some challenges typically faced by local and state health departments in the US, and opportunities to build and strengthen public health capacity to respond to emerging infectious diseases.

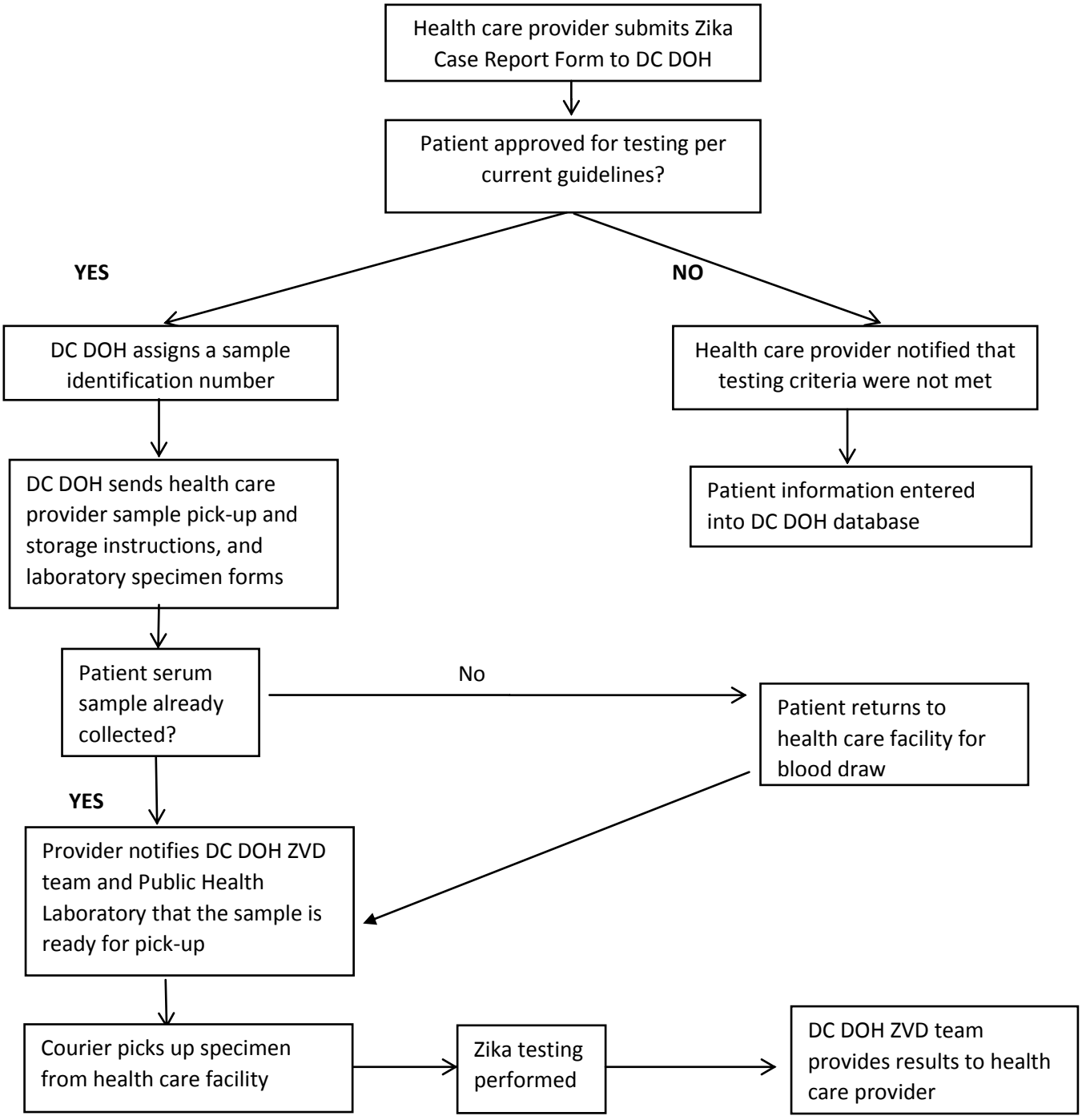
Zika Virus Preparedness and Response:

The DC Department of Health (DC DOH) Zika Virus Surveillance Program was initiated in January 2016. DC DOH Epidemiologists conducted active surveillance for travelers returning from areas with ongoing ZVD transmission in collaboration with health care workers when patients present to DC health care facilities (Figure 1). Due to the large number of international travelers in the Washington, DC metropolitan area, health care workers within the city were asked to screen all patients about their recent travel history outside the US. Patients who had traveled to areas with ongoing ZVD transmission within the previous two weeks are screened for the following symptoms: fever (both subjective and objective), non-purulent conjunctivitis, rash, and arthralgia. Non-pregnant patients displaying at least one symptom are recommended for Zika virus testing. Pregnant patients (and those who become pregnant within 8 weeks of returning from an area with ongoing ZVD transmission) are recommended for Zika virus testing 2 to 12 weeks from the last day of travel, regardless of symptom status. The DC Public Health Laboratory (PHL) performs Polymerase Chain Reaction (PCR) testing for Zika virus RNA on all samples collected within 7 days of symptom onset. Immunoglobulin M (IgM) antibody testing is performed at CDC facilities in Fort Collins, Colorado, on samples collected more than 7 days after symptom onset and for all samples from asymptomatic pregnant patients (or patients that became pregnant within 8 weeks of travel) (Figure1).

Mosquito Control:

Starting in April 2016, DC DOH is enhancing its vector-borne disease surveillance program by beginning surveillance activities two months earlier than in previous years, and therefore expanding the surveillance period to 6 months. Surveillance involves trapping adult mosquitoes in each of the eight DC wards, using gravid traps and carbon dioxide (CO2) traps. Trapped mosquitos are sorted by both sex and species weekly and submitted to the DC PHL for PCR Testing. The DC PHL performs testing on all female mosquitos for the following diseases of public health importance: Chikungunya virus, Dengue virus, West Nile virus, and Zika virus. Test results are posted on the DC DOH website daily, and weekly totals are reported to the CDC. DC DOH mosquito-control personnel also place insecticides that target the juvenile larval-stage of mosquitoes (larvicides) in areas with standing water and catch basins. DC DOH will hold two community education campaigns during the mosquito season to present information on how to reduce mosquito breeding sites in the community and around homes, as well as preventative measures individuals can take to reduce personal exposure to mosquito.

Figure 1: District of Columbia Department of Health (DC DOH) Zika Patient Processing Protocol



Challenges:

Communication with stakeholders:

Communication with stakeholders is always a critical part of response activities. As previously mentioned, Washington, DC has a large population of frequent travelers, which means that there is a large population of residents who potentially needed testing. This creates a challenge responding to e-mails and telephone calls from stakeholders who request guidance or have questions. Responding to inquiries can become time consuming to the extent that it hinders our ability to perform other response activities, such as reviewing and processing case report forms and interviewing patients referred for testing. Responding to stakeholders on an individual basis becomes even less feasible when intense media attention increases public fear, as was the case with ZVD.

DC DOH is responsible for providing official data on cases of Zika virus among DC residents to the media (such as through press releases) and responding to media inquiries. One of the challenges this creates is balancing the responsibility to share information with the need to ensure the individual privacy of patients. This has been particularly important given that the number of confirmed cases in DC (all travel-associated) is very small (n=4 as of May 9, 2016).

Another challenge in communicating with stakeholders is that instead of a single message, multiple, targeted messages must be developed and distributed to various audiences. For example, health care workers need detailed technical information so that they can appropriately manage patients and refer patients for Zika virus testing. Patients suspected to have Zika virus need specific information regarding testing and risk of infection. In addition, the messages communicated to each group evolve over time. When the CDC updates its guidance or releases new recommendations on testing criteria, mosquito control practices, as potential for Zika virus exposure changes over time (e.g., during mosquito season or summer vacation), or as we implement changes in our local surveillance protocol (e.g., updated Zika case report form), new messages need to be released. The public also needs general information presented in lay terms on prevention of mosquito bites. Development of a communications plan that includes public education about preventing the breeding of mosquitoes, personal protection guidance, and the participation of the necessary agencies and other stakeholders is critical to the success of the program.

Regional Coordination:

As the response heightened, DC DOH increasingly received ZVD case report forms for residents of the neighboring states of Maryland and Virginia who visited DC health

care facilities. Each jurisdiction had developed their own process for specimen collection and routing, submission of appropriate documentation by providers (e.g., case report and laboratory forms), and testing approval criteria. However, it soon became evident that each jurisdiction could not operate in isolation. This created a challenge to not only develop and optimize a DC ZVD surveillance protocol, but also to develop a regional protocol in collaboration with Maryland and Virginia.

Testing Limitations:

There have been several challenges associated with testing persons for ZVD. A major challenge has been that testing for Zika virus cannot be performed by commercial laboratories. Initially testing was only possible at the CDC Arbovirus Diagnostic Laboratory. Even with the expansion of PCR testing at the DC PHL, confirmatory testing must still be performed by the CDC for all samples. In addition, PCR testing is only appropriate for persons whose serum sample was collected within 7 days of symptom onset and very few patients met these criteria. Testing requires coordination of multiple partners both internal and external to DOH. When a sample is approved for testing, information must be communicated to all partners in a timely manner to facilitate timely testing and minimize sample storage times.

Recommendations about who should be tested and test result interpretation has been challenging because the epidemiology of ZVD is not well understood at this point in time. Testing criteria have changed over the course of the response as more data have become available, particularly with regard to sexual transmission. Many persons with a positive travel history but without symptoms want to be tested, especially since the general public is aware that 80% of people do not develop symptoms. However, the predictive value of the test in asymptomatic individuals is unknown and, therefore, test in this population is not currently recommended. As testing criteria expanded to include all pregnant women with a positive travel history, the wait-times for results increased past 4 weeks as the number of samples received daily by the CDC increased. This makes it difficult for patients and health care providers to make any clinical decisions based on test results alone, and have led to prolonged anxiety, especially among pregnant women.

Lessons Learned:

As part of the Zika virus response, DC DOH was tasked with balancing the need to respond to inquiries for guidance and information, while also performing other response activities, maintaining awareness of media messages, developing multiple communications tailored to specific stakeholders, and providing accurate and updated information in a timely manner. As the outbreak expanded, this communication

needed to transition from one-on-one interaction to more efficient strategies.

The most efficient means of addressing these communication challenges, particularly for the public, was to develop a specific webpage on Zika on the DC DOH website. The website directs members of the public to contact or visit their health care provider to determine whether they should be tested for ZVD. DC health care providers are e-mailed updated health notices, which can be accessed through a link on the DC DOH ZVD webpage. The health notices provided information about testing criteria, protocols for reporting suspected cases, and coordinating sample pick-up for testing. Members of the public are advised to send an e-mail to the DC DOH ZVD team using an e-mail address displayed on the DC DOH ZVD webpage if they needed additional information. A general telephone line was reserved as another means for health care providers to contact DC DOH, in addition to the DC DOH ZVD team e-mail address. As new information is posted on the DC DOH ZVD website or shared with the media, the levels of details included are closely monitored due to privacy concerns. Protecting the privacy of the patient is of paramount importance, and must be balanced when communicating public health information. We also discovered the importance of establishing key contacts at each health care facility and at the CDC to ensure that protocols were followed and to facilitate accurate and timely testing. Once we communicate information to the key contact(s) at health care facilities, they can then convey our messages to all the health care providers working at their facility.

In a situation where fear can play a large role, addressing misconceptions in the community early is important. This supports health care workers in providing appropriate care for their patients, and allows DC DOH to plan and execute an appropriate response to address current healthcare needs. Because ZVD is a mosquito-borne disease, there were continual questions from the community and the media regarding vector control. To mitigate fears, the DC DOH ZVD team presented information at community meetings as well as during a community-based educational campaign to take place throughout the mosquito season. There has also been focused communications prepared to inform residents that there has been no local transmission of ZVD by mosquitoes in the continental US and to address other misconceptions around ZVD.

Given the uniqueness of the Washington, DC metropolitan area, DC DOH could not work in isolation to develop its Zika Virus response activities. Therefore, DC DOH held weekly conference calls with Maryland and Virginia to share state and local protocols and establish a process for handling cases from neighboring jurisdictions. These conference calls were also an opportunity to share strategies and challenges. Close collaboration with neighboring jurisdictions also ensured that DC

DOH could appropriately inform health care providers about the processes that needed to be followed based on their patient's state of residence, and that health care providers received consistent messages about how to report suspected ZVD cases regardless of the health department they contacted for guidance.

DC DOH worked closely with key contacts at health care facilities to explain testing criteria and the reasons people were not cleared for testing to ensure testing was only performed when appropriate. To account for changing testing criteria, records were retained for all patients who were not approved for testing so that if they were to become eligible in the future as guidelines changed, their health care providers could be contacted.

CONCLUSIONS:

Although we faced several challenges, this experience continues to add to our effectiveness in addressing the demands of controlling future emerging infectious diseases. Meeting these challenges when they occur will ensure the accomplishment of better outcomes in the future. Priorities for control of ZVD must include provision of adequate information and education to stakeholders, who visit endemic areas, prevention of transmission by local vectors, and developing an integrated vector management program. In our rapidly changing and unpredictable environment, developing detailed protocols and increased collaborative efforts are essential keys to success.

Author Contributions:

John Davies-Cole supervised the surveillance and response activities and led the writing; Preetha Iyengar, Sasha McGee and Andrew Hennenfent conducted surveillance and response activities and wrote separate sections. Vito DelVento supervised the mosquito control activities and reviewed the manuscript. Anicet Dahorou coordinated samples referral and laboratory testing. Fern Johnson-Clarke reviewed and edited the manuscript.

REFERENCES:

1. World Health Organization (WHO). Zika Outbreak: WHO's Global Emergency Response Plan. WHO website. March 3, 2016. http://www.who.int/emergencies/zika-virus/response/en/. Accessed March 21, 2016.
2. The World Health Organization (WHO). The History of Zika Virus. WHO website. 2016.http://www.who.int/emergencies/zika-virus/timeline/en/. Accessed March 21, 2016.
3. Centers for Disease Control & Prevention (CDC). Zika: Symptoms, Diagnosis and Treatment. CDC Website. March 11, 2016. http://www.cdc.gov/zika/symptoms/index.html. Accessed March 20, 2016.
4. Carod-Artal FJ. Epidemiology and neurological complications of infection by the Zika virus: a new emerging

neurotropic virus. Rev Neurol. 2016; 62:317-328.

5. Kleber de Oliveira W, Cortez-Escalante J, De Oliveira WT, do Carmo GM, Henriques CM, Coelho GE, Araújo de França GV.Increase in reported prevalence of microcephaly in infants born to women living in areas with confirmed Zika virus transmission during the first trimester of pregnancy - Brazil, 2015. MMWR Morb Mortal Wkly Rep. 2016; 65: 242-7. doi: 10.15585/mmwr.mm6509e2.
6. Teixeira MG, da Conceição N Costa M, de Oliveira WK, Nunes ML, Rodrigues LC. The epidemic of Zika virus-related microcephaly in Brazil: detection, control, etiology, and future scenarios. Am J Public Health. 2016; 106:601-5. doi: 10.2105/AJPH.2016.303113.
7. Hills SL, Russell K, Hennessey M, Williams C, Oster AM, Fischer M, Mead P. Transmission of Zika virus through sexual contact with travelers to areas of ongoing transmission - continental United States, 2016. MMWR Morb Mortal Wkly Rep2016; 65:215–216
8. Villa, R. Zika, or the burden of uncertainty. Clin Ter.2016; 167:7-9. doi: 10.7417/CT.2016.1907.
9. Wong SS, Poon RW, Wong SC. Zika virus infection-the next wave after dengue?J Formos Med Assoc. 2016; Mar 7. pii: S0929-6646(16)00077-2. doi: 10.1016/j.jfma.2016.02.002.
10. Snair J, Hermann J, Brown L, Wollek S, Balogh E, Maxfield K. Potential Research Priorities to Inform Public Health and Medical Practice for Domestic Zika Virus: Workshop in Brief (2016). Institute of Medicine; Division on Earth and Life Studies; National Academies of Sciences, Engineering, and Medicine, Washington (DC). February 2016. http://www.nap.edu/read/23404/chapter/1#8. Accessed March 19, 2016.
11. Duchin JS. US public health preparedness for Zika and other threats remains vulnerable. Disaster Med Public Health Prep. 2016; 8:1-2.

ZIKA: A RE-EMERGING INFECTIOUS VIRUS DISEASE OF PUBLIC HEALTH CONCERN

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ABSTRACT:
Zika is caused by a flavivirus transmitted by mosquitoes of the Aedes species, mainly *Aedes aegypti.* It causes a mild self-limiting illness in people that it infects, leaving most people asymptomatic. However, the recent rise in the spread of Zika virus predominantly in Latin America has been accompanied by unprecedented rise in a number of children being born with abnormally small heads-identified as microcephaly. In addition several countries, including Brazil, which has experienced the world largest Zika outbreaks, reported a steep increase in Guillain Barre Syndrome- a neurological autoimmune disorder that could lead to paralysis and death. Although it has not been definitively proven, evidence is growing that Zika virus causes both microcephaly and Guillain Barre Syndrome. Obviously, these reports made the World Health Organization to declare Zika as a significant global public health concern. Apart from using insecticides to control the spread of mosquitoes, several other approaches are being implemented to prevent Zika virus infection. These include vaccine development and impairing egg-laying female mosquito's ability to transmit infection and also genetic modification and sterilization of male *Aedes aegypti.*

Keywords: Zika Virus, Public Health Concern, Brain Damage, Preventive Strategies
Submitted March 2016; Accepted May 2016

INTRODUCTION:

Nature abhors vacuum and so as the frenzy of Ebola appears to be in recess, the void has to be filled with the advent of Zika, a re-emerging infectious disease spreading explosively around the world and predominantly transmitted by mosquitoes of the *Aedes* species such as the tiger mosquito *Aedes aegypti,* which also transmits Yellow Fever, (Figure 1) and potentially *Aedes albopictus.* The Zika virus (ZIKV) is an RNA arbovirus that belongs to the virus family Flaviviridae and the genus Flavivirus and is therefore related to the Dengue, Yellow Fever, Japanese Encephalitis, Chikungunya and West Nile viruses. It is an enveloped virus with icosahedral symmetry and non-segmented single-stranded RNA genome [1, 2]. ZIKV has also been isolated from *Aedes*

africanus, Aedes apicoargentus and *Aedes vittatus,* to mention a few. Zika virus derived its name from the Zika forest of Uganda, just as Ebola got its name from the Ebola River in Zaire and Lassa from a town in North Eastern Nigeria. It was first isolated in 1947 from a rhesus macaque monkey by scientists of Yellow Fever Research Institute [3 - 5]. A second isolation from *Aedes africanus* followed at the same time at the same site in 1948. When the monkey developed a fever, researchers isolated from its serum a "filterable transmissible agent" that was named Zika virus in 1948 [6]. ZIKV, like other arboviruses, such as Yellow Fever, Dengue or Chikungunya is maintained in enzootic transmission cycles in the forested areas of Africa, Asia, South America and French Polynesia with the vertebrate hosts as primarily monkeys in the so-called monkey-mosquito-monkey cycle, with occasional transmission to humans.

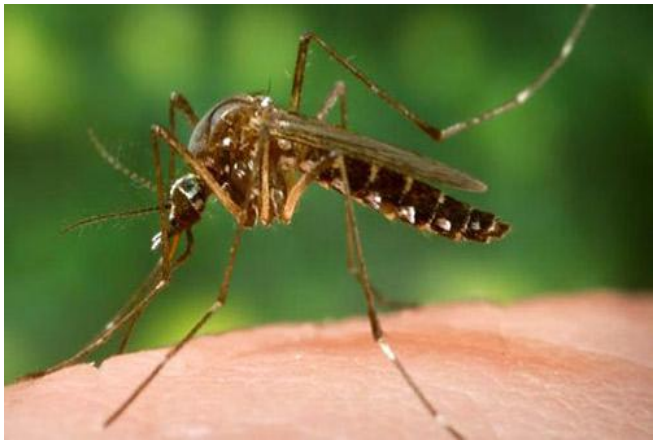

Figure 1: Adult female yellow fever mosquito, Aedes aegypti (Linnaeus), in the process of seeking out a penetrable site on the skin surface of its host Photograph by James Gathany, Courtesy: Center for Disease Control Public Health Image Library www.cdc.gov/features/stop

As of February, 2016 there are no confirmed cases of ZIKV transmission through blood transfusions, although a potential risk is suspected based on a study conducted between November 2013 and February 2014 during the Zika outbreak in French Polynesia, in which 42 (2.8%) blood donors tested positive for ZIKV RNA and were asymptomatic at the time of blood donation [7, 8]. As a safety measure to protect blood and transplant recipients, the Centers for Disease Control and Prevention (CDC) recommends that blood, tissues or organs should not be obtained from donors diagnosed with ZIKV within six months from date of diagnoses, travelled to a ZIKV hotspot or had sex with a patient diagnosed with ZIKV [9].

Is it possible for the Zika virus to be transmitted through urine, saliva and semen?

Brazilian Research Institute recently found active ZIKV in the urine and saliva of some infected patients, but the ability of the virus to infect people through these two body fluids requires to be established through further research [10, 11]. The story with semen is different. In 2016 three cases of sexual transmission were reported. ZIKV was grown from semen. Zika antibodies were demonstrated in a United States biologist studying mosquitoes in Senegal [10], also in 2016 the Dallas County Health and Human Services Department reported a person contacted Zika fever after having sexual contact with an infected person. Fourteen additional cases of possible sexual transmission are being investigated. Reports also showed that ZIKV can stay in the semen indefinitely [11]. This is why men should be more concerned about Zika than women. Common sense therefore dictates that they should be having protected sex to prevent a possible transmission to their partners.

There are two lineages of the ZIKV: African and Asian. Phylogenetic studies indicate that the ZIKV spreading in the Americas is mostly closely related to the Asian strain, whereas Western ZIKV is found to be 89% identical to African genotypes, but is most closely related to the strain found in French Polynesia during the 2013 - 2014 Zika outbreaks [12].

Symptomatology: As in malaria, when a person is bitten by a mosquito that has the ZIKV they harbor the virus in their blood, (just as the Anopheles mosquito transmits plasmodia in the blood). When they get bitten by another mosquito, the virus is passed along. Symptoms of ZIKV infection are usually mild. Majority of people (80%) are asymptomatic. Infection manifests as fever, maculopapular rash, muscle and joint pain, malaise, headache and conjunctivitis. These symptoms generally last for 2-7 days [9].

Treatment: There is no specific treatment for Zika. Symptoms are palliatively alleviated with over-the-counter medications: Analgesics and antipyretics. Patients are advised to rest and take enough fluids to prevent dehydration and to avoid taking specific non-steroidal anti-inflammatory drugs (NSAIDS), such as, Ibuprofen and Aspirin until the diagnosis of Dengue is ruled out to reduce the risk of bleeding. Acetaminophen (Tylenol) or Paracetamol are recommended [13]. There are no vaccines currently available.

Complications: Zika fever is mild but not its complications. Unfortunately babies have to bear the brunt of this seemingly innocuous infection. New research associates the ZIKV

with a condition in which the immune system attacks nerves of fetuses causing muscle weakness, paralysis and even death. This autoimmune disorder is called Guillain Barre Syndrome. In pregnant women also, the virus has been linked to an alarming increase in the rate of birth defect known as microcephaly-an abnormally small head which may cause brain damage, mental retardation, delays in speech, movement and growth. It is suspected that this can only occur during the first trimester of pregnancy when the brain is being formed. However, this relationship has not been established by researchers [4]. More than 4000 new microcephaly cases are suspected to be Zika-related. CDC recommends that pregnant women delay travel to areas where Zika is active; these areas have been expanded to include 37 countries of the Americas, Oceania and the Pacific Islands. CDC current guidelines recommend that pregnant women returning from these areas get tested for Zika. More of the cases in the USA of pregnant travelers are being investigated by CDC [14]. In 2015, Zika virus was detected in the amniotic fluid of 2 pregnant women, whose fetuses had microcephaly, indicating that the virus had crossed the placenta and could have caused mother-to-child infection [14]. In a cohort study of pregnant women in Brazil, Zika infection was associated with growth retardation and fetal death, placental insufficiency and CNS injury and abnormally small heads [15].

Epidemiology: Zika was first reported in one of the African countries, and as was earlier mentioned, was discovered in rhesus monkeys in the Zika forest of Uganda in 1947 [3 – 5]. Researchers found that it lived in mosquitoes. First evidence of human ZIKV infection was published in 1952 following the results of serological studies in Uganda, Tanzania and Nigeria. Among 84 people of all ages, 50 individuals had antibodies to ZIKV, all above 40 years old were immune [16]. But it was not until 1954 that the isolation of the ZIKV from humans was published [16]. Subsequently outbreaks have been reported from 1957 - 1981 throughout Africa and Asia and in French Polynesia in 2007 and spread to Latin America in 2014. To date there have been ZIKV outbreaks in 41 countries. Some 312 travel-associated cases in the United States with Zika-viremia have been reported, including 27 pregnant women and 6 sexually transmitted, and also a total of 352 locally acquired cases in the United States territories, including a case of Guillain-Barre Syndrome [11]. Since Brazil reported the ZIKV in May 2015, infections have occurred in about 24 countries of the Americas. The disease now has explosive pandemic potential. A German biotechnology company-Genekam- claims to have developed a DNA-based test that can detect ZIKV in the blood and this can determine if a person is a carrier of ZIKV [17]. If it proves to be true it will be a

great tool in epidemiological studies and an adjunct to detection of Zika antibodies.

Prevention and Control: Prevention of ZIKV infection is completely dependent on the control of the mosquito vector and limiting person-person contact, the goal of mosquito-based surveillance is to quantify human risk by determining local vector presence and abundance. In order to quickly identify and mitigate a mosquito-borne disease outbreak, establishing and maintaining a local surveillance program is critical. The vector for Zika*, Aedes aegypti*, is an "urban mosquito" which likes to feed on people and breed in water-filled habitats like plant containers, bird-bath and pools of standing water which we too often leave around our dwellings. First line of approach in getting rid of mosquitoes is to get rid of their habitats. Spraying of insect repellents is another strategy. Some people use a combination of 20% Picaridin and 30% oil of lemon eucalyptus. Chemical pesticides ("larvicides" and "adulticides") are effective in killing mosquito eggs, larvae, pupae and adult mosquitoes. It is also advisable, just as it is recommended in the case of West Nile virus, to wear long sleeve shirts and trousers when outside during dusk and dawn when mosquitoes are most active [9, 18].

As it has always been the case in diseases that have no vaccine, Non-governmental organizations (NGOs) should be involved in ZIKV awareness by mobilizing community members to take specific actions, as has been advised, to prevent further infections with the ZIKV. One of WHO's responses to the reduction of mosquito population and thus contain Zika is providing training on clinical management, diagnosis (strengthening capacity of laboratories to detect the virus) and vector control (providing larvicide to treat standing water sites) through a number of its collaborating centers [9].

Forrest innovations- an Israeli-based biotech company has another solution to contain the spread of disease-carrying mosquitoes, especially *Aedes aegypti* that transmits the ZIKV. They plan to breed and release sterile mosquitoes to prevent reproduction and eventually reduce its population. The company's mosquito control program called "NoMoreMos" uses a technique- "sterile insect technique" that sterilizes male mosquitoes at a larval stage by applying a topical solution that renders them sterile but does not modify their genetic code. The company targets Rio de Janeiro, Brazil which has seen the world's largest Zika outbreaks and will host the 2016 Summer Olympics. Its more immediate concern is to prevent transmission among visitors and athletes. To achieve this, the company plans to release some 25 million sterile mosquitoes starting in June and through the Olympics in August [19]. The choice of male mosquitoes is

justified because sterilized male mosquitoes can no longer fertilize female eggs and male mosquitoes do not bite.

Another approach to contain the Zika disease was pioneered by a British biotech firm, Oxitec working with Brazil has genetically modified the Aedes mosquito in such a way that the males produce off-springs that cannot reproduce. "The USA FDA has granted preliminary approval for Oxitec to release the insects in Florida, after determining that there would be no significant impact to human, animal and plant life from the experiment or reducing mosquito populations that spread Dengue, Chikungunya and Zika virus" [20].

The Australian approach to contain the spread of mosquitoes is to infect them with *Wolbachia* bacterium that lives only in insect cells and impairs the mosquito ability to transmit infections such as Dengue and Zika. If mosquitoes cannot become infected with ZIKV, they cannot transmit the virus between people [19].

As was mentioned earlier there is no vaccine or preventative drug for Zika. According to the WHO experts, the priority should be to develop inactivated vaccines that are safe to use in women of reproductive age and pregnant women. Vaccine production generally is very technically challenging, need to be pathogen-specific and also capital intensive [21]. Subsequently, as of March 2016 a total of 18 companies and institutions, including the National Institute of Health (NIH) Vaccine Research Center and India's Bharat Biotech International that started developing Zika vaccines have faced the challenges using two approaches: "Recombinant" involving genetic engineering and "Inactivated" where the virus is incapable of reproducing itself but can still trigger immune response [21 – 25]. Some other companies involved in vaccine development are Brazil's Butantan institute, Public Health Agency of Canada, New link Genetics, Merck & Co, Sanofi, Glaxo Wellcome and Japanese Takeda Pharmaceutical. The Director of National Institute of Allergy and Infectious Diseases (NIAID) in the USA - Anthony Fauci recently, in a CNN television interview stated that researchers on West Nile virus have developed a "platform" for a flavivirus vaccine that might be quickly adaptable to Zika if the process can skip the regulatory hurdles of the USA FDA.

CONCLUSION:

The Director-General of WHO-Margaret Chan, speaking recently in Geneva said that nobody could predict how far the ZIKV would spread, causing more and more cases of Guillain Barre Syndrome and Microcephaly in newborns when pregnant women are infected. But "if this pattern is confirmed in and beyond Latin America and the Caribbean, the world will face a severe crisis". Subsequently on February 1,

2016 the WHO declared ZIKV infection a public health emergency of international concern [26]. In 1992 the USA National Academy of Sciences (NAS) warned that we have not yet conquered infectious disease as a consequence of human activities and we were likely to see more and more pathogens spreading beyond their ancestral ranges. In essence what NAS was saying is that human factors are responsible for human plight that we experience from time to time. Some of these factors are increasing human populations going into new places and coming in contact with new pathogens either emerging or re-emerging such as Ebola or Zika. Other factors are more and faster travels, growing urbanization and erosion of traditional public health infrastructures, such as mosquito control programs. To the list we can add climate change which can be conducive for some mosquito-borne diseases. A key lesson learned from the 2014 Ebola outbreaks is the need for galvanizing appreciable international response and avoiding panic and overreaction [28]. I think the same should be applicable in the ZIKV disease outbreaks.

In the absence of a vaccine or a preventative therapy the only option remaining is preventive strategies including public enlightenment. It is on this premise that I would like to suggest what I call the 7 “Commandments” for the prevention of ZIKV infection [27].

1. You should avoid mosquito bites, particularly at dusk and dawn when the mosquito is most active.
2. You should wear long-sleeved shirts and long pants to conceal body parts that may serve as targets.
3. You should stay in places with air conditioning or that use window or door screens to keep mosquitoes outside.
4. You should sleep under a mosquito bed net if you are in Zika-infested areas and not able to protect yourself otherwise from mosquito bites.
5. If you are suspected of having Zika then remember to wear condom if you cannot observe abstinence to prevent sexual transmission of the virus to your partner.
6. Use Environmental protection Agency (EPA) approved, and therefore safe and effective, insect repellent such as Permethrin as directed.
7. Do not use insect repellent on babies younger than 2 months of age. Instead dress infants or small children with clothing that covers arms and legs to prevent mosquito bites.

Even when vaccines become available these recommendations should still be in force as a public health norm.

REFERENCES:

1. Knipe DM and PM Howley. Fields Virolgy (5th Edit) Lippincott Williams & Wilkins 2007, pp. 1156 & 1199.
2. Faye OF, Freire CCM, Iamarino A, Faye O, de Oliveira JVC, Diallo M, Zanotto PMA, Sall AA and B Bird B. Molecular evolution of Zika virus during its emergence in the 20th century. Neglected Tropical Diseases 8 (1): 2014, e 2636.
3. Sikka V, Chattu VK, Popli RK, Galwankar SC, Kelka D, Sawicki SG, Stawicki SP and

TJ Papadimos. The emergence of Zika virus as a global security threat. A review and a Concensus Statement of the INDUSEM Joint Working Group. Journal of Global Infectious Diseases 8(1):2016,3-15.

4. Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Scheinder AB, Zimler R, Talton J, Cobb RR, Ruzic I, Smith-Gagen J, Janies D and J Wilson. Zika virus: Medical countermeasure development challenges. Neglected Tropical Diseases 10 (3): 2016, e0004530.
5. Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, Huy R and SC Weaver. Genetic characterization of Zika virus strains: Geographic expansion of the Asian Lineage. Neglected Tropical Diseases 6 (2): 2012, e1477.
6. Enfissi A, Codrington J, Roosblad J, Kazanji M and D Rousset. Zika virus genome from the Americas. Lancet 387 (10015): 2016, 227-228.
7. "Zika virus infection outbreak, Brazil and the pacific region". Stockholm: European Center for Disease Control and Prev. May 25, 2015.
8. Musso D, Nhan T, Robin E, Roche C, Bielaire D, Zisou K, Shan Yan A, Cao-Lormeau VM and J Broult. " Potential for Zika virus transmission demonstrated during outbreak in French Polynesia, Nov. 2013-Feb. 2014. Euro-surveillance 19 (14): PMID 24739982, 2014.
9. "Zika Situation Report". World Health Organization, February 5, 2016.: www.who.com
10. Zanluca C, de Melo VC, Dos Santo GI and K Luz. First Report of autochthonous transmission of Zika virus in Brazil. Memorias de Instituto Oswaldo Cruz 110 (4): 2015, 569-572.
11. Center for Disease Coinrol and prevention Mor. Mortal. Wkly Rep. 2016.
12. Lanciotti RS, Lambert AJ, Holodniy M, Saavedra S and CC Leticia. Phylogeny of Zika virus in Western Hemisphere. Emerging Infectious Diseases 22 (5): 10. 3201, 2016.
13. Symptoms, Diagnosis and Treatment. Center for Disease Control and Prevention, Atlanta. 4 Mach, 2016. www.cdc.gov/features/stop
14. Oduyebo T, Petersen EE and SA Rasmussen. Update: Interim Guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure-United States, 2016. Morb Mortal Wkly Rep 65: 1-6, 2016.
15. Martines RB, Bhatnagar J and MK Keating. " Notes from the Field: Evidence of Zika Virus infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses-Brazil, 2015" Morbid Mortal Wkly Rep 65 (06): 1-2, 2015
16. Zika virus (06) Overview 2016-02-09 19: 58:3. Pro. MED-mail. International Society for Infectious Diseases, 2016.
17. Ugbomoiko US. Lassa and Zika fevers: Poor disease control fuels killer viruses in Nigeria 2016.. www.vanguardngr.com
18. Mitchell C. Pan American Health Organisation (PAHO) Statement on Zika Virus Transmission and Prevention. www.paho.org, 2016.
19. Mosquito control program. No More Mos. www.forrestinnovations.com, 2016.
20. Researchers release genetically modified mosquitoes in Brazil. www.dailymail.co.uk/zikavirus, 2012.
21. Maron DF. First Dengue Fever Vaccine Gets Green Light in 3 Countries. Scientific American, January, 2016.
22. World Health Organization and experts prioritize vaccines, diagnostics and innovative control tools for Zika R&D, WHO 9 March, 2016. **www.who.com**
23. Stemberg S. Vaccine efforts underway as Zika virus spreads. US News and World Report. 28 January, 2016.
24. Bagla P. How Bharat Biotech made its breakthrough in developing a vaccine for Zika virus. Huntington Post (India) February, 9 2016.
25. Siddiqi Z. Bharat Biotech says working on two possible Zika vaccines. Reuters, 8 February, 2016.
26. World Health Organization declares Zika as a global emergency. BBC online. 1 February, 2016.
27. Centers for Disease Control and Preventions, www.cdc.gov/features/stop Mosquitoes, 2016.
28. Anyiwo CE. Ebola: Enough of the hysteria. Pac J. Med. Sci. vol. 14 No. 1 Jan, 2014, 30-37: www.pacjmedsci.com .

THE PUBLIC HEALTH CHALLENGE OF DENGUE FEVER IN PAPUA NEW GUINEA

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INTRODUCTION AND KEY FACTS

Dengue Fever (DF) is a mosquito-borne disease of public health concern in both tropical and subtropical countries, especially influenced by rainfall, temperature and unplanned rapid urbanization [1]. World Health Organization (WHO) member states have reported on average 2.4 million cases of DF annually over the past 5 years [1]. Even with these figures, other data suggests the number of dengue infections could be as high as 390 million annually, of which up to 96 million show clinical manifestation[1]. Global reporting has therefore not been good, and Papua New Guinea (PNG) is one of the countries that have not yet reported national DF surveillance data.

DF does not feature among the leading burden of diseases reported in PNG's National Health Plan 2011-2020, and it is not clear whether lack of reliable reporting was the reason. In 2015, DF was reported as being only rarely diagnosed and possibly having a low index of clinical suspicion in PNG. That same report further stated that dengue haemorrhagic fever (DHF) has not been reported in PNG for over a decade [2].

Three reports of the DF situation in the Western Pacific region from 2010 to 2012 state that there was no DF-specific surveillance in PNG [3-5]. However, DF's presence was verified from case importation to Queensland for which surveillance in Queensland is actively conducted [6].

DF surveillance in PNG is challenged by geographical isolation of its remote, mountainous, coastal, and island sparsely distributed and diverse rural communities [7]. This situation limits access, provision and coverage of health services. These challenges only add to those posed by DF itself, resulting in a paucity of information about its presence in PNG.

Transmission

There are four serotypes of the dengue virus: DEN-1, DEN-2, DEN-3, and DEN-4 [1], all of

which have been identified since the first isolation of the dengue virus (DENV) in 1943 [8]. Dengue is transmitted through bites by an infected female species of the *Aedes aegypti* mosquito that bites mainly in the early morning and in the evening before dusk. It is worth noting that this same mosquito also transmits chikungunya, yellow fever and the Zika virus infection [1]. Infected humans are the main carriers of the virus (4-12 days incubation period after the infected bite) and therefore the source of the virus for uninfected mosquitoes to complete the cycle of infection.

Symptoms

DF presents in both children and adults, characterized by high fever, and combination of the following symptoms: muscle and joint pains, pain behind the eyes, nausea, severe headache, vomiting, nausea, swollen glands or rash, and a drop in blood pressure. It can also be completely asymptomatic. The symptoms can last 2-7 days, even longer. It is usually more complicated or potentially deadly when blood plasma leaks, or there is fluid accumulation or severe dehydration, severe abdominal pain, bleeding either in vomit or gums, fatigue and restlessness [1].

Diagnosis, Treatment and Control

There is no specific treatment for DF other than just managing the symptoms such as through use of acetaminophen (paracetamol) for pain relief and replenishing the patient's body fluid volumes. Medical care by physicians and nurses, especially for DHF, also known as severe dengue, has been known to decrease mortality rates [1].

Recovery from infection by one serotype provides a lifelong immunity against that particular serotype. However, subsequent infections by other serotypes have been noted to increase the risk of developing DHF.

A recently developed vaccine, Dengvaxia (CYD-TDV), has been registered in several countries. The WHO will be following up with a Vaccine Position Paper recommendation on its use sometime in mid-2016 [1].

Several public health prevention measures should be taken to control the transmission of infection, including destroying the mosquito breeding sites, covering domestic water containers, using insecticides and wearing long-sleeved clothes. These should be accompanied by active monitoring and surveillance of vectors to determine effectiveness of control interventions.

Historical Perspective of DENV

The DENV was introduced into the Americas by the mosquito vector *Stegomyia aegypti* from Africa via slave ships and other commercial vessels which crossed the Atlantic Ocean during the 18th and 19th centuries, and five centuries prior to that [7]. The ancestor of the viruses has been postulated to have emerged

about 1000 years ago from sylvatic cycles involving non-human primates [7]. Two monkey species, the African green monkey (*Chlorocebus sabaeus*) and the Guinea baboon (Papiopapio), widely found across the African continent, have been the non-human primates reservoir of the virus in the sylvatic cycle. The virus jumped to humans due to low DENV virulence, thereby facilitating its sustenance and transmission. The DENV later exploited the mosquito vector *Aedes aegypti* to achieve transmission to humans [9].

DF was clinically diagnosed and reported to be widespread in North and South America, the Caribbean basin, Asia, and Australia during the 18th and 19th centuries [7]. The introduction of mosquito-eradication program between 1946 and 1970 in South America saw a decline in the incidence of DF. Unfortunately, an increase in the introduction and spread of mosquitoes by transportation for commercial and military purposes led to the re-emergence of DF as a major public health problem during the mid and later parts of the 20th century [7]. For example, during the Second World War, Southeast Asia experienced an increase in DF, with the vector continuing to intensify across affected geographic areas of the region. In addition, further spread occurred as a result of shipping and air traffic globally as well as ecological and demographic changes [7].

The successive epidemics of the 1980s and 1990s in Brazil involved three serotypes of the DENV. Low numbers of cases of DHF were reported, unlike in Asia, where reported epidemics occurred in large numbers of children. The reason for the differences was due to the presence of resistant genes in those with African ancestry. This was confirmed by high levels of antigenic antibodies against the American DENV-2 genotype and the cross-reactive DEN-1, both of which had been endemic in Latin America for many years [10].

Today, all the DENV serotypes circulate in Africa, South and Southeast Asia, the Caribbean basin and Central and South America and the Western Pacific regions [7]. The vector *Aedes* sub group *Stegomyia* is endemic in the Pacific region and may have been derived from a single original species unintentionally introduced by the first Austronesian navigators 1500 to 2000 years ago [11]. Due to strict isolation and ecological conditions in the islands, different species emerged. The introduction of *Aedes aegypti* into different islands over time may be linked to the Pacific history of human migration. This mosquito species introduction was first recorded in the Pacific in the late 19th and early 20th centuries [11]. The WHO reports that currently, over 70% of the world's dengue fever disease burden is borne by South-East Asia and Western Pacific countries [12].

Papua New Guinea's Current Situation

Several countries in the Pacific Region have no functioning surveillance centres, including PNG [5], where no surveillance was conducted before 2010. Reports from Australia's Northern Queensland and the Torres Strait Islands show evidence of imported cases from PNG [3]. However, the first DENV2 in PNG was reported earlier in 1944 [8]. Studies have shown over time that the disease is endemic in PNG [13]. The first epidemic of DF was reported in 1971 in Port Moresby and Rabaul [14]. One report noted a high prevalence of Arboviral antibodies in PNG, and that DF was endemic in PNG [13]. With no treatment yet available for DF, prevention is achieved through effective public health interventions such as vector control using treated mosquito nets, community action and participation, and public awareness [15].

Public health response at the national, provincial, district and community levels has been varied. Daru Hospital reported 170 cases (126 clinical presentations and 44 confirmed) in November 2015, and the National Capital District (NCD) reported 15 cases [16], while during the same period, no cases were reported from other provinces.

The National Department of Health (NDOH) continues to monitor the current 2016 outbreak with weekly updates [16]. Only 7 of the 170 cases in Daru developed severe disease needing hospitalization; however, all recovered and were discharged. Children below 5 years of age accounted for 12% (21/170) of the Daru cases.

Ongoing Routine Surveillance

The NDOH surveillance team reported that confirmed cases were reported in all three electorates of the NCD in February 2016 [15].There is clinic testing with rapid diagnostic test kits, with weekly samples being sent to either the Central Public Health Laboratory (CPHL) or the PNG-Institute of Medical Research (PNGIMR) for confirmatory testing. For example, between 25th April and May 6th, 2016, the CPHL tested 1855 blood samples with dengue Rapid Diagnostic Tests (RDT), of which 15% (335) of these samples were positive for DF. The CPHL and PNGIMR also tested the samples for other viruses, such as Chikungunya and Zika viruses. There have been no deaths reported in any of the major clinics in NCD such as Gerehu, Kilakila, 6-Mile and Kaugere clinics during the 2016 outbreak. Among a total of about 700 blood samples collected before 25th April, 2016, 40% tested positive for DF.

Public Health Response

Public health response in Port Moresby has been positive and improving with the National Capital District Commission (NCDC) as the lead implementing agency in carrying out the public health response in the city. Interventions envisioned include fogging, cleaning and

drainage as well as community awareness creation sessions. Additional interventions could include going from house to house and spraying the environment. Risk communication and awareness creation in communities is being conducted by the several agencies: NDOH, NCD, and the NCDC. Interventions proposed include focusing on cleaning and draining in each district and also targeting a day for the interventions. More DF awareness is likely also needed by the clinical staff as well as in communities, so that prompt notification, testing, tracing and examination of contacts and investigation of patient environments can be undertaken by the public health authorities to enable prompt care and necessary measures to be taken.

Coordination and Partnership

The NCDC, NCD Health, IMR, CPHL, WHO and NDOH are involved in the outbreak response and providing updates. While the current 2016 epidemic created an opportunity for collaborating with other sectors as part of the public health response, there are still many challenges. The NDOH report [15] highlighted challenges in implementing the program. These included:

- Lack of an effective, functioning surveillance system that would quantify the emergence, patterns of spread and magnitude of the problem;
- Lack of funding support for timely and progressive fogging in the city;
- Lack of community sustainability of the mosquito control activities;
- Inadequately coordinated communication and awareness creation and
- Lack of funding to enable dissemination of DF Information Education and Communication [IEC] materials (posters) that werealready designed.

Way Forward

There is room for other partners to be involved and actively participating in the response activities. The University of Papua New Guinea (UPNG) School of Medicine and Health Sciences (SMHS) Division of Public Health can facilitate support in terms of providing technical assistance support to developing and conducting operational research and data analysis and building community awareness and strengthened vigorous prevention strategies.

However, we cannot meet the DF challenge in PNG without first closing the surveillance gap described in this article. To achieve progress and mount an appropriate response, we need more and better data than we have now to count the not yet counted and make the now invisible visible. Without surveillance data we have no idea who is getting DF, where they

are, what their behaviours are, who is dying from it, or what the effects of any control measures might be. This information and more is needed to effectively target our response, and also to further learn from comparisons with DF surveillance data from other countries and areas in our region.

Then, building on the resulting surveillance information, more awareness in the community based on that evidence could more appropriately empower individuals, families, groups, clinicians, organizations, communities and the health services generally to play active roles in achieving, sustaining and protecting their own and the public's health and managing the various aspects of the DF threat and burden confronting us. Effective IEC strategies that are then appropriately tailored and targeted would help all stakeholders learn to make better decisions, modify their behaviours and change key areas of the social conditions necessary to overcome the DF challenge.

REFERENCES

1. World Health Organization, "Dengue and severe dengue," 17 May 2016. [Online].Available:www.who.int/mediacentre/factsheets/fs117/en/.
2. V. Asigau, E. K. Lavu, W. McBride, E. Biloh, F. Naroi, E. Koana, J. Ferguson and M. Laman, "Prevalence of patients with acute febrile illnesses and positive dengue NS1 tests in a tertiary hospital in Papua New Guinea," *American Journal of Tropical Medicine and Hygiene,*vol. 2, no. 2, pp. 4-8, 2011.
3. Y. Arima and T. Matsui, "Epidemiologic update of dengue in the Western Pacific Region, 2010," *Western Pacific Surveillance and Response Journal,* vol. 2, no. 2, pp. 4-8, 2011.
4. Y. Arima, Z. Edelstein, H. Han and T. Matsui, "Epidemiologic update of dengue situation in the Western Pacific Region, 2011," *Western Pacific Surveillance andResponse Journal,* vol. 4, no. 2, pp. 47-54, May 2013.
5. Y. Arima, M. Chiew and T. Matsui, "Epidemiologic update on the dengue situation in the Western Pacific Region, 2012," *Western Pacific Surveillance and Response Journal,* vol. 6, no. 2, pp. 82-89, April 2015.
6. J. Hanna and S. Ritchie, "An apparent recent decline in importations of dengue from Papua New Guinea into north Queensland," Communicable Diseases Intelligence Quarterly Report, vol. 33, pp. 34-35, 2009.
7. E. Viennet, S. Ritchie, H. Faddy, C. Williams and D. Harley, "Epidemiology of dengue in a high-income country: a case study in Queensland, Australia," Parasites and Vectors, vol. 379, pp. 1-16, 2014.
8. M. Jonduo, G. Bande and P. Horwood, "Arboviruses of human health significance in Papua New Guinea," PNG Medical Journal, vol. 55, no. 1, pp. 35-44, 2012.
9. World Health Organization, "Situation update," 22 April 2016. Available: www.wpro.who.int/southpacific/programmes/communicablediseases/disease_surveillance_response/page/.

10. J. Messina, O. Brady, T. Scotty, C. Zou, D. Pigott, K. Duda, S. Bhatt, L. Katzelnick, R. Howes, K. Battle, C. Simmons and S. Hay, "Global spread of dengue virus types: mapping the 70 year history," Trends in Microbiology, pp. 138-146, 2014.
11. R. Rodriguez-Roche and E. A. Gould, "Understanding the dengue viruses and progress towards their control," Biomed Research International, pp. 1-20, 2013.
12. N. Vasilakis, J. Cardosa, K. Hanley, E. Holmes and S. Weaver, "Fever from the forest: prospects for the continued emergence of sylvatic dengue virus and its impact on public health," Nature Reviews Microbiology, vol. 9, no. 7, 2011, pp. 532.
13. E. Calvez, L. Guillaumot, L. Millet, J. Marie, H. Bossin, V. Rama, A. Faamoe, S. Kilama, M. Teurlai, F. Mathieu-Daude and M. Dupont-Rouzeyrol, "Genetic diversity and phylogeny of Aedes aegypti, the main arbovirus vector in the Pacific," PLoS Neglected Tropical Diseases, Vol. 10, no. 1, p. e0004374, 2016.
14. M. Chan, E. Christophel, D. Gopinath and R. Abdur, "Challenges and future perspective for dengue vector control in the Western Pacific Region," Western Pacific Surveillance Response Journal, vol. 2, no. 2, pp. 9-16, 2011.
15. National Department of Health, "Sitrep4 – NCD Dengue Outbreak," National Department of Health, Port Moresby, 2016.
16. World Health Organization, 2016. [Online].Available:/www.who.int/features/qa/54/en/. [Accessed 23 May 2016].

DENGUE FEVER: AN OVERVIEW

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INTRODUCTION:

Dengue Fever is caused by one of the arthropod –borne viruses of the genus *Flavivirus* in the family *Flaviviridae* [1]. They are also called arboviruses. The genus includes a number of other viruses transmitted by mosquitoes and ticks that cause diseases in humans; these are yellow fever, West Nile, Japanese encephalitis, and tick-borne encephalitis viruses [1].

Aedes aegypti is the main vector for the dengue virus (DENV) worldwide. In nature, infection by the DENV involves mainly humans and *Aedes* mosquitoes, although in Malaysia and West Africa dengue transmission have been reported in monkeys and forest *Aedes* spp [1]. The vector as well as the less common species have been reported to live around homes biting humans mainly during the day and breed where there are small collections of fresh water, such as in cisterns and even in backyard litters. For example, surveys in Texas revealed that up to 25% of premises had *A. aegypti* breeding in their water containers [1]. It has been reported that humans are uniformly susceptible and that age, race and gender do not appear to influence this susceptibility [1, 2].

In 1943, Ren Kimura and Susumu Hotta first isolated the dengue virus [3]. These two scientists were studying blood samples of patients taken during the 1943 dengue epidemic in Nagasaki, Japan. A year later, Albert B. Sabin and Walter Schlesinger independently isolated the dengue virus. These scientists working in different countries isolated the virus now referred to as dengue virus 1 (DEN-1) [3].

Dengue Virus (DENV) Genome and Structure:

The genome of DENV is a single strand positive-sense RNA (ss RNA) of approximately 11 kilobase. The positive-sense implies that the RNA can be translated directly into polypeptide. The RNA genome of DENV encodes 10 genes. During translation the DENV genome produces a single long polypeptide chain, which is later fragmented into 10 separate proteins [4].

The 10 proteins are made up of 3 structural proteins and 7 non-structural proteins. The

structural proteins are the Capsid (C), Envelope (E) and Membrane (M). The non-structural proteins are NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5. They are involved in viral replication and assembly [4].

The DENV is roughly spherical in shape. The Nucleocapsid that forms the viral core is made up of the viral genome and the Capsid (C) proteins. The viral envelope is the lipid bilayer (membrane) that surrounds the Nucleocapsid. There are about 180 copies of proteins E and M embedded in the viral envelope and span the lipid bilayer. These proteins form the protective outer layer that regulates the entry of the DENV into the host cells [4]. The glycoprotein E contains most of the antigenic determinants of the DENV and is essential for viral attachment and entry into the host cell.

During infection, the DENV attaches to the surface of the host cell and enters the cell via Endocytosis. Inside the cell, the DENV fuses with the endosomal membrane and is released into the cytoplasm. The DENV particle comes apart, releasing the viral genome. The positive-strand viral RNA is then translated into a single polypeptide, which is fragmented into 10 proteins. The viral RNA is replicated by using the genetic materials of the host [4]. When production of the structural proteins and RNA genome are completed, the assembly of new DENV occurs on the endoplasmic reticulum. The immature viral particles are transported through the trans-Golgi network (TGN), where they mature and are converted to their infectious form. When the mature DENV are released they then infect new cells [4].

Infected white blood cells respond by producing cytokines, such as interferon that are responsible for most of the symptoms characteristics of dengue fever, the flulike symptoms and severe pains [4, 5]. In severe infection, large amount of the DENV are produced and many more tissues and organs (such as the liver and the bone marrow) are affected. Dysfunction of the bone marrow can cause thrombocytopenia that increases the risk of bleeding, which is one of the major complications of severe dengue [4, 5].

Dengue Serotypes:

Four closely related dengue viruses named DEN-1, DEN-2, DEN-3, and DEN-4 are known to cause dengue infections [1, 4 – 7]. Each of the four viruses has different interactions with antibodies in the human host serum, thus they are called Serotypes. Genetically, the four dengue viruses are similar because they share about 65% of their genomes; however, within a single serotype, there is some genetic variation. Despite these variations, infection with each of the dengue serotypes results in the same disease and range of clinical symptoms.

Infection with one serotype provides life-time protection only against that particular serotype. However, it is still possible to become infected

by other serotypes, which may develop into severe dengue [4 – 7].

According to the WHO expert consensus groups, dengue is a single entity with different clinical presentations [6, 7]. Infected patients may present with a range of clinical symptoms that vary according to severity and age. Infection by any of the four dengue serotypes may be asymptomatic or may lead to classic dengue fever (DF), or to more severe forms of the disease, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) [6, 7]. In 1997 the dengue case definition was limited in terms of its complexity and applicability. This recognition of the limitations led to a multicenter study in seven countries in Asia and Latin America. A new case definition emerged from this study. The new WHO classification for dengue severity was divided into Dengue without Warning Signs, Dengue with Warning Signs, and Severe Dengue (DHF) [6, 7].

Epidemiology of dengue and severe dengue:

The DENV is endemic in many areas of the tropics and subtropics, Asia, Oceania, Africa and parts of North and South America. Outbreaks have been known to occur in the Caribbean and the USA (Rio Grande Valley of Texas). In 1981, 350,000 cases of dengue were recorded in Cuba of which 158 died [8]. According to the current WHO database, only 9 countries had experienced severe dengue epidemics before 1970. However, the disease is now endemic in more than 100 countries in the WHO regions of Africa, the Americas, the Eastern Mediterranean, South-East Asia and the Western Pacific [9,10]. The America, South-East Asia and Western Pacific regions are the most seriously affected [9 – 11]. In 2008 the cases across the Americas, South-East Asia and Western Pacific exceeded 1.2 million and over 3 million in 2013 [9 – 11]. The threat of a possible outbreak of dengue fever in Europe was raised because local transmission was reported in France and Croatia in 2010 and imported cases were detected in 3 other European countries. In 2012, an outbreak of dengue on the Madeira Islands of Portugal resulted in over 2000 cases and imported cases were detected in mainland Portugal and 10 other countries in Europe. In 2013, severe dengue cases occurred in Florida (USA) and Yunnan province of China. Dengue also continues to affect several South American countries, notably Costa Rica, Honduras and Mexico. In Asia, Singapore has reported an increase in cases after a lapse of several years and outbreaks have also been reported in Laos. In 2014, trends indicate increases in the number of cases in China, the Cook Islands, Fiji, Malaysia and Vanuatu, with DEN-3 affecting the Pacific Island countries after a lapse of over 10 years. Dengue was also reported in Japan after a lapse of over 70 years. A total of 2.35 million cases of dengue

were reported in the Americas alone in 2015, of which 10200 cases were diagnosed as severe dengue causing 1181 deaths [10 – 11]. The year 2015 was characterized by large dengue outbreaks worldwide, with the Philippines reporting more than 169000 cases and Malaysia exceeding 111000 suspected cases of dengue, representing a 59.5% and 16% increase in case numbers to the previous year, respectively. Brazil alone reported over 1.5 million cases in 2015, approximately 3 times higher than in 2014. Delhi, India in 2015 recorded its worst outbreak since 2006 with over 15000 cases. The Island of Hawaii USA was affected by an outbreak with 181 cases reported in 2015 and ongoing transmission in 2016. The Pacific island countries of Fiji, Tonga and French Polynesia have continued to record cases. An estimated 500000 people with severe dengue require hospitalization each year, a large proportion of which are children. About 2.5% of those affected died [10 – 11].

In the recent and ongoing outbreak in Papua New Guinea (PNG) a total of 170 cases were seen at the Daru Hospital Outpatient Department, Daru Western Province from 4 November 2015 to 8 January 2016 [12]. There were a total of 126 clinical cases and 44 confirmed cases (2 confirmed by PCR as DENV-2). Age of cases ranged between 6 to 35 years with children less than 5 years representing 12% of the cases. Seven severe clinical cases were hospitalised; all of them recovered and discharged. Several other cases have been reported in Port Moresby General Hospital with no fatalities reported [12].

Clinical Manifestations of dengue:

Infections by the DENV may not be apparent or may be subclinical. When symptoms are obvious, three classes may be recognized: Classic dengue (dengue with warning signs), dengue haemorrhagic fever (DHF, also known as Severe Dengue) and an atypical form (dengue without warning signs) [6, 7, 13]. Classic dengue is also known as “break bone fever” (because of the associated muscle and joint pains) and it occurs mainly in non immune people. The usual incubation period is 5 to 8 days. These patients may have mild conjunctivitis and coryza which may be followed a few hours later by a sudden onset of severe headache with pain in the back of their eyes as well as in the lower back. About three quarters of these patients may have sore eyes with some photophobia. Rigors are commonly seen later. Patients in this category may have some difficulty sleeping, anorexia and a bitter taste. Quite a few of them may experience some weakness at this stage [6, 7, 13]. About a quarter of these patients may have a sore throat with some rhinitis. Cough is hardly seen in this group. Some patients may present with bleeding noses and gums, haematuria and black stool (melaena). In one study where 26 patients were recruited, 13% had bleeding peptic ulcers on endoscopy. Ninety percent

have red eyes which were tender upon pressing [1, 14]. Some of these patients may present with non tender palpable lymph nodes in the posterior cervical, the epitroclear and the inguinal groups. Over half of these patients may have small vesicles in the posterior part of the soft palate. The tongue is often coated in these patients and they have skin rash which vary from diffuse flushing over the thorax and inner aspect of the arms. Later these give way to a more definite maculopapular rash on the trunk on the third to the fifth day and spreads peripherally. This rash may be pruritic and ends with drying or scaling.

Extreme bradycardia is rare in this group of patients. About 2 to 3 days after the onset of the illness, the fever as well as the other symptoms may almost subside completely. This remission however may last for 2 days only to be followed by the return of fever and the other symptoms, although they are usually not as severe as during the initial attack. This is described as a saddleback diphasic phase of the illness although it may not occur in some patients [1, 6, 7, 13, 14]. This febrile illness may last 5 to 6 days and terminates abruptly. Some patients may experience fatigue for several months after the attack of dengue fever.

The atypical mild illness may be seen in some patients. Symptoms include fever, anorexia, headache and muscle aches. Clinical examination may reveal skin rashes but involvement of lymph nodes is usually absent. The course of the illness is usually less than 3 days [1, 6, 7].

In both the classic and mild dengue, the leukocyte count may be low or normal. By the third to the fifth day the leukocyte counts of less than 5000 per microliter and neutropenia are common. Sometimes albuminuria of moderate degree may be seen [14].

Severe Dengue {Dengue Haemorrhagic fever (DHF)}:

This is the third category of Dengue infection. Severe dengue (also known as Dengue Haemorrhagic Fever DHF) was first recognized in the 1950s during dengue epidemics in the Philippines and Thailand. Today, severe dengue affects most Asian and Latin American countries and has become a leading cause of hospitalization and death among children in these regions [6, 7, 13].

All the 4 dengue serotypes can cause Severe Dengue and Dengue Shock Syndrome (DSS). This may occur in about 5% of patients, especially in patients who have previously been infected with another serotype of DENV. This is referred to as “Secondary Infection”. The major reason why secondary infection with a different serotype of DENV places individuals at risk of developing Severe Dengue Fever and DSS is not clear. However, the most widely accepted hypothesis is that of antibody-dependent enhancement (ADE). Severe dengue and DSS

are the most serious clinical manifestations of DENV infection. Some researchers have suggested that ADE and immunopathological mechanisms are implicated in such complications [6, 7, 13].

In Asia, children suffer more from severe dengue, with one peak occurring under the age of 1 and a second in older children aged 3 to 5. In infants, the disease is associated with primary infection in the presence of maternal antibodies. Studies in Thailand have estimated the frequency of DSS as 11 per 1000 secondary dengue infections with the disease being more common in girls. DSS tends to occur more frequently in the indigenous populations. It seems to be rare in people of European descent [6, 7, 13, 14].

Clinical Manifestations of Severe Dengue:

The illness begins abruptly and is characterized by fever, cough, pharyngitis, headache, anorexia, nausea, vomiting and abdominal pain which is often severe. This usually lasts for 2 to 4 days. Muscle pain, joint pain and bone pains are unusual compared to the classical disease [1, 6, 7].

Physical signs include fever ranging from 38.3 to 40.6^{o}C, redness or inflammation of tonsils and pharynx, palpable lymph nodes and liver. The initial stage is usually followed by sudden deterioration, with rapid onset of weakness and lassitude. On examination, the patient (usually a child), may be found to be restless, with cold clammy hands and feet, a warm trunk and with cyanosis. Petechiae, caused by broken capillaries, are often found on the forehead and extremities in 50% of cases [1, 6, 7]. There may be a macular or maculopapular rash. The extremities are often cyanotic. Hypotension with narrowing of the pulse pressure, and tachycardia are often noted. Pathologic reflexes may be present. Most fatalities occur in the fourth or fifth day of the illness. Poor prognostic signs include melaena, haematemesis, coma, or unresponsive shock.

Laboratory findings:

Haemo-concentration may be present in 20% of affected children. The majority of children may develop leukocyte count between 5000 and 10,000 per microliter with about one third showing leukocytosis. Usually about 10% of children may have true leukopenia. The most characteristic findings are thrombocytopenia, rarely with blood platelets under 75,000 cells per microliter, positive tourniquet test and prolonged bleeding time. Prothrombin time and Partial Thromboplastin Times (PTT) are usually near the normal values [6, 7]. Depression of clotting factors V, Vll, IX and X may be present. Bone marrow examination may reveal maturation arrest of megakaryocytes.

In a case study in Manila and in Bankok, haematuria was frequent even with other bleeding signs; however in Tahiti gross haematuria was common [14]. The cerebrospinal fluid (CSF) examinations are

usually normal in most patients. Other abnormal laboratory findings may include hyponatremia, acidosis, elevated blood urea and nitrogen levels, elevation of Aspartate Transaminase (AST) level, mild hyperblirubinaemia and hypoproteinaemia [14]. ECG may reveal diffuse myocardial abnormalities. Two thirds of patients may have radiological evidence of pneumonia; many of them may show pleural effusions. Ultrasonography is useful in detecting pleural effusions, ascites and thickening of the bladder wall.

Diagnosis of severe dengue:

The WHO has established criteria for the diagnosis of severe dengue (DHF). Acute onset high fever continuous and lasting for 2 – 7days; haemorrhagic manifestations, including at least a positive tourniquet test and any of the following: petechiae, purpura, ehymoses, epistaxis, bleeding gums, haematemesis or melaena, enlargement of the liver, thrombocytopenia of less than 100,000 cells per microliter, haemoconcentration, haematocrit increased by more than 20% [1, 6, 7].

Criteria for DSS: rapid weak pulse with narrowing of the pulse pressure of less than 20%, or hypotension with cold, clammy skin and restlessness. The WHO classification includes grading of severity (table 1). Minor haemorrhagic manifestations may be seen during the course of Classic Dengue fever without meeting WHO criteria for severe dengue [1, 6, 7].

Table 1: (Modified) World Health Organisation's clinical classification of Severe Dengue or Haemorrhagic fever (DHF)

Grades	Clinical Features	Laboratory findings
I	Fever, constitutional symptoms, positive tourniquet test	Haemoconcentration, Thrombocytopenia
II	Grade 1 plus spontaneous bleeding (eg. Skin, gums, git)	Haemoconcentratiion, Thrombocytopenia
III	Grade ll plus circulatory failure, agitation	Haemoconcentration, Thrombocytopenia
IV	Grade ll plus profound shock (BP =0)	Haemoconcentration, Thrombocytopenia

NB: Grades I – IV = DHF (Dengue Haemorrhagic Fever)
III & IV =DSS (Dengue Shock Syndrome)
Git = Gastrointestinal tract

Treatment for Severe Dengue:

The mainstay is correction of circulatory collapse while avoiding fluid overload. Administration of 5% glucose in 0.5N saline at a rate of 40ml/kg will restore blood pressure within 1 to 2 hours in most of the patients. When stable, the rate of administration of IV fluids can be reduced to 10ml/kg per hour. If improvement does not occur, plasma or plasma expander (20ml/kg) may be administered. Transfusion of whole blood is not recommended. Oxygen should be administered. Glucocorticoids have been used but doses of 25mg/kg have not resulted in significant improvement. Since the evidence for severe disseminated intravascular coagulation is questionable, the use of heparin is not clear-cut, although in a group of Philipino children with DEN 3, administration of heparin (1.0mg Sodium Heparin per kilogram) was associated with a dramatic rise in number of platelets and level of plasma fibrinogen. Antibiotics are not indicated; sympathomimetic amines and Salicylates are contraindicated [1, 6, 7]. Paracetamol can be taken to bring down fever and reduce joint pains. However, aspirin or ibuprofen should not be taken since they can increase the risk of bleeding.

Recovery from vascular collapse usually occurs within 24 to 48 hours at which time diuretics and digitalis may be necessary. An uncontrolled trial of interferon was conducted during the 1981 epidemic in Cuba with some indication of efficacy [1].

Prognosis:

Mortality has varied from 1- 23%. Deaths have been most common in infants under 1 year of age [6, 7].

Prevention:

At present there is no specific dengue therapeutics; vector control is the only preventive method available. As a precautionary approach, patients can adopt measures to reduce transmission by sleeping under treated bed nets especially during the period of illness with fever. However, the growing global epidemic of dengue is of mounting concern, thus a safe and effective vaccine is urgently needed [6, 7, 15].

Status of dengue vaccine development:

According to the WHO [15], the first dengue vaccine, Dengvaxia (CYD-TDV) by Sanofi Pasteur, was registered in Mexico in December, 2015. CYD-TDV is a live recombinant tetravalent dengue vaccine that has been evaluated as a 3-dose series on zero / six / twelve month schedule in Phase III clinical studies. The vaccine has been registered for use in individuals 9-45 years of age living in endemic areas. There are approximately five additional vaccine candidates under evaluation in clinical trials,

including other live-attenuated vaccines, as well as subunit, DNA and purified inactivated vaccine candidates. Additional technological approaches, such as virus-vectored and VLP-based vaccines, are under evaluation in preclinical studies [15].

REFERENCES:

1. Peters CJ: Infections caused by Arthropod- and Rodent-Borne Viruses: Dengue fever; In Harrison's Principles of Internal Medicine 18th Edition, 2012; McGraw-Hill Companies, Inc. USA, ISBN 978-0-07174889-6; MHID 0-07-174889-X
2. Centers for Disease Control and Prevention: Update: Management of patients with suspected viral hemorrhagic fever—United States. MMWR 44:475, 1995 (www.cdc.gov): In Harrison's Principles of Internal Medicine 18th Edition, 2012, 2012; McGraw-Hill Companies, Inc. USA, ISBN 978-0-07174889-6; MHID 0-07-174889-X
3. Mukhopadhyay S, Kuhn RJ and MG Rossmann. A structural perspective of the flavivirus life cycle; Nature Reviews Microbiology 2005, 3, 13–22. doi:10.1038/nrmicro1067
4. Alcaraz-Estrada SL, Yocupicio-Monroy M and R María del Angel. Insights into dengue virus genome replication. Future Virol. 2010, Vol 5 (5), 575–592: www.futuremedicine.com
5. Srinivas V and VR Srinivas. "Dengue Fever: A Review Article". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 29, April 09; Page: 5048-5058, DOI:10.14260/jemds/2015/736
6. Dengue Guidelines for Diagnosis, Treatment, Prevention and Control: A joint publication of the World Health Organization (WHO) and the Special Programme for Research and Training in Tropical Diseases (TDR), New Edition 2009, www.who.int/mediacentre/factsheets
7. WHO; Global strategy for dengue prevention and control 2012-2020; Publication of the World Health Organization, available on WHO web site: www.who.int
8. Micks DW and WB Moon. Aedes aegypti in a Texas coastal country as an index of dengue fever receptivity and control. Am. Journal of Trop Med Hyg 29: 1382 1980. In Harrison's Principles of Internal Medicine 13th Edition.
9. Epidemiology of dengue and severe dengue;CDC2016.www.cdc.gov/Dengue/epidemiology/
10. Global database on dengue, updates 2016.www.nature.com/scitable/topicpage/dengue-viruses.
11. Dengue fever, Zika and Chikungunya updates. www.arphs.govt.nz/health-information/communicable-disease/dengue-fever-zika-chikungunya
12. WHO/WPRO; Emerging disease surveillance and response: Weekly Pacific Syndromic Surveillance Reports on emerging diseases in Pacific. WPRO regional report 2016. www.wpro.who.int/southpacific/programmes/communicable_diseases/disease_surveillance_response
13. WHO and TDR. Handbook for clinical management of dengue; WHO 2012 www.wpro.who.int/mvp/documents/handbook_for_clinical_management_of_dengue.
14. World Health Organization and Pan American Health Organization (WHO & PAHO) Number of Reported Cases of Dengue and Severe Dengue (SD) in the Americas, by Country: Figures for 2016, Epidemiological Week / EW 18 (Updated Mayo 13, 2016) www.paho.org/hq/index.php?option
15. WHO: Dengue vaccine research. WHO document, WHO Geneva 2016. www.who.int/immunization/research/development/dengue_vaccines/en/

CHILDHOOD BURNS REQUIRING HOSPITALIZATION IN WESTERN FIJI: A RETROSPECTIVE STUDY

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ABSTRACT:

The objective of this study was to access the causative factors in burn injuries in patients, five years and younger, admitted to the burns unit at Lautoka Hospital. Data was collected for analysis from the Hospital computer database and from case folders. There were 178 burn admissions, most of them under 20% of body surface area (BSA). Among the 178 patients 70 (39.3%) were children of 5 years of age or less; only those data were included in the study. Of the 70 children 92.9% were three years of age or less. The mean age of all the children was 19.8 months. Gender distribution of the children indicated 47 (67.1%) male and 23 (32.9%) were female. Distribution by ethnicity indicated 70.0% ethnic Fijians, 25.7% ethnic Indians and 4.3% were of other races. Clinical examination shows 97.1% were scalding burns and most of them occurred during cooking (44) or serving (22) food. Household electric kettles were involved in causing the burn injuries in 28.5% of the cases.

In conclusion almost all the burns in our present study were due to scalds. The results show a very low incidence of flame, contact, chemical or intentional burns as compared to other studies. Electric kettles were involved in almost one third of the cases.

Keywords: Pediatric burns, scalds, incidence, Fiji

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INTRODUCTION:

Burns are a common cause of pediatric injury worldwide and most of these are caused by hot liquids at home [1]. The mechanism of burn injuries in children is markedly different from that in adults. Whereas flame, chemical and workplace injuries predominate in adults, in children, burns are usually scalds in the home environment [2, 3]. The inherent playful, curious and ignorant nature of children makes them more prone to burn injuries. Socio cultural factors also play a major part in the mechanism

of childhood burns resulting in different causes in different cultures [4,5,6,7,8]. Most childhood burns are not life threatening, but they cause significant pain and physical and psychological suffering. They also entail a huge drain on precious health care resources. The objective of this study was to access the causative factors in burn injuries in patients five years and younger, admitted to the burns unit at Lautoka Hospital.

METHODS:

This was a retrospective study conducted on admissions to the Burns Unit at Lautoka Hospital, Fiji between January 2011 and December 2013. This tertiary hospital is the receiving centre for all burns in the Western Division of the country. It caters to a population of 365379 [9]. Patient data was collected for analysis from the admission register, the Hospital computer database and from case folders retrieved from Medical Records. Burn percentages were calculated using the Lund and Browder chart for children [10].

RESULTS:

There were a total of 178 burn admissions in the Burns Unit in the years 2011 to 2013. Out of these 70 (39.3%) were children of 5 years of age or less and were included in the study.

Table 1: Age Distribution of the 70 children included in the study

Age in years	Number (%)
< 1	15 (21.4%)
1 – 2	37 (52.9)
2 – 3	13 (18.6%)
3 – 4	2 (2.9%)
4 – 5	3 (4.3%)

Of these 65 (92.9%) were three years of age or less. The mean age of all the children was 19.8 months; the youngest child was 4 months old. Table 1 shows the age distribution of all the children. Of the 70 children, 47 (67.1%) were male and 23 (32.9%) were female. Distribution of the children according to their ethnicity shows that 49 (70.0%) were ethnic Fijians while 18 (25.7%) were ethnic Indians and 3 (4.3%) were of other races. Clinical examination shows that 68 (97.1%) suffered scalding injury, one had a flame burn and one was burnt with a hot

iron. Of the 68 children who were scalded, 44 (64.7%) were injured during the cooking, 22 (32.4%) during serving of food and only 2 (2.9%) by hot bathing water. Among the 68 scalding burns 20 (29.4%) were caused by the use of electric kettles. Most of the burns (92.9%) were under 20% of BSA.

The number (%) of cases with the percentage burn areas are presented in Table 2:

Table 2: Number (5) of cases with burn percentage

Burn area	Number (%)
1 – 5%	17 (24.3%)
6 – 10%	24 (34.3%)
11 – 15%	16 (22.9%)
16 – 20%	8 (11.4%)
> 20%	5 (7.1%)

In the period covered in this study mortality was recorded; a 13 month old girl with 40% scalds burns, caused after the nanny put the child in a tub of hot water to bathe her. This was the only case in which an intentional motive was suspected. All other burns were unintentional.

DISCUSSION:

Burns are the fourth most common type of trauma worldwide and comprise between three to eight per cent of all childhood injuries [11] and are a major cause of mortality and morbidity, particularly in low and middle income countries (LMIC) where 95% of burn deaths occur [12]. The incidence of burn injuries and their sequela in children have shown a significant decline in developed countries due to better preventive and management strategies [12]. In LMIC implementation of advanced burn management is usually not feasible because of resource competition from other important health care issues such as infections and non-communicable diseases. Thus, for LMIC it is important to understand local causation so that maximum returns on health expenditure can be achieved through properly targeted prevention.

Burns in children five years and less accounted for 39.3% of all burn admissions in our present study and this is comparable to that found by other researchers [13]. Children under three years of age are most prone to unintentional scalds [14]. Their increasing mobility combined

with the lack of knowledge about dangerous objects puts them at risk [15].

Male children outnumber females in most worldwide studies as well as in our study [1, 11, 14, 15]. In the older child, reasons for this gender differences are apparent. In many societies boys tend to play outdoors and are more likely to sustain flame and chemical injuries, while girls may be more involved in kitchen and household work. However it is difficult to explain this gender difference in children less than three years of age. One would expect these children to have similar behaviour and receive similar treatment from caregivers. It is obvious that further thought and study is needed to elucidate this problem [1].
Most burns occurred in the ethnic Fijian population as compared to the local Indian population. Socio cultural and lifestyle factors need to be investigated to find the reasons for this difference between the two major ethnic groups in Fiji.

The scalding burn rate obtained in the present study was 97.1%. Only two children in our study did not suffer a scalding burn. This is in variance with other published studies in which scalds comprise between 59.0 – 92.0% of childhood burns [5, 14, 17, 18, 19] with the rest being flame, contact and chemical burns.

Only in one child (2.9%) in our study was intentional injury suspected (but not proven). This is a very low rate as the incidence reported elsewhere is between 10.0 – 12.0% [19, 20].

The common causes of injury in our study were related to the child accidentally spilling of hot food while it was on the stove or on the floor or on a table. Only two children were injured by hot bath water and this was in a basin and not by running water.

In 29% of cases electric kettles were involved. These kettles are used commonly in Fiji not only for cooking but to heat water for bathing and other activities and are a danger as they are often kept on a table or refrigerator and have trailing cords. This aspect of burn injuries has also been commented upon by J G Ray [16] and Rafii [14, 20].

Awareness on the ways in which children get scalded at home should be disseminated by health care workers to the public. Children should be restricted from entering or playing in cooking areas in dwellings. Some simple child proof barriers for e.g. movable storage shelves can be used for this purpose.

Electric kettle spills can be reduced if families with toddlers can be motivated to purchase the squat (traditional) shaped electric kettle rather

than the currently popular tall, narrow based kettles that are commonly available and are more easily toppled.

CONCLUSIONS:

Results obtained in the present study population indicated that almost all burns in the under five age group are caused by hot liquids. Most injuries occur during cooking and serving food with a significant number involving electric kettles. The incidence of flame, contact, chemical and intentional injuries were very low.

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REFERENCES:

1. Janine Duke, Fiona Wood, James Semmens, Dale W. Edgar, Katrina Spilsbury, Delia Hendrie and Suzanne Rea. Burn hospitalizations for children younger than 5 years of age: 1983 – 2008. Pediatrics; originally published online 2011 March 7; DOI: 10.1542/peds.2010-3136. Available from: www.pediatrics.aappublications.org/content/early/2011/03/07/peds.2010-3136
2. Atiyeh B.S, Rubeiz M, Ghanimeh G, Nasser A.N, Al-Amm C.A. Management of Paediatric Burns. Annals of Burns and Fire Disasters - vol. XIII - n. 3 - Sept 2000
3. Nele Brusselaers, Stan Monstrey, Dirk Vogelaers, Eric Hoste, Stijn Blot. Severe burn injury in Europe: a systematic review of the incidence, etiology, morbidity, and mortality. Critical Care 2010, 14:R188. Available from: www.ccforum.com/content/14/5/R188
4. Hammig BJ, Ogletree RJ. Burn injuries among infants and toddlers in the United States, 1997-2002. Am J Health Behav. 2006 May-Jun; 30(3):259-67. PMID: 16712440
5. Labib J R, Shalaby S F. Epidemiology and outcomes of pediatric burn injuries in Cairo University Hospital – Egypt. British Journal of Medicine and Medical Research. 2014; 4(4): 1056-1068. ISSN: 2231-0614
6. Ahmed M; Ann Burns Fire Disasters. 2010 Mar 31; 23(1): 25–27, published online Mar 31, 2010, PMCID: PMC3188237. Available from: www.ncbi.nlm.nih.gov/pmc/articles/PMC3188237/
7. Forjuoh SN. Burns in low- and middle-income countries: a review of available literature on descriptive epidemiology, risk factors, treatment, and prevention. Burns. 2006 Aug;32(5):529-37. Epub 2006 Jun 14
8. WHO Burns Fact Sheet N°365 Updated April 2014. Available from: www.who.int/mediacentre/factsheets/fs365
9. Ministry of Health Annual Report 2013. Pg. 21. Available from: www.health.gov.fj/PDFs/Annual%20Report/Annual%20Report%202013.pdf
10. Demetrius A Miminas. A critical evaluation of the Lund and Browder chart. Wounds UK, 2007,Vol 3,No 3
11. Mercier C, Blond M H. Epidemiological survey of childhood burn injuries in France. Burns. 1996 Feb; 22 (1): 29-34. doi:10.1016/0305-4179(95)00073-9
12. A WHO plan for burn prevention and care. Geneva, World Health Organization. 2008. Page 5. Available from: www.whqlibdoc.who.int/publications/2008/9789241596299_eng.pdf
13. Grisolia G A, Pinzauti E, Pancani S, Pavone M. Paediatric Burns in the acute phase: Specific Aspects. Annals of Burns and Fire Disasters. 2005 Dec; XVIII (4)

14. Kai-Yang L, Zhao-Fan X, Luo-Man Z, Yi-Tao J, Tao T, Wei W, Bing M, Jie X, Yu W, Yu S. Epidemiology of pediatric burns requiring hospitalization in China: a literature review of retrospective studies. Pediatrics. 2008 Jul; 122 (1): 132-42. doi: 10.1542/peds.2007-1567,PMID: 18595996
15. Michael H. Toon, Dirk M. Maybauer, Lisa L. Arceneaux, John F. Fraser, Walter Meyer, Antoinette Runge, Marc O. Maybauer. Children with burn injuries-assessment of trauma, neglect, violence and abuse. J Inj Violence Res. 2011 Jul; 3(2): 98-110. doi: 10.5249/jivr.v3i2.91
16. World report on child injury prevention. Page 98, ISBN 978 92 4 156357 4. Available from: www.whqlibdoc.who.int/publications/2008/9789241563574_eng.pdf
17. Ray J G. Burns in young children: a study of the mechanism of burns in children aged 5 years and under in the Hamilton, Ontario burn Unit. Burns, 1995 Sep 6; 21 (6): 463-466. doi:10.1016/0305-4179(95)00020-C
18. Spinks A, Wasiak J, Cleland H, Beben N, Macpherson A K. Ten-year epidemiological study of pediatric burns in Canada. J Burn Care Res. 2008 May-Jun; 29(3):482-8.doi: 10.1097/BCR.0b013e3181776ed9, PMID: 18388560
19. Lowell G, Quinlan K, Gottlieb L J. Sources of Scald Injuries in Young Children. Pediatrics. 2008; 122: 799-804 Medscape. Mar 18, 2009. Available from: www.medscape.com/viewarticle/589353
20. Rafii MH, Saberi HR, Hosseinpour M, Fakharian E, Mohammadzadeh M. Epidemiology of Pediatrics Burn Injuries in Isfahan. Arch Trauma Res. 2012; 1(1):27-30. DOI: 10.5812/atr.5295. Available from: www.archtrauma.com/?page=article&article_id=5383

THE DIAGNOSTIC DILEMMA OF ORAL PSORIASIS: A REVIEW

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ABSTRACT:
Psoriasis is chronic immunologically mediated inflammatory skin disorder affecting 1–3% of Swedish population. It is associated with impairments quality of life even in mild cases, while in severe cases it excess mortality .Oral manifestations of psoriasis are rare and has various clinical presentations which are often difficult to diagnose. Oral psoriasis is a rare entity that might be confused with other oral mucous membrane dermatoses; hence, it should be considered under differential diagnosis of oral mucous membrane disorders and confirmed histo-pathologically. The occurrences of cutaneous lesions along with oral lesions that are diagnosed histo-pathologically give definite diagnosis for oral psoriasis.

Key words: Psoriasis, histopathology, Koebner phenomenon, fissured tongue, geographic tongue.
Submitted January 2016; Accepted April 2016

INTRODUCTION:

Psoriasis is a chronic immunologically mediated inflammatory skin disorder affecting 1–3% of the Swedish population. It is associated with impairments quality of life even in mild cases, while in severe cases it excess mortality [1].

The term psoriasis is derived from the Greek word ‘psora’ meaning itch. It occurs at any age of life with peak between 50-60 Years, slightly more in women, with remissions and exacerbations. The earlier occurrence of psoriasis, the wider spread and more recurrent.10-30% of old age psoriatic patients has rheumatic psoriasis.

Psoriasis vulgar is most common, in which well‑delineated pappulo-squamous plaques, are salmon pink or red color and covered by gray or white scales. Lesions are generally distributed symmetrically, involving most commonly the extensor aspects of elbows and knees, scalp, lumbosacral region, and umbilicus (fig 1). Nail changes are common (fig 2) with positive Koebner phenomenon, in which new lesions develops at the site of pressure or trauma [2].

Psoriasis is characterized by abnormal keratinocyte differentiation, epidermal hyper-proliferation, excess Th-1 inflammation and angiogenesis with blood vessel dilatation [1]. The issue of whether psoriasis can manifest itself in the oral mucosa has been debated for many years. In 1903, the first case of oral psoriasis was reported [3].

Oral manifestations of psoriasis are less well recognized than skin lesions, and treatment for oral lesions is not standardized .Oral lesions can appear on the lips, tongue, palate, buccal mucosa and gingiva showing no consistent lesion pattern. The clinical appearance of reported oral psoriatic lesions is varied, It may appear as White lesions which is plaque shaped can have a punctate or striated texture, or erythematous lesions that could be generalized, patchy, or papular in appearance ,it can also presented as lesions with mixed appearance include both erythema and white striations [4].

The prevalence of oral manifestations in patients with cutaneous psoriasis is uncertain; reports indicate that oral manifestations of psoriasis are rare [5]. Several studies have reported increased presence of fissured tongue (FT) and geographic tongue (GT) in patients with psoriasis [6] fig (3) but the connection has been questioned. Authors who claim an association between GT or FT and psoriasis have focused on the histo-pathologic similarities, but others argue that a parallel course between the conditions is required for a true correlation to exist [7].

Pathophysiology:

Psoriasis is a prototypical Th-1 inflammatory disease characterized by activation and expansion of Th-1 cells, Th-1 cytokines and antigen presenting cells. Elevation in the circulating levels of Th-1 cytokines, adhesion molecules such as E-selectin, ICAM-1 and angiogenic factors, as vascular endothelial growth factor (VEG-F) in psoriasis [8]. The inflammatory cytokines, such as TNF-α, are elevated in the blood and skin of patients with psoriasis, promoting epidermal hyper-proliferation and angiogenesis [9].

The central role of IL-17 and IL-20 in the pathogenesis of psoriasis has been illustrated [10].IL-17 is secreted by a subclass of CD4+, Th1 cells; It is involved in the pathogenesis of psoriasis as well as activates inflammation in many organ systems [11, 12]. Angiogenic factors, such as VEG-F which encourage angiogenesis and endothelial cell activation are produced by immunocytes and keratinocytes in psoriatic skin. The serum level of VEG-F correlates with clinical severity of psoriasis and increased in plaque lesions [8].

Decreased folic acid levels and increased Homocysteine levels promote oxidative stress in psoriasis [13, 14]. Genetics play important role in psoriasis susceptibility. Over 20 genetic loci have been associated with psoriasis susceptibility with no other identified function.

The strongest association was identified on chromosome 6p21 known as PSORS1, a locus within the class I major histocompatibility complex (MHC I) [15]. Some of the Triggers for psoriasis include Stress, Skin injury, Streptoccocal infection, medications such as beta-blockers, anti-malarial and non- steroidal anti- inflammatory drugs [16].

Oral psoriasis:

Oral psoriasis has been seen to manifest in broadly four types of lesions:

First, Well-defined yellowish-white lesions, round to oval in shape, which are independent of cutaneous psoriasis; second, White, circulate, lacy, elevated lesions on the tongue and mucosa that are congruent with skin lesions; third, Redness or erythema of the entire oral mucosa associated with acute exacerbation of psoriasis; forth, Geographic tongue, found more frequently in patients with cutaneous psoriasis than in controls. Oral psoriasis can involve any part of the oral mucosa [17].

Histopathogical features of oral psoriasis:

Para-keratotic epithelium occur n 91% of reported cases of oral psoriasis and long rete ridges and show clubbing or thickening in the lower portion. Epithelial acanthus is seen in up to 65% of cases. Elongated Connective tissue papillae and in many areas the epithelium over the papillae is very thin and at the tips of the connective tissue papillae dilated capillaries.

The uppermost epithelial layers are infiltrated with polymorph nuclear neutrophils in 74% of cases. Lamina propria infiltrate with mononuclear cells. No clear-cut monromicro-abscesses are encountered. Few mitotic figures are observed in the basal epithelium. Epithelial turnover rate is increased to 4 days for the skin and 5-8 days for normal oral mucosa compared with 28 days for normal skin and mucosa fig (4). Although psoriatic lesions are not premalignant, dystrophic changes may occur after treatment with arsenicals or radiation. The fact that the regeneration of epithelial cells in the oral cavity is more rapid than those in the skin may account for lack of documented oral changes in psoriasis patients. It is also possible that the oral environment itself may alter oral lesions, both clinically and histologically [2].

A definitive diagnosis of oral psoriasis is also more convincing when the oral lesion follows that of the skin disease. However, there are reports of oral manifestations without concurrent skin lesions [18].

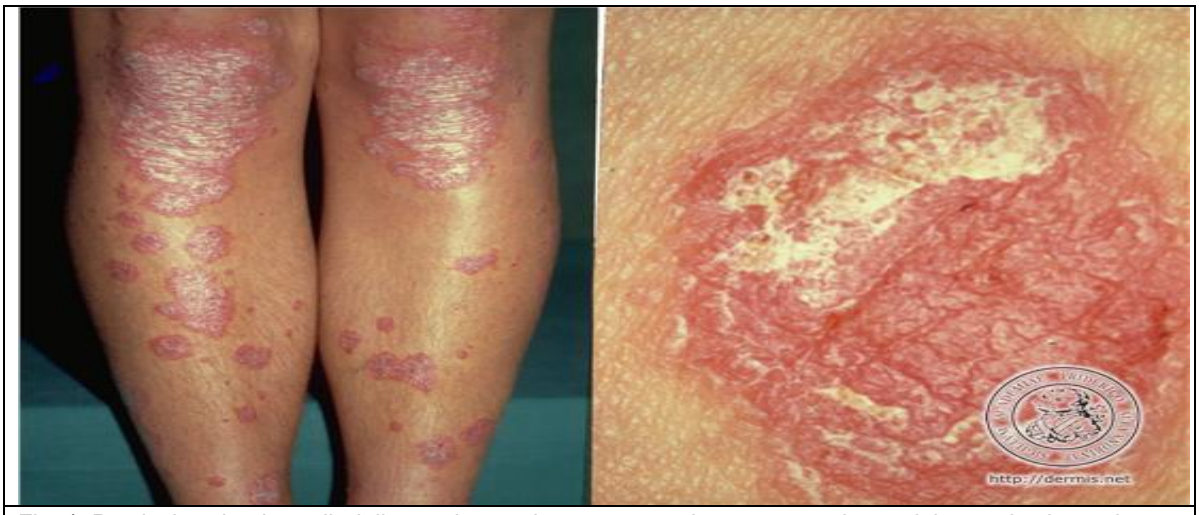

Fig. 1: Psoriasis vulgaris, well-delineated pappulo-squamous plaques, are salmon pink or red color and covered by gray or white scales symmetrically distributed [2]

Fig 2: Nile changes in psoriasis [2]

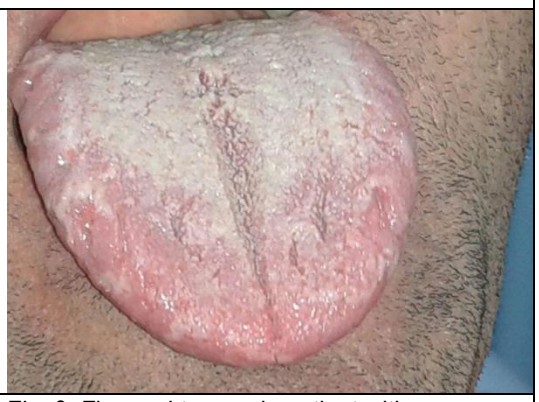

Fig. 3: Fissured tongue in patient with cutaneous psoriasis [6].

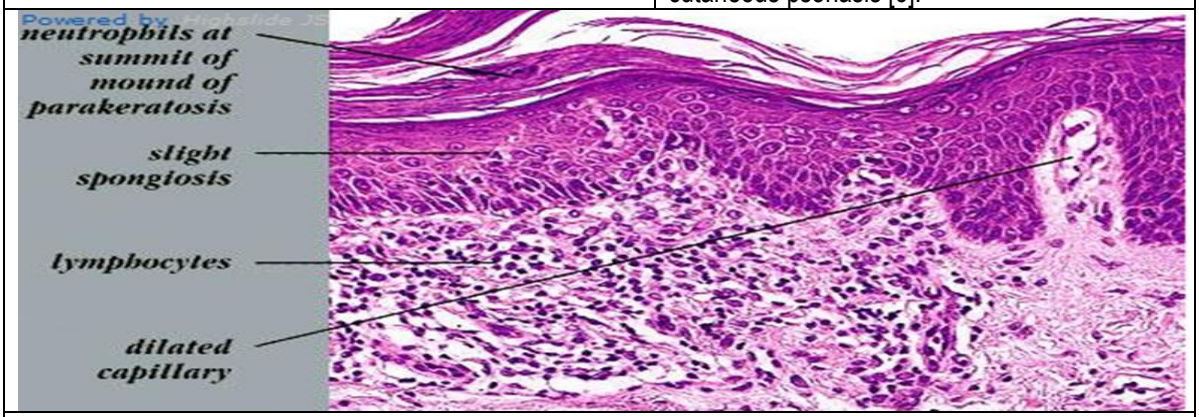

Fig. 4: Histopathology features of psoriasis [18]

Differential diagnosis:

The basic criteria in the diagnosis of oral psoriasis comprise simultaneous occurrence of skin and oral mucosal lesions that are confirmed histo-pathologically. Positive family history of cutaneous psoriasis and positive Human Leukocyte Antigen (HLA) typing antigen such as B13, B17, B37, Cw04, and Cw06, encounters for psoriasis diagnosis [19].

The differential diagnosis of oral psoriasis includes lichen planus, candidiasis, leukoplakia, pemphigoid, pemphigus, eczema, lupus erythematosis, neurodermatitis, syphilis, idiopathic gingivostomatitis, Reiter's syndrome, stomatitis medicamentosa, palatal hyperplasia, and squamous cell carcinoma [2].

In patients where cutaneous manifestation of psoriasis is absent, immune-pathological assays are helpful in excluding psoriasis from other oral dermatoses; however, sometimes there still exists a doubt regarding its diagnosis, making oral psoriasis an enigma or more specifically a diagnostic dilemma [20].

Treatment:

Goal of treatment is palliative (remission from symptoms) not curative. Treatment of such conditions ranges from topical corticosteroid to Vitamin D3, topical Ratinoid to cytotoxic agents as Methatroxite and Cyclosporine. Life -long therapy is needed. For oral psoriasis, palliative treatment includes topical anesthetic (Benadryl), an emollient toothpaste (Orábase) or Maalox, as a coating mucosal protectant, and alkaline rinses are appropriate. Topical corticosteroids, such can be used for symptomatic patients. The oral healthcare provider should focus on the removal of irritants, bacterial plaque, restoration of caries and repair of poorly fitting dentures or prosthetics or sharp or broken teeth.

Occasionally, patients may complain of xerostomia and stomadynia (changes in sensory perception/burning/taste). 26% of people living with moderate or severe forms of this disease have been forced to change or discontinue their normal life style. Living with psoriasis can be both physically and emotionally challenging [21].

DISCUSSION:

There are 3 main phenotypes of psoriasis; the most common is psoriasis vulgaris (chronic plaque), Children and adolescents may develop a self-limiting phenotype, known as guttate psoriasis, with papular lesions on the trunk following a b-hemolytic streptococcal or viral infection. A third and acute phenotype is generalized pustular psoriasis (von Zumbusch psoriasis), there is small, sterile pustules develop on painful inflamed skin. Erythroderma is an unusual but serious form, in which the entire body is covered with psoriasis lesions

[22]. By most researchers, psoriasis is a multifactorial disease in which several genes interact with one another and with environmental stimuli. There is also a hereditary influence [23].

Several studies found an increased prevalence of FT and GT in patients with cutaneous psoriasis [7], but the majority of individuals with FT and GT do not have psoriasis. Although patients with psoriasis show an increase of both GT and FT prevalence, these lesions should not immediately be interpreted as oral manifestations of psoriasis but, rather, as clinical and immunologic reaction patterns in the oral mucosa that some patients with cutaneous psoriasis may, for some reason, be more prone to develop.

Whether the remission observed in oral lesion parallel with skin lesion remission is unknown. The suggestion by most researchers that there must be a parallel course between oral and dermal lesions for a true association to exist is, theoretically, justified [24].

The majority of published studies are based on cross-sectional material in which a simultaneous existence of cutaneous and oral lesions has been found [5].

The onset of oral lesions is usually unknown, and the chronologic coexistence is therefore uncertain. Furthermore, no longitudinal studies have been conducted in which parallelism in intensity of oral and dermal lesions has been evaluated over time at a group level, which makes the existence of parallel clinical courses difficult to assess. In addition, psoriasis may affect various parts of the body at different times, making the chronologic connection of oral and cutaneous lesions of psoriasis, an issue of uncertain value [5].

Currently there are no established histo-pathologic criteria for a conclusive diagnosis of oral psoriasis. Criteria in current use have been adapted from dermato-pathology and may not be entirely relevant for the oral mucosa and are not clearly related to known pathogenetic events. The presence of Munro microa-bscesses has been suggested to be pathognomonic for oral and cutaneous psoriasis, but may absent in some cases [7].

Consequently, a number of different histopathologic findings have been used to consider an oral lesion as consistent with psoriasis, but there is no individual criterion or combination that can be regarded as unequivocally diagnostic.

In addition, the criteria of oral involvement are essentially adopted from dermal disease and may not be relevant for oral lesions. From a diagnostic aspect, the histopathologic changes associated with oral psoriasis are thus relatively nonspecific and may be found in other mucosal lesions.

CONCLUSION:

Oral psoriasis is a rare condition and can be confused with other dermatomes of oral mucous membrane. The presences of cutaneous lesions along with oral lesions that are diagnosed histo-pathologically give definite diagnosis for oral psoriasis. On the other hand, varied clinical and histo-pathological appearance of psoriasis and that the lesions resemble other diagnostic entities makes the diagnosis speculative. To date, from the evidence available, it is still unclear whether oral psoriasis is a distinct entity or whether, indeed, it exists, making it a diagnostician's dilemma. Importantly, there are currently no definite accepted clinical or histopathologic criteria by which an oral lesion can be unequivocally associated with psoriasis. In addition, several case reports have been classified as involving oral psoriasis despite no dermal involvement. Definitive diagnosis of oral psoriasis is therefore difficult to establish with absolute certainty.

Future studies on oral psoriasis that should be of a longitudinal and prospective character; otherwise, speculation concerning whether oral psoriasis really exists and the possible nature of these lesions will persist.

REFERENCES:

1. Rahat S. Azfar, Joel M. Gelfand. Psoriasis and Metabolic Disease: Epidemiology and Pathophysiology, Curr Opin Rheumatol. 2008; 20(4): 416–422.
2. Saif Khan, Sufian Zaheer1, N. D. Gupta. Oral psoriasis: A diagnostic dilemma. European Journal of General Dentistry .2013:2 (1):67-71.
3. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol. 2013; 133:377-385.
4. Lois N. Dreyer; Gwen Cohen Brown, Oral Manifestations of Psoriasis. The New York State Dental Journal 2012:14-18.
5. U. Mattsson, G. Warfvinge and M. Jontell. Oral psoriasisda diagnostic dilemma: a report of two cases and a review of the literature Oral surgery, Oral medicine ,Oral pathology ,Oral radiology., 2015: 120(4) 183-188.
6. Costa SC, Hirota SK, Takahashi, Andrade H Jr, Migliari DA. Oral lesions in 166 patients with cutaneous psoriasis: a controlled study. Med Oral Patol Oral Cir Bucal. 2009;14:e371-e375.
7. Germi L, De Giorgi V, Bergamo F, Niccoli MC, Kokelj F. Psoriasis and oral lesions: multicentric study of Oral Mucosa Diseases Italian Group (GIPMO). Dermatol Online J. 2012; 18:11.
8. Griffiths CEM, BJ Pathogenesis and clinical features of psoriasis. Lancet. 2007;370:263–271.
9. Setty AR, CG, Choi HK. Obesity, waist circumference, weight change, and the risk of psoriasis in women: Nurses'

Health Study II. Arch Int Med. 2007;167(15):1670–1675.
10. Wolk K, Witte E, Warszawska K. The Th17 cytokine IL-22 induces IL-20 production in keratinocytes: a novel immunological cascade with potential relevance in psoriasis. Eur J Immunol 2009; 39:3570.
11. Arican O, AM, Sasmaz S, Ciragil P. Serum levels of TNF-alpha, IFN-gamma, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. Mediators Inflammation. 2005; 2005 (5): 273–9.
12. Sabat R, PS, Hoflich C, Kreutzer S, Wallace E, Asadullah K, Volk H-D, Sterry W, Wolk K. Immunopathogenesis of psoriasis. Exper Dermatol. 2007;16:779–798
13. Lentz SR Mechanisms of homocysteine-induced atherothrombosis. J Thromb Haemost. 2005; 3(8):1646–1654.
14. Malerba M, GP, Radaeli A, Sala R, Pinton PGC, Girolomoni G. Plasma homocysteine and folate levels in patients with chronic plaque psoriasis. Br J Dermatol. 2006; 155: 1165–1169.
15. Stephen K. Richardson and Joel M. Gelfand. Update on the natural history and systemic treatment of psoriasis. Adv Dermatol. 2008; 24: 171–196.
16. Psoriasis Genetics Research Yields Discovery. Psoriasis Advance; Jan/Feb 2004.
17. Yesudian PD, Chalmers RJ, Warren RB, Griffiths CE. In search of oral psoriasis. Arch Dermatol Res 2012; 304: 1-5.
18. Haines C. emedicine.medscape.com, Psoriasis Symptoms and Triggers. 2005.
19. Migliari DA, Penha SS, Marques MM, Matthews RW. Considerations on the diagnosis of oral psoriasis: A case report. Med Oral 2004; 9: 300-3.
20. Yesudian PD, Chalmers RJ, Warren RB, Griffiths CE. In search of oral psoriasis. Arch Dermatol Res 2012; 304:1-5.
21. Lois N. Dreyer; Gwen Cohen Brown, Oral Manifestations of Psoriasis. The New York State Dental Journal, 2012: p14-18.
22. Lloyd P, Ryan C, Menter A. Psoriatic arthritis: an update. Arthritis. 2012; 2012:176 -298.
23. Raychaudhuri SP. A cutting edge overview: psoriatic disease. Clin Rev Allergy Immunol. 2013; 44: 109-113.
24. Migliari DA, Penha SS, Marques MM, Matthews RW. Considerations on the diagnosis of oral psoriasis: a case report. Med Oral. 2004; 9:300-303.

CASE REPORT

DENTURE STOMATITIS – A CASE REPORT

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ABSTRACT:
Denture stomatitis is an inflammatory reaction and the intensity of inflammation varies depending on the tissues involved as well as on the intensity of forces acting on the tissue. It may be associated with a number of bacterial and candida organisms as well as some predisposing factors.

Keywords: denture, stomatitis, candida albicans.
Submitted March 2016; Accepted May 2016

INTRODUCTION:

Candida albicans (C. albicans) is an innocuous commensal of the microbial communities of the human oral cavity [1]. The role of Candida, and specifically C. albicans, in development of denture stomatitis is associated with pathogenic overgrowth of Candida on denture surfaces and the oral mucosa, and is widely accepted as a leading etiological factor [2].

It affects 24-60% of denture wearers, and it is usually found on the palatal mucosa beneath the fitting surface of the upper denture. Dental prostheses may produce a local environment of lowered pH and anaerobic conditions by decreasing the flow of oxygen and saliva to the underlying tissue; these conditions favour fungal overgrowth. Biofilms in denture plaque represent a protective reservoir for oral microbes [2].

Candida-associated denture stomatitis has been found in 60-65% of the subjects carriers of prosthesis with more diffused clinical manifestations [3]. C. albicans may be found in two major forms, yeast and hyphae form. The yeast form is usually associated with mucosal commensalism, although the conversion yeast-to-hyphae is commonly related to the invasion of superficial layers of the oral epithelium, leading to clinical infection [1].

Case Report:

A 19 year old male patient reported to Dental Out Patient Department with complaints of missing tooth with respect to upper front tooth region since 2 years. Patient gave history of wearing removable partial denture during night time. Medical history was non-contributory. Patient had a habit of smoking cigarette since last 2 years. Personal history revealed brushes twice daily with toothbrush and tooth paste. General physical examination and extra oral examination were non-contributory. On intraoral examination, reddish erythmatous area seen on the palatal mucosa & rughae region (fig.1) and was non tender on palpation, with missing maxillary right and left central incisors. Considering the history and examination of the patient we arrived at the provisional diagnosis of Denture Stomatitis type II.

Discontinuation of denture use and re-fabrication of the denture was advised to the patient and topical application of Candid mouth paint (Clotrimazole 1%) four times daily for 15days was given. Patient was instructed to remove the denture and put in water during night time and oral hygiene instructions given. Patient recalled after one month for review. On examination lesion was completely healed.

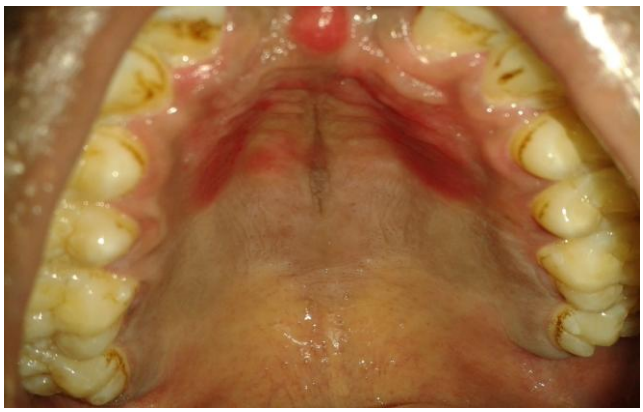

Fig 1: Erythematous area in denture bearing region in maxilla

DISCUSSION:

Denture-associated stomatitis (DAS) (Candida-associated denture stomatitis, denture-sore mouth) is a chronic infection of the oral mucosa caused solely by Candida species or in association with bacteria [2].

Pathogenesis:

The pathogenesis of the Candida-associated denture stomatitis is elaborate and multifactorial. It includes local and systemic

factors (Table 1) related to the host and to the Candida capability to adhere and proliferate in the host epithelial tissues. Candida-associated denture stomatitis is able to rise up when the conditions of the micro oral environment are favourable for the growth and the adhesion of the yeast and also when systemic factors of the host cause depression of the mechanisms of defence [1]. As in our case it is type II denture stomatitis.

Table 1: Predisposing Factors [1]

Systemic factors	Local factors
Physiological (denture stomatitis) Endocrine dysfunctions Nutritional deficiencies Neoplasia's Immuno-suppression	Antimicrobials and topical or inhaled corticosteroids Carbohydrate rich diet Tobacco and alcohol consumption Hypo salivation Deficient oral hygiene Wearing dentures (especially through night)

Classification:

According to Newton's classification, three types of denture stomatitis are distinguished.

Type I - A localized simple inflammation or pin point hyperaemia

Type II - An erythematous or generalized simple type presenting a more diffuse erythema involving some part or the entire denture covered mucosa, as can be seen in the present case, which is type II.

Type III - A granular type inflammatory papillary hyperplasia commonly involving the central part of the hard palate and the alveolar ridges [3].

Complications:

The affected mucosa is atrophic providing less support for the dentures. Some patients complain of burning sensation or tingling sensation beneath the denture. In some patients oral candidiasis may also lead to secondary complications such as oesophageal candidiasis [5].

Management and preventive measures:

Plaque control - Proper cleanliness of denture is important. The denture should be scrubbed with soap and water after every meal. The mucosa in contact with the denture also should be kept clean.

Denture should be properly finished and polished; ill-fitting dentures should be relined or newly made [3]. If the denture stomatitis is due to allergy to denture base material, a patch test should be done.

Newly fabricated dentures should be kept in water to remove the free monomer.

Denture stomatitis associated with Candida infection can be treated by local application of Nystatin, Amphotericin B, Miconazole or

Clotrimazole; Systemic therapy with Ketoconazole or Fluconazole [3].

To prevent the risk of relapse, the treatment should be continued for 4 weeks. When lozenges are used, the patient should be instructed to take out the dentures when the medicine is consumed. Meticulous oral and denture hygiene should be maintained. The denture should be kept in disinfectant solution during night. Old dentures fitting surface should be removed to 1-2 mms and relined for use during the treatment period.

CONCLUSION:

The causes of denture stomatitis are multifactorial. A proper history and oral examination will help to treat the patient successfully. A proper oral & denture hygiene are required to prevent and avoid denture stomatitis.

REFERENCES:

1. Andréa Araújo de Vasconcellos Amanda Araújo de Vasconcellos Rômulo Bomfim Chagas and Letícia Machado Gonçalves. Candida-Associated Denture Stomatitis: Clinical Relevant Aspects. Clin Microbial 2014, 3:4
2. Najla S. Dar-Odeh, Mohammad Al-Beyari and Osama A. Abu-Hammad. The role of antifungal drugs in the management of denture-associated stomatitis .The International Arabic Journal Of Antimicrobial Agents 2012; Vol. 2 No. 1:1
3. Lylajam S. Prasanth V. Denture stomatitis – Etiological factors and management. Journal of Clinical Dentistry Vol. 2 No.1 December 2011
4. Carmen Salerno Michelangelo Pascale María Contaldo Vincenzo Esposito Maurizio Busciolano Lucio Milillo Agostino Guida Massimo Petruzzi Rosario Serpico. Candida-associated denture stomatitis. Med Oral Patol Oral Cir Bucal. 2011 Mar 1; 16 (2):e139-43.
5. Anna Giorgi. Oral Thrush. Health Line. 2016. www.healthline.com

ORAL VASCULAR LESION: A CASE REPORT

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ABSTRACT:
Vascular lesions are tumors or malformations of the vasculature. Vascular tumors are the most common tumors in infancy; it is seen in 1.1 to 2.6% of newborn infants and 10 to 12% of children by the first year of life. There persistence in adulthood however presents as a challenge to the physician. Most of the case reports of vascular lesions in the oral cavity have been presented in relation to tongue, lips and in the palate. Report of classical lesion in the buccal mucosa has not been reported in the near past. Asymptomatic lesions tend to get neglected by patients. In this case report we present one such rare case of a vascular lesion in an adult. Classification of vascular lesions and there treatment is discussed.

Keywords: oral vascular lesion, hemangioma, buccal mucosa.
Submitted March 2016; Accepted May 2016

INTRODUCTION:

Vascular lesions are tumors or malformations of the vasculature. It is the most common tumor in infancy; it is seen in 1.1 to 2.6% of newborn infants and 10 to 12% of children by the first year of life [1, 2]. There persistence in adulthood however presents as a challenge to the physician [2,3]. The hemangioma involutes with time and symptomatic lesions are effectively managed by various means [2,3]. Most of the case reports of vascular lesions has been presented in relation to, lips, tongue and some in the palate [4,5,6,7]. Asymptomatic lesions tend to get neglected by patients. In this case report we present one such rare case of a vascular lesion intraorally in an adult female patient.

CASE REPORT:

A 49 year old female patient presented to the department of oral medicine and radiology at century dental college with chief complaint of decayed teeth. There were no associated symptoms. Her history did not reveal any significant detail. She was moderately built and nourished with steady gait and normal

cognition. On General and extra oral examination no abnormality was detected. On intraoral examination there was a large purple coloured swelling on the right buccal mucosa. The swelling was sessile with broad base and was located at the line of occlusion opposing upper right teeth region. It measured about 3*2 cm, its surface was smooth and lobulated, rubbery on palpation and did not empty on application of pressure (Figures 1 &2). At the anterior margin of the swelling a pulsatile vessel could be palpated. The lady was aware of the swelling and said that it was present since 20- 25 years; it had waxed and waned in size. It never bled nor was it associated with any discomfort. In her previous visit to dentists she was advised to ignore it. She was not interested in getting treatment done for the same. We advised her to get an ultrasonography done. She however did not get any investigation done. She was reluctant in even getting a noninvasive diagnostic procedure like diascopy performed. Provisional diagnosis of low flow vascular anomaly and differential diagnosis of Non Involuting Capillary Hemangioma (NICH) and Arteriovenous malformation was made. The patient was advised to be watchful of the same and report to the nearest hospital in case of bleeding from the same.

As in this patient, the lesions are asymptomatic and tend to get neglected. They also refuse to carry out investigations for the same. This makes it difficult to diagnose the lesion accurately.

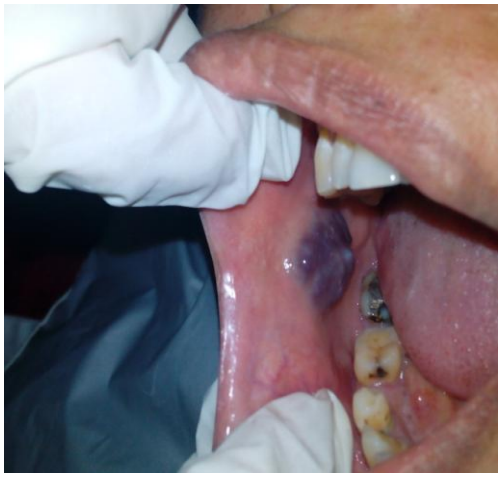

Figure 1 Clinical picture showing raised lesion at the level of occlusion on the right buccal mucosa.

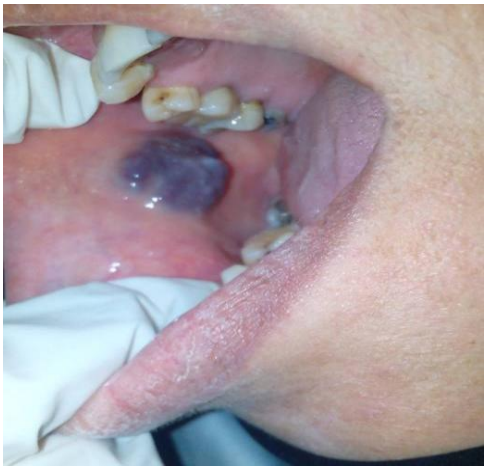

Figure 2. The swelling is dome shaped and purple in colour. The contents of the swelling did not empty on application of pressure.

DISCUSSION:

Vascular anomalies are congenital lesion of abnormal vascular development. They were first classified by Mulliken and Glowacki In 1982 [8] Recent classification of vascular lesions has clarified their diagnosis beyond doubt. Currently they have been described by International Society for the Study of Vascular Anomalies (ISSVA) classification. Revised in 2014 as given below

Vascular anomalies

Vascular tumors	**Vascular malformations**		
	Simple	**Combined**	**others**
Benign Locally aggressive or borderline Malignant	Capillary malformations Lymphatic malformations Venous malformations Arteriovenous malformations Arteriovenous fistula	capillary-venous malformation CVM capillary-lymphatic malformation CLM capillary-arteriovenous malformation CAVM Lymphatic-venous malformation LVM capillary-lymphatic-venous malformation CLVM capillary-lymphatic-arteriovenous malformation CLAVM capillary-venous-arteriovenous malformation CVAVM capillary-lymphatic-venous-arteriovenous CLVAVM	Anomalies of major named vessels (aka "channel type" or "truncal" vascular malformations) Vascular malformations associated with other anomalies Provisionally unclassified vascular anomalies

Benign vascular tumors are further classified as: Infantile hemangioma / Hemangioma of infancy, congenital hemangioma

(a) Rapidly involuting (RICH); (b) Non-involuting (NICH); (c) partially involuting (PICH)

Tufted angioma, Spindle-cell hemangioma, Epithelioid hemangioma, Pyogenic granuloma (lobular capillary hemangioma);

Locally aggressive or borderline vascular tumors: Kaposiform hemangioendothelioma, Retiform hemangioendothelioma,Papillary intralymphatic angioendothelioma (PILA), Dabska tumor, Composite hemangioendothelioma, Kaposi sarcoma

Malignant vascular tumors: Angiosarcoma, Epithelioid hemangioendothelioma

Clinical diagnosis of malignant lesions is challenging. It is usually diagnosed by histopathological examination.

Syndromes associated with vascular lesions:
Blue rubber bleb nevus (Bean) syndrome VM,
Klippel-Trenaunay syndrome: CM + VM +/- LM + limb overgrowth;
Parkes Weber syndrome: CM + AVF + limb overgrowth;
Servelle-Martorell syndrome: limb VM + bone undergrowth Sturge-Weber syndrome: facial + leptomeningeal CM + eye anomalies +/- bone and/or soft tissue overgrowth;
Limb CM + congenital non-progressive limb hypertrophy
Maffucci syndrome: VM +/- spindle-cell hemangioma + enchondroma
Macrocephaly - CM (M-CM / MCAP);
Microcephaly - CM (MICCAP);
CLOVES syndrome: LM + VM + CM +/- AVM + lipomatous overgrowth
Proteus syndrome: CM, VM and/or LM + asymmetrical somatic overgrowth
Bannayan-Riley-Ruvalcaba sd: AVM + VM +macrocephaly, lipomatous overgrowth

VASCULAR TUMORS:

Vascular tumors are common during infancy [8]. The infantile hemangioma is the commonest of the vascular lesions and is prevalent in infancy. It is rarely apparent at birth, evident in the first three months. It gradually involutes. It has been described in literature as going through three distinctive phases: proliferation 1-3 months, quiescence 9-12 months and involution by 5-9 years [1-3,8,9]. They may be superficial, deep and compound. They appear as red or nodular raised lesion. They require intervention only if problematic. Some of the complications that have been reported are: hemorrhage, ulceration, infection and disfigurement [9]. In certain cases depending on the location on compression of vital organs and may cause airway obstruction and cardiac failure [10].

As these lesions involute over time no treatment is required in majority of the cases. Only cases with severe or recurrent hemorrhage or those that interfere with vital structures require treatment. Various therapies with steroid, interferon and vincristine have

been tried with variable rates of success. Surgical excision or laser therapy has been used in lesions unresponsive to medication [9]. The recent literature suggests the usage of propranalol with higher safety profile [10].

VASCULAR MALFORMATIONS:

Vascular malformations, by contrast, are present at birth and grow proportionately with the child. They are composed of dysplastic arterial, venous and/or lymphatic vessels rather than proliferating cells. They are named according to the predominant vessel type and are further classified as 'high-flow' and 'low-flow' lesions [9].

Lesions that demonstrate arteriovenous shunting such as arteriovenous malformations (AVMs) and arteriovenous fistulae (AVF) are described as high flow, whereas venous malformations (VMs), lymphatic malformations (LMs) or combined lympho-venous/veno-lymphatic malformations (VLMs), together with CMs are described as low flow. AVM the lesion enlarges due to hormonal changes, infection, trauma and surgical injury.

INVESTIGATION:

Ultrasonography or MRI can be used as the first modality of examination [11]. They help in differentiating between fast and slow flow lesions. Doppler sonography can be used to differentiate AVM from other lesions. MRI helps in defining the extent of the lesion, volume of the affected area. CT however is useful to identify osseous involvement of the lesion and to identify phleoboliths. Characteristic shining pearl appearance has been reported in vascular malformations [12]. Ultrasound guided needle placement is utilized for sclerotherapy [13].

TREATMENT:

Pulsed dye laser treatment is the 'gold standard' for capillary malformations. Per cutaneous image guided sclerotherapy has become mainstay in treatment of venous malformation. Various agents have been used such as ethanol, bleomycin, sodium tetradecyl sulfate, polidoconal, OK-432. Of these absolute ethanol have been associated with most complications and least have been noted with sodium tetradeyl sulfate [12,13]. High-power lasers have an excellent therapeutic option for this type of lesion in the oral cavity. Their coagulative properties allow procedures to be done without the risk of bleeding, which promotes a better healing pattern and a differentiated postoperative appearance. Surgical excision combined with intravascular embolization is treatment of choice for AVM however extensive AVM are still not curable [13].

Review of literature:

There have been many case reports of haemangioma in the literature, although earlier

most of venous or capillary malformations were reported as hemangiomas [4,5,6,7]. The current classification of vascular anomalies which is based on clinical, radiological, and histological differences helps in differentiating accurately between vascular tumors and malformations and also helps in predicting prognosis [3].

Vascular lesions of the lip [5,6], tongue and palate[7] have been reported frequently in adult patients. Intramuscular hemangiomas involving masseter has been commonly reported and cases involving buccinators also has been found [14]. Multifocal hemangiom [15] have also found mention in recent literature.

CONCLUSION:

Vascular lesion of the buccal mucosa has not been reported in an adult individual in the recent past. However we are limited in our diagnosis because the patient was not interested in getting any further investigations done or therapy as the lesion had not caused any problem to her. Based on the clinical presentation alone the most plausible diagnosis would be a low flow venous malformation. The aim of this case report is to establish the innocuous presence of this rare benign lesion and also justifies watchful neglect for most of these.

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REFERENCES:

1. Leung AKC, Barankin B, Hon KL. Infantile Hemangioma. Pediatr Neonatal Nurs Open Journal. 2014; 1(1): 6-11.
2. Lo K, Mihm M, Fay A. Current theories on the pathogenesis of infantile hemangioma. Semin Ophthalmol. 2009; 24(3): 172-177.
3. Richter GT, Friedman AB. Hemangiomas and vascular malformations: current theory and management. Int J Pediatr. 2012; Article ID 645678, 10 pages.
4. Avila ED, Molon RS, Conte Neto N, Gabrielli MA, Hochuli- Vieira E. Lip Cavernous hemangioma in a young child. Braz Dent J. 2010; 21:370–4.
5. Jasper J, Camilotti RS, Pagnoncelli RM, Poli VD, da Silveira Gerzson A, Gavin Zakszeski AM. Treatment of lip hemangioma using forced dehydration with induced photocoagulation via diode laser: report of three cases. Oral Surg Oral Med Oral Pathol Oral Radiol. 2015; 119(3):e89-94.
6. Awni S, Conn B. Caliber-Persistent Labial Artery: A Rarely Recognized Cause of a Lower Lip Swelling-Report of 5 Cases and Review of the Literature.J Oral Maxillofac Surg. 2016 Jan 18.pii: S0278-2391(16)00107-5
7. Goyal L, Sharma VK, Gupta ND, Bansal P. Rare occurrence of lobular capillary hemangioma on the palate: possible mechanism and treatment

considerations. J Mich Dent Assoc. 2014;96(10):48-51

8. Kate Mahady, Stefanie Thust, Rupert Berkeley, Sam Stuart, Alex Barnacle, Fergus Robertson, Kshitij Mankad. Vascular anomalies of the head and neck in children. Quant Imaging Med Surg 2015;5(6):886-897
9. Eivazi B, Werner JA. Management of vascular malformations and hemangiomas of the head and neck--an update. Curr Opin Otolaryngol Head Neck Surg. 2013; 21(2):157-63.
10. Broeks IJ, Hermans DJ, Dassel AC, van der Vleuten CJ, van Beynum IM. Propranolol treatment in life-threatening airway hemangiomas: a case series and review of literature. Int J Pediatr Otorhinolaryngol. 2013;77(11):1791-800
11. Bhat V, Salins PC, Bhat V. Imaging spectrum of hemangioma and vascular malformations of the head and neck in children and adolescents. J Clin Imaging Sci. 2014: 24; 4:31.
12. Buckmiller LM, Richter GT, Suen JY. Diagnosis and management of hemangiomas and vascular malformations of the head and neck. Oral Dis. 2010; 16(5):405-18.
13. van der Vleuten CJ, Kater A, Wijnen MH, Schultze Kool LJ, Rovers MM .Effectiveness of sclerotherapy, surgery, and laser therapy in patients with venous malformations: a systematic review. Cardiovasc Intervent Radiol. 2014 August; 37(4):977-89.
14. Doddanna SJ, Dawar G, Rallan NS, Agarwal M. Intramuscular cavernous hemangioma: a rare entity in the buccinator muscle. Indian J Dent Res. 2014 Nov-Dec; 25(6): 813-5. doi: 10.4103/0970-9290.152211.
15. Yogesh T Lakkasetty, Sangeeta Malik, Akshay Shetty and Kourosh Nakhaei. Multiple vascular malformations in head and neck - Rare case report. J Oral Maxillofac Pathol. 2014 Jan-Apr; 18(1): 137–142.

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