A Pandemic of Aching Bones

An otherwise healthy 34-year old New York woman sought medical help because of fever, headache, chills, severe aches in her limbs and some pain behind her eyes. She was treated conservatively but with no remission of her symptoms. Additional laboratory tests revealed that she was suffering from dengue fever. Further questioning disclosed that she had recently returned from a trip to Key West, Florida.

The Florida Health officials were promptly notified, and 27 further cases of dengue were identified in residents of the Florida keys. During the interval between 1946 and 1980, no locally-acquired cases of dengue had been reported within the continental United States. Since that time, however, periodic outbreaks have been recorded in the southern states, particularly along the Texas-Mexican border.

In the last decade, dengue has become virtually epidemic in many tropical and sub-tropical regions. In New Delhi, for example, one hospital was inundated with over 700 cases on one Sunday. And the United States Public Health Service now declares: "Dengue is the most common vector (insect)-borne viral disease in the world, causing 50 – 100 million infections and 25,000 deaths each year."

What is dengue ? The name is probably derived from a Swahili word, *dinga,* describing a person who walks stiffly as if his bones caused much pain. A similar Spanish word, *dengue,* (often pronounced, dandy), means a stiffness or awkwardness in walking.

The disease, transmitted by dengue virus-infected *Aedes Aegyptii* female mosquitoes, probably originated in Sub-Saharan Africa, was carried, after the 15th Century, by the slave trade to the Western Hemisphere, where an abundance of local *Aedes* mosquitoes facilitated the spread of the disease throughout the Caribbean and the Americas.

It must be stressed that the bite of an *Aedes* mosquito by itself does not cause dengue fever. The spread of the disease occurs when an *Aedes* mosquito bites a victim of acute dengue and takes in the victim's blood containing the dengue virus. This "loaded" mosquito may then transmit the virus – and hence the disease – to its next biting victim.

If there are no *Aedes*-genus mosquitoes lurking, then there is no way of contracting dengue except perhaps by receiving a blood transfusion from a dengue victim. Sadly, though, the *Aedes* mosquitoes are widespread: 2.5 billion humans share their living space with these invertebrate predators.

By the 18th Century the disease spread north involving most of the Atlantic colonies, initiating an epidemic of the pestilence in colonial Philadelphia. Benjamin Rush, a local physician (and, incidentally, a signer of the Declaration of Independence) took note of the disease. Medical historian credit him as the first to define, in writing, the clinical characteristics of an ailment that he called Breakbone Fever.

Dengue is now endemic to all of Central America, the Caribbean, much of South America, southern Asia and particularly China, which is burdened by immense numbers of cases.

The classical symptoms of dengue include a suddenly developing fever accompanied by intense headache, pains behind the eyes, troublesome joint and muscle pains and frequently a truncal rash. The fever tends to subside within a few days only to rise again within a week. Thus this biphasic temperature pattern is often referred to as a "saddle-back fever."

There are four closely related forms of the dengue virus. Recovery from one antigenic-variant of the virus (let us call it type A) confers a reasonable immunity if the human later encounters the same viral variant. But what happens if a patient recovers fully from an attack of dengue fever caused by Type A and then, perhaps a year later, is then bitten by an *Aedes* mosquito bearing the virus of Type B dengue fever?

Type A dengue virus has imprinted itself on the immune system of the recovered patient. He is then afflicted with a type B dengue virus, a virus quite biologically similar to Type A. The body, instead of forming new immunological defenses against type B (which it would have done were it not for the prior attack by type A) settles for using its older immune defenses designed to combat type A, under the feeble reasoning that "it was good enough against type A; so it should work against type B which is almost identical to type A". Dr. Thomas Francis, Jr., the great virologist, first described this curious phenomenon, calling it "The Doctrine of Original Antigenic Sin."

This biological phenomenon is now shown to be operative for many viral diseases, such as influenza, with more than one antigenic type of infective virus. And the clinical consequence with this phenomenon? Since the body does not mount an adequate protective response to type B, the outcome carries a much more serious, sometimes fatal, prognosis. A sad example of a bad outcome when the body fails to respond when the second metaphoric cry of "Wolf" is uttered.

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Disclosure of Financial Interests

Stanley M. Aronson, MD, and spouse/significant other have no financial interests to disclose.

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