ACS Chemical Neuroscience

Editorial

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Torn from the Headlines: Surviving the "Brain Eating Amoeba"

Recently, *ACS Chemical Neuroscience* commissioned and published two exceptional Viewpoint pieces on *Naegleria fowleri*, "the brain eating amoeba" that discussed the diagnosis, pathophysiology, and treatments for the disease that manifests upon infection, primary amoebic meningoencephalitis (PAM).[1,2] The Baig Viewpoint discussed nasal entry mechanism of the amoeba, receptor targets and challenges in both diagnosis and drug treatment.[1] According to the Center for Disease Control (CDC), there have been 138 cases of PAM caused by *N. fowleri* in the United states in the past 50 years, and there have only been three survivors.[1−3] The triumphant story of one patient's survival, and course of treatment, was recounted in the Viewpoint by Levy and Pugh, and focused on early diagnosis, induced hypothermia to lower intracranial pressure, and cocktail antibacterial therapy.[2] I finally took notice the past two summers and noted 1−3 stories each year in the mainstream news media describing adolescents acquiring *Naegleria fowleri* from swimming in fresh water sources, typically in the south, where they developed PAM, and with tragic, fatal outcomes. The stories were all very similar, and typically unraveled with late and/or misdiagnosis and/or no access to key medicines. Critical to the success story of Levy and Pugh[2] was rapid diagnosis and access to miltefosine **1** (Figure 1), an investigational medication supplied by the CDC,

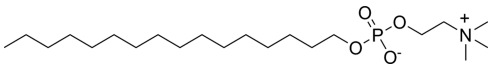

Figure 1. Structure of the investigational drug, miltefosine (**1**), to treat PAM.

as part of the therapeutic regimine.[2,3] Due to the rarity of PAM and the investigational nature of **1**, it is not available at most hospitals and the drug is usually flown in for the patient from the CDC.[3,4]

Miltefosine **1** (trade names: Impavido and Miltex) is categorized as a broad spectrum phospholipid antimicrobial agent related to the signaling molecule, lysophosphatidylcholine,[5] but its origin can be traced back to the 1980s as an experimental oncology agent. Later, it was found effective against the *Leishmania* parasites, and its application in this vein continued to evolve, where in 2013 **1** was recommended by the CDC to treat PAM.[5,6] In 2014, **1** was approved by the FDA for the treatment of *Leishmania* parasites in patients 12 and older.[3]

While every summer, as I mentioned, tragic news related to *Naegleria fowleri* and PAM (a fatality rate of ∼97%) is relayed, the fourth survivor (out of 139 cases) was just reported.[4] Moreover, the wonderful news was once again due to treatment as described by Levy and Pugh and included **1**.[2] The Florida teen was rapidly diagnosed (amoeba detected in the spinal fluid), hypothermia and a coma were induced, and miltefosine **1** was administered. However, this last point was a miracle. The hospital did not have miltefosin on hand; fortunately, the manufacturer of **1**, Profounda, Inc., was located in Orlando, Florida, so the son of the CEO dropped the life-saving drug off at the hospital![4] *Naegleria fowleri* and PAM are fatal, and disease progression is very rapid; therefore, medication must be readily available for positive outcomes. Many hospitals, especially those in southern states, should keep miltefosine on hand during summer months—many physicians are arguing this point. Short of this and to further get the word out on miltefosine, the CDC site states that a clinician with a patient with suspected *Naegleria fowleri* should contact the CDC Emergency Operations Center at 770-488-7100 to consult with an a CDC expert regarding the use of, and access to, **1**.

In the past few years, the odds of beating *Naegleria fowleri* and PAM are increasing.[1−4] Rapid diagnosis and proper therapeutic agents, such as **1**, are essential. With the recent success stories in Arkansas[2] and Florida,[4] hopefully new therapeutic approaches and agents will be developed to effectively combat *Naegleria fowleri* and PAM with further enhanced survival rates. Hint, hint... this would be a great research project with significant impact on human health.

While not standard *ACS Chemical Neuroscience* content to date, I welcome Articles, Letters, Viewpoints, and Reviews on CNS pathogens, CNS oncology, and other diseases of the brain, and that target the brain. CNS-focused medicinal chemists are uniquely poised to develop novel therapeutic treatments for CNS pathogens and cancers with drugs that can readily access the pathogen/tumor within the brain—for all of my neuroscience colleagues—initiate a collaboration with an anti-infective colleague or an oncologist... great things will result.

Craig W. Lindsley, Editor-in-Chief

AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

REFERENCES

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(2) Pugh, J. J., and Levy, R. A. (2016) *Naegleria fowleri*: Diagnosis, pathophysiology of brain inflammation and antimicrobial treatments. *ACS Chem. Neurosci.*, DOI: 10.1021/acschemneuro.6b00232.

(3) For information on PAM, miltefosine and *Naegleria fowleri* from the CDC, see http://www.cdc.gov/parasites/naegleria/treatment.html.

(4) For the recent survivor's story, see http://www.foxnews.com/health/2016/08/24/florida-teen-survives-rare-amoeba-infection-that-kills-most-people.html.

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