RESPONSE TO LETTER TO THE EDITOR


We thank Dr. Figaji for his thoughtful commentary\(^1\) on our recent systematic review addressing intracranial pressure monitors in traumatic brain injury (TBI)\(^2\). We completely concur with his eloquent summary of the limitations of the literature. Although Dr. Figaji takes slight issue with our contention that in order to improve outcome, intracranial pressure (ICP) monitoring “... must be acted upon in a standardized and reproducible manner”, we feel our statement is in fact congruous with his central thesis. This is illustrated nicely in his discussion: elevated ICP is simply a number which may represent various pathophysiologic mechanisms which themselves may have very different treatment approaches.

Intracranial pressure monitoring may be considered analogous to the pulmonary artery catheter (PAC) which generates objective physiologic information which the clinician must then interpret to both diagnose the problem and prescribe a remedy. However, the “right” response is predicated on correct interpretation by clinicians, who perform poorly in this regard\(^3\). Previous trials on PAC use have been criticized for both lack of training of study personnel on variable interpretation and lack of treatment algorithms in response to PAC data\(^4\). Because interventions (in this case ICP monitors) generally have small treatment effects, standardization of clinical decisions is requisite for rigorous scientific evaluation\(^5\). Dr. Figaji illustrates the challenges with developing a standardized algorithm to approach ICP monitoring. However, standardization of care has resulted in improved outcomes in other complex systems, including patients with TBI\(^6\). Hopefully neuromonitoring will lead to an improved understanding of the pathophysiologic mechanisms underlying our this complex disease process. As always, the goal is to improve care for our patients, something we can all agree on.

Donald E. G. Griesdale\(^1,3,5\), Asher A. Mendelson\(^1\), Chris Gillis\(^2\), William R. Henderson\(^1,3\), Juan J. Ronco\(^1,3\), Vinay Dhingra\(^1,3\)
University of British Columbia\(^1,2\);
Vancouver General Hospital\(^3,4\);
Vancouver Coastal Health Research Institute\(^5\)
Vancouver, British Columbia, Canada
Email: donald.griesdale@vch.ca

REFERENCES

TO THE EDITOR

Bacillus Thuringiensis Poisoning Related Acute Transverse Myelitis

A 25-year-old Asian woman with acute spinal shock was referred to our institution for therapy. She attempted suicide by drinking 250mg of insecticide containing Bacillus thuringiensis (8000Iu/mg) seven days prior to admission. She felt nausea soon after drinking the insecticide, but did not vomit nor did she go to see the doctor until five days later when she felt headache, abdominal pain, sudden weakness on her both legs, and was unable to urinate.

On clinical examination, we found the patient to have normal temperature, pulse, blood pressure and respiration, without mental disorders. The patient experienced a stiff neck. Neurologic evaluation revealed paresis of both lower limbs of grade 0/5 and hypotonia, without Babinskii’s sign, knee and ankle deep tendon reflexes were elicited, T10-level sensory deficit, impaired joint position sensation of the lower limbs, and absence of anal sphincter tone. Her cranial nerve functions were normal.

Cerebrospinal fluid (CSF) analysis showed translucent fluid with an opening pressure of 300cmH\(_2\)O. The CSF glucose, chloride and adenylate deaminase contents were normal and CSF protein was as high at 98 mg/dL. The CSF leukocyte count was high (440 x10\(^6\)/L, of which 97 percent was neutrophils and 3 percent was lymphocytes). The CSF erythrocyte count was also high (440 x10\(^6\) /L), however, traumatic puncture was denied and CSF culture for bacteria and fungus showed negative results.

Her serum immunological examination and peripheral blood tests were normal. Tests for antibodies of Coxsackie virus, CMV, EBV, HBV, HCV, HIV, HSV1, HSV2, VZV, bacillus tuberculosis, syphilis in serum and CSF, as well as tumor markers in serum revealed no etiological values. Cultures of her urine, stool, and blood were all negative.

Her first spinal magnetic resonance imaging (MRI), taken on the onset day of paralysis, which was five days after her suicide attempt, was normal (Figure 1). Her second spinal MRI, which was taken eight days after her suicide attempt, indicated diffused abnormalities in whole spinal cord, along with severe swelling of spinal cord (Figure 2). Cerebral MRI was normal.

Electroencephalogram and visual evoked potentials were normal. Electromyography and peripheral nerve conduction velocity both indicated upper-neuron damage of all four limbs.
After admission, the patient kept suffering from severe abdominal pain, accompanied by poor appetite, and her feces test indicated continuous bloody stools. Her abnormal sensory level kept ascending, and weakness gradually spread to her upper limbs. Three weeks of treatment with intravenous antibiotics, cortisone, mannitol and vitamin B had no effects. The levels of anesthesia and paralysis kept ascending. Four weeks after onset, her levels of anesthesia stayed at T4, and both upper limbs were force less of grade 2/5 and hypotonia, without respiratory muscle injuries. She was transferred for rehabilitation exercise. One year of follow-up revealed no improvement of her disabilities.

**DISCUSSION**

As a final diagnosis, we considered the most likely one to be acute transverse myelitis resulting from *Bacillus thuringiensis* poisoning. The clinical diagnosis was based on the Transverse Myelitis Consortium Working Group Criteria for Idiopathic Acute Transverse Myelitis. The etiological diagnosis was based on the history of intake of high doses of *Bacillus thuringiensis*. Other common etiologies, such as viral infection, syphilis, tuberculosis, multiple sclerosis, vertebral dislocation, spinal cord hemorrhage, tumor, spinal-contusion, spinal-vascular malformation, serologic or clinical evidence of connective tissue diseases were all excluded. Although we did not finish the specific tests of *Bacillus thuringiensis* or Cry toxins in blood or CSF, the accordance of onset time with swallowing pesticides highly indicated that poisoning was the etiology.

After consulting the literature, we think this case of acute transverse myelitis based on *Bacillus thuringiensis* poisoning is the first ever described in humans.

*Bacillus thuringiensis* is an aerobic, gram-positive, spore-forming bacterium from the Bacillus cereus group. They can...
produce Cry toxins (delta-endotoxins) during the sporulation phase, which are pore-forming toxins that have insecticide activity. One feature that distinguishes Cry toxins is their remarkable specificity, and they are therefore harmless to non-target insects and animals\(^1\). Nowadays, they are widely used in insect control in agriculture and forestry, in the control of mosquito-borne human diseases, and in the development of transgenic insect resistant plants. Based on former laboratory studies, field experience and epidemiology studies, it has been widely accepted that products of Bacillus thuringiensis are safe to humans, animals, and the environment.

However, some recent laboratory studies put the safety of the pesticides in question. According to Cerstiaens’s study, one of the Cry toxins, Cry1C, has been proved to be toxic to primary cultured neurons of Lymantria, in a concentration of 20 ug/ml \textit{in vitro}\(^2\). Likewise, it is possible that the pesticides also possess neurotoxicity to humans. On the other hand, a recent study addressed the effect of sub-lethal doses of biological and synthetic pesticides of Bacillus thuringiensis on female rats’ reproduction apparatus during pregnancy; no miscarriages or malformations of the neonates occurred. But the pups, who received more or less of the insecticide, produced similar lesions in the kidneys, livers and lungs and had reduced fertility. This study suggested that sublethal doses of insecticides possibly provide chronic toxicity to humans\(^3\).

There are only two literature reports of Bacillus thuringiensis infection in man between the year 1997 and the present, and all infected individuals had experienced either extensive burns or a blast injury, which predisposed them to infection\(^4\). Based on the literature, the symptoms of Bacillus thuringiensis infection or poisoning included mild irritative pulmonary symptoms, theoretical risk of respiratory infection in immunocompromised individuals, single corneal ulceration, mild gastroenteritis with heavy ingestion\(^5\).

In this case, the patient had no vomiting, diarrhea or gastrolacage after swallowing the pesticides. We speculated that, high doses of insecticides were absorbed through the gastrointestinal tract, which secondarily induced diffused spinal cord injury. However, the specific mechanisms of this injury are unknown. It is possible that Cry toxins directly attacked neurons and lead eventually to cell death. Alternatively, the toxins possibly induced auto-immune responses against neurons.

We know that most poisonings from pesticides do not have a specific antidote. Therefore, decontamination is the most effective intervention. Unfortunately, the patient missed the best chance for treatment, which lead to her bad prognosis.

In conclusion, few human tests with high dose of Bacillus thuringiensis have been performed. In line with the increased spread of the use of such pesticides in agriculture and transgenic plants, the side effects of their long term applications deserve more consideration.

\[\text{Jing Han, Yan Cheng, Mei-sheng Wang}\
\text{Department of Neurology, Tianjin Neurology Institute, Tianjin Medical University General Hospital, 154 Anshan Road Heping District, Tianjin 300052, China}\
\text{Email: quartz945@163.com}\]

\textbf{REFERENCES}
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\section*{CASE PRESENTATION}

A 69-year-old Caucasian man was admitted to the emergency department because of acute onset right arm weakness and speech impairment, lasting 30 minutes. A computed tomogram (CT) brain scan showed leukoaiaosis and mild cortical atrophy. The patient complained of a similar episode one day before. He was a smoker and moderate alcohol drinker; he had referred with higher blood pressure and mild carotid atherosclerosis for two years. He was taking ramipril, aspirin 100 mg and low-dose statin. ABCD2 score was moderate. At the admission to the Stroke Unit his blood pressure was 130/80 mmHg, heart rate was sixty rhythmic, and the neurological examination was normal. Epiaortic ultrasound study showed mild atherosclerosis; Transcranial doppler (TCD) ultrasound was normal as well as CT cerebral angiography. We thought transient ischemic attacks (TIA) episodes and started higher dose antiaggregation with aspirin 300 mg and atorvastatin 80 mg. The day after, the patient...