



Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Rosewell, A;Dagina, R;Murhekar, M;Ropa, B;Posanai, E;Dutta, S;Barr, I;Mola, G;Zwi, A;Raina MacIntyre, C

Title:

Concurrent influenza and shigellosis outbreaks, Papua New Guinea, 2009

Date:

2011-01-01

Citation:

Rosewell, A., Dagina, R., Murhekar, M., Ropa, B., Posanai, E., Dutta, S., Barr, I., Mola, G., Zwi, A. & Raina MacIntyre, C. (2011). Concurrent influenza and shigellosis outbreaks, Papua New Guinea, 2009. *Emerging Infectious Diseases*, 17 (4), pp.756-758. <https://doi.org/10.3201/eid1706.101021>.

Persistent Link:

<https://hdl.handle.net/11343/269521>

License:

CC BY

blockade (5). Other opportunistic infections that have been reported in clinical trials include *Pneumocystis jirovecii* pneumonia, herpes zoster, EBV hepatitis, tuberculosis, and asymptomatic *Mycobacterium avium-intracellulare* (6–10). Thus, CMV disease should be considered when patients receiving tocilizumab have febrile syndromes.

**David van Duin,
Cyndee Miranda,
and Elaine Husni**

Author affiliation: Cleveland Clinic,
Cleveland, Ohio, USA

DOI: 10.3201/eid1704.101057

References

- Nishimoto N, Yoshizaki K, Miyasaka N, Yamamoto K, Kawai S, Takeuchi T, et al. Treatment of rheumatoid arthritis with humanized anti-interleukin-6 receptor antibody: a multicenter, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2004;50:1761–9. DOI: 10.1002/art.20303
- European Medicines Agency. Actemra (tocilizumab): summary of product characteristics, 2009 [cited 2009 Mar 23]. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000955/WC500054890.pdf
- Kim SY, Solomon DH. Tumor necrosis factor blockade and the risk of viral infection. *Nat Rev Rheumatol*. 2010;6:165–74. DOI: 10.1038/nrrheum.2009.279
- Ramshaw IA, Ramsay AJ, Karupiah G, Rolph MS, Mahalingam S, Ruby JC. Cytokines and immunity to viral infections. *Immunol Rev*. 1997;159:119–35. DOI: 10.1111/j.1600-065X.1997.tb01011.x
- Dixon WG, Symmons DP, Lunt M, Watson KD, Hyrich KL, Silman AJ. Serious infection following anti-tumor necrosis factor alpha therapy in patients with rheumatoid arthritis: lessons from interpreting data from observational studies. *Arthritis Rheum*. 2007;56:2896–904. DOI: 10.1002/art.22808
- Genovese MC, McKay JD, Nasonov EL, Mysler EF, da Silva NA, Alecock E, et al. Interleukin-6 receptor inhibition with tocilizumab reduces disease activity in rheumatoid arthritis with inadequate response to disease-modifying antirheumatic drugs: the tocilizumab in combination with traditional disease-modifying antirheumatic drug therapy study. *Arthritis Rheum*. 2008;58:2968–80. DOI: 10.1002/art.23940
- Smolen JS, Beaulieu A, Rubbert-Roth A, Ramos-Remus C, Rovensky J, Alecock E, et al. Effect of interleukin-6 receptor inhibition with tocilizumab in patients with rheumatoid arthritis (OPTION study): a double-blind, placebo-controlled, randomised trial. *Lancet*. 2008;371:987–97. DOI: 10.1016/S0140-6736(08)60453-5
- Nishimoto N, Miyasaka N, Yamamoto K, Kawai S, Takeuchi T, Azuma J. Long-term safety and efficacy of tocilizumab, an anti-IL-6 receptor monoclonal antibody, in monotherapy, in patients with rheumatoid arthritis (the STREAM study): evidence of safety and efficacy in a 5-year extension study. *Ann Rheum Dis*. 2009;68:1580–4. DOI: 10.1136/ard.2008.092866
- Yokota S, Imagawa T, Mori M, Miyamae T, Aihara Y, Takei S, et al. Efficacy and safety of tocilizumab in patients with systemic-onset juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled, withdrawal phase III trial. *Lancet*. 2008;371:998–1006. DOI: 10.1016/S0140-6736(08)60454-7
- Nishimoto N, Ito K, Takagi N. Safety and efficacy profiles of tocilizumab monotherapy in Japanese patients with rheumatoid arthritis: meta-analysis of six initial trials and five long-term extensions. *Mod Rheumatol*. 2010;20:222–32. DOI: 10.1007/s10165-010-0279-5

Address for correspondence: David van Duin, Department of Infectious Diseases, Mailcode G21, Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195, USA; email: vanduid@ccf.org

Concurrent Influenza and Shigellosis Outbreaks, Papua New Guinea, 2009

To the Editor: A high case-fatality ratio has often been associated with outbreaks of a new influenza virus but is less commonly reported in association with seasonal influenza. Nevertheless, in developing countries, seasonal influenza has been associated with a high proportion

of deaths, especially among remote populations. In Madagascar, seasonal influenza mortality rates of 2.5% have been reported (1), with even higher rates (15%) reported in Indonesia (2) and in the highlands of Papua New Guinea (9.5%) (3). High mortality rates during influenza outbreaks in the developing setting have been ascribed to a lack of access to antimicrobial drugs to treat cases of secondary pneumonia and lack of access to health care in general (1).

Diarrheal disease is a major cause of illness and death throughout the world, with diarrheal outbreaks causing a substantial proportion of deaths (4). Endemic shigellosis is responsible for ≈10% of all cases of diarrhea among children <5 years of age living in developing countries and up to 75% of diarrheal deaths (5,6). Although epidemic *Shigella dysenteriae* causes the most dramatic form of *Shigella* spp. infections in developing countries with high attack rates and mortality rates, approximately half of the *Shigella* spp. infections are caused by endemic *Shigella* spp. (4). Despite the endemicity of both influenza viruses and *Shigella* spp. in developing countries, data on their co-infection are lacking.

In mid-August 2009, an outbreak of bloody diarrhea and influenza-like illness (ILI) was reported to health authorities in Menyamya, a remote highland region of Morobe Province, with an estimated population of 10,000 persons. On August 28, an investigation was conducted to identify the cause and extent and to implement control measures.

Two sets of data were collected at the Hakwange Aid Post in Menyamya: 1) laboratory-investigated cases, 2) verbal autopsies. An additional dataset of clinical cases was subsequently collected from surrounding facilities in the district.

Rapid verbal autopsies were conducted by using standardized questionnaires. Bloody diarrhea was

defined as acute onset of fever and diarrhea with visible blood in the stool. ILI was defined as acute onset of fever with cough or sore throat or both. Twenty deaths were identified in the Hakwange Aid Post catchment area, of which 11 were associated with bloody diarrhea and 9 with respiratory illness. Molecular methods were used to identify and characterize respiratory pathogens, and sequencing was used to identify genes that conferred enhanced pathogenicity. Influenza A virus was identified in 14 of 20 respiratory samples collected, of which 10 were subtyped as H3N2; the virus was A/Perth/16/09-like. During the investigation, patients with ILI were given oseltamivir.

Rectal swab specimens were transported in Cary-Blair media and were cultured within hours before serologic and biochemical testing were performed. Antimicrobial drug resistance testing was performed by using the Kirby-Bauer method. *S. flexneri* serotype 3 was isolated in 3 of 14 investigated cases of bloody diarrhea, with no other pathogens identified. *Shigella* spp. were resistant to amoxicillin, chloramphenicol, and co-trimoxazole but susceptible

to ciprofloxacin. Patients received co-trimoxazole and, following sensitivity test results, ciprofloxacin or norfloxacin. Community health education sessions were conducted, and soap, jerry cans, and Aquatabs (Medentech Ltd, Wexford, Ireland) were distributed to households.

Early detection and intervention in disease outbreaks enable timely public health measures and may limit illness and death (7). Twenty deaths had already occurred in this provincial border community before our assessment, and an additional 200 deaths were associated with these conditions in neighboring provinces (8). The delayed reporting of these events from extremely isolated areas resulted in a delayed and less effective response. Although dealing with an outbreak is extremely challenging in this setting, strengthening the system for reporting such events from the district level has the potential to save lives.

Despite the high number of deaths associated with this outbreak of seasonal influenza A (H3), phylogenetic analysis showed that the strain was similar to the low pathogenicity seasonal influenza virus that had

circulated in the region during the previous 12 months. In our assessment, only 29% of those who sought treatment for respiratory symptoms and difficulty breathing were given antimicrobial drugs. The facility-based case-fatality ratios suggested a greater likelihood of death associated with possible co-infection (odds ratio 2.1, 95% confidence interval 0.5–7.4) (Table), but the difference was not significant. The major limitation of this investigation is the lack of microbiologic confirmation to allow wider assumptions to be made about possible co-infections, their effects (if any), and the role of other pathogens that cause similar clinical features.

Ciprofloxacin is now recommended as the drug of choice for all patients with bloody diarrhea, regardless of their age (9). *Shigella* spp. have widespread resistance to the recommended treatment for bloody diarrhea in Papua New Guinea, co-trimoxazole, and no resistance to ciprofloxacin. This outbreak strain was resistant to co-trimoxazole, and its administration would have contributed little to limiting disease and its subsequent transmission. In the context of widespread illness

Table. Descriptive epidemiology of concurrent outbreaks of bloody diarrhea and influenza-like illness, Menyama District, Papua New Guinea, 2009

Variable	No. (%) patients*				Total, n = 704
	Bloody diarrhea, n = 50	Influenza-like illness, n = 431	Possible co-infection, n = 131	Nonfebrile respiratory illness, n = 92	
Aid post					
Hakwange	25 (50.0)	256 (59.4)	50 (38.2)	67 (72.8)	398 (56.5)
Kome	10 (20.0)	64 (14.9)	27 (20.6)	12 (13.0)	113 (16.1)
Kulolonguli	15 (30.0)	111 (25.8)	54 (41.2)	13 (14.1)	193 (27.4)
Male sex	24 (48.0)	206 (47.8)	71 (54.2)	40 (43.5)	341 (48.4)
Age group, y					
<5	11 (22.0)	118 (27.4)	33 (25.2)	10 (10.9)	172 (24.4)
5–14	14 (28.0)	103 (23.9)	23 (17.6)	22 (23.9)	162 (23.0)
15–44	21 (42.0)	169 (39.2)	58 (44.3)	50 (54.4)	298 (42.3)
≥45	4 (8.0)	39 (9.1)	17 (13.0)	8 (8.7)	68 (9.7)
Unknown	0	2 (0.5)	0	2 (2.2)	4 (0.6)
Date of onset					
June	0	6 (1.4)	3 (2.3)	2 (2.2)	11 (1.6)
July	9 (18.0)	36 (8.4)	21 (16.0)	7 (7.6)	73 (10.4)
August	29 (58.0)	294 (68.2)	76 (58.0)	57 (62.0)	456 (64.8)
Unknown	12 (24.0)	95 (22.0)	31 (23.7)	26 (28.3)	164 (23.3)
Died	1 (2.0)	8 (1.9)	5 (3.8)	2 (2.2)	16 (2.3)

*Categories are mutually exclusive.

and death, possibly associated with multidrug-resistant *Shigella* spp., a review of the national policy for the management of bloody diarrhea is urgently needed.

Acknowledgments

We thank Darrel Cecil, Temas Ikanofi, Leomeldo Latorre, and Luisa Wanma for their diagnostic support; and Anthony Gomes, Irwin Law, Carmen Aramburu, and Eigil Sorensen for their technical support.

**Alexander Rosewell,
Rosheila Dagina,
Manoj Murhekar, Berry Ropa,
Enoch Posanai, Samir Dutta,
Ian Barr, Glen Mola,
Anthony Zwi,
and C. Raina MacIntyre**

Author affiliations: World Health Organization, Port Moresby, Papua New Guinea (A. Rosewell, M. Murhekar); University of New South Wales, Sydney, New South Wales, Australia (A. Rosewell, A.

Zwi, C.R. MacIntyre); National Department of Health, Port Moresby (R. Dagina, B. Ropa, E. Posanai); Port Moresby General Hospital, Port Moresby (S. Dutta); World Health Organization Collaborating Center for Reference and Research on Influenza, Melbourne, Victoria, Australia (I. Barr); and University of Papua New Guinea, Port Moresby (G. Mola)

DOI: 10.3201/eid1704.101021

References

1. Outbreak of influenza, Madagascar, July–August 2002. *Wkly Epidemiol Rec.* 2002;77:381–4.
2. Corwin AL, Simanjuntak CH, Ingkoku-sumo G, Sukri N, Larasati RP, Subianto B, et al. Impact of epidemic influenza A-like acute respiratory illness in a remote jungle highland population in Irian Jaya, Indonesia. *Clin Infect Dis.* 1998;26:880–8. DOI: 10.1086/513917
3. Sungu M, Sanders R. Influenza virus activity in Papua New Guinea. *P N G Med J.* 1991;34:199–203.
4. Clemens J, Kotloff K, Kay B. Generic protocol to estimate the burden of *Shigella* diarrhoea and dysenteric mortality. Geneva: World Health Organization; 1999.
5. Bennish ML, Wojtyniak BJ. Mortality due to shigellosis: community and hospital data. *Rev Infect Dis.* 1991;13(Suppl 4):S245–51.
6. Kotloff KL, Winickoff JP, Ivanoff B, Clemens JD, Swerdlow DL, Sansonetti PJ, et al. Global burden of *Shigella* infections: implications for vaccine development and implementation of control strategies. *Bull World Health Organ.* 1999;77:651–66.
7. Grais RF, Conlan AJK, Ferrari MJ, Djibo A, Le Menach A, Bjørnstad ON, et al. Time is of the essence: exploring a measles outbreak response vaccination in Niamey, Niger. *J R Soc Interface.* 2008;5:67–74. DOI: 10.1098/rsif.2007.1038
8. Situation report—diarrhoeal disease outbreaks in Papua New Guinea. Port Moresby (Papua New Guinea): Surveillance Unit, National Department of Health; 2009.
9. World Health Organization. Guidelines for the control of shigellosis, including epidemics due to *Shigella dysenteriae* type 1 [2010 May 20]. <http://www.who.int/topics/cholera/publications/shigellosis/en/index.html>

Address for correspondence: Alexander Rosewell, World Health Organization, 4th Floor, AOPI Centre, PO Box 5896, Port Moresby, Papua New Guinea; email: rosewella@wpro.who.int

Vol. 16, No. 12

An online Technical Appendix was omitted from the article *Mycobacterium tuberculosis* Infection of Domesticated Asian Elephants, Thailand (T. Angkawanish, et al.). The article has been corrected online (<http://www.cdc.gov/eid/content/16/12/1949.htm>).

Get the content you want delivered to your inbox.



**Table of Contents
Podcasts
Ahead of Print Articles
Medscape CME™
Specialized Content**

Online subscription: www.cdc.gov/ncidod/eid/subscribe.htm