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April 27, 1988

Mark id. Groedel , Atty .
Reminger & Reminger, LPA
Leader Bldg.
Cleveland, OH 44114 .

Re: Philip McIntosh

Dear Mr. Croedel:

At your request, I examined Mr. Philip McIntosh, presently a 41 year old right-handed male. The history was obtained from the patient. Also available for review were records you forwarded to me. These records consist of the following:

- letter from Howard Tucker, M.D. , dated 5/22/87
- reports of tests ordered'by Howard Tucker dated 6/9/87 including EEG, CT brain scan (unenhanced), skull x-rays, CT scan of the cervical spine, cervical spine x-rays
- cervical myelogram report dated 12/9/85 from Christine Wirtz, M.D.
- physician progress notes dated 12/9 - 12/11/85
- 12/9/85 CT brain scan report
- neurologic consultation report from Romeo Craciun, M.D.
- discharge summary from post-myelogram hospitalization
- followup office notes by Dr. Craciun

PROBLEM:

Ongoing symptomatology dating back to job-related injury on July of 1985 with accentuation of symptoms following a myelogram on 12/9/85.

PRESENT ILLNESS:

In July of 1985, the patient was involved in an accident in his job with CEI. . He slipped and grabbed onto something with his right arm in an attempt to stabilize himself. This led

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to a significant amount of pulling on the arm, particularly in light of Mr. McIntosh's weight. He states that those symptoms were aggravated by a myelogram which was being performed to evaluate his neck and right upper arm pain. Following the myelogram (accompanied by complications to be discussed later), the patient states his symptoms were worsened. These symptoms continue to the present.

At present, the patient complains of the following symptoms:

- headaches
- light sensitivity (photophobia) associated with headaches
- eye soreness
- discomfort, right arm and right shoulder
- popping sensation in neck when turning head
- low back soreness (at the site of the lumbar puncture for the myelogram)

Headache:

The patient traces his headache back to the accident in 1985. Since the myelogram, he claims that the headaches have been worse. The headaches tend to be "frontal and occipital in location." They tend to have a pressing quality. At the present time, they are virtually constant but tend to wax and wane. They are generally accentuated by physical activity. Prior to the myelogram, the headaches tended to be intermittent. They occurred "once in a while." On reviewing Dr. Craciun's office notes from the early part of 1986, he does not report much headache, but he does report the patient's complaint of neck stiffness. This is most probably a manifestation of the patient's headache, given that a significant amount of his headache is occipital in location. Diagnostic procedures including a CT brain scan and EEG both done during 1987 were normal.

The patient is currently not taking any medications for his headaches.

Light Sensitivity/Photophobia:

This actually appears to be a component of the patient's headache. When the headache builds up, he becomes aware of increased sensitivity to light.

Eye Pain:

This also is probably a component of his headache, although he lists it as being separate from the headache. When his headache builds in intensity, he notices more peri-orbital pain. He states that if he rubs his eyes during those times, it will hurt.

Arm Discomfort:

This would appear to be patient's most aggravating symptom. It dates back to the time of the accident in July of 1985. The patient reports that he had pain in his neck and right shoulder stretching inferiorly into the scapular region and into the right upper arm. It was for this problem that he was hospitalized in December of 1985 for a myelogram to rule out a cervical radiculopathy. Following the myelogram, the patient has continued to have arm discomfort. He states that the discomfort is greater than it was prior to the myelogram. Along with the proximal arm pain and scapular region pain, he describes a sense of heaviness in the arm and also numbness in the right hand and fingers, particularly the fourth and fifth fingers. With an increase in physical activity, the heaviness and numbness as well as the pain increased. The numbness is always in the fourth and fifth digits, but with increased activity, it spreads to the other digits of the hand. He finds it difficult to elevate his right arm above the horizontal since it accentuates his symptoms. The ongoing discomfort has made it impossible for him to return to his original job at the Cleveland Electric Illuminating Company. He used to be a "line mechanic." We now is a meter reader.

On reviewing Dr. Craciun's 1986 notes and Dr. Tucker's 6/22/87 letter, there is no mention of numbness in the right upper extremity, although there is mention of neck, right shoulder, and right upper arm pain. The patient states that the numbness began sometime after the accident and as already mentioned, became worse after the myelogram.

It should be noted that he had a right rotator cuff tear, probably several years before the June 1985 accident. He states, however, that he made a complete recovery from that injury prior to the accident.

"Neck Popping:"

The patient reports a sensation of neck popping with rotation of the head. He dates this back to the accident. He states that if he rotates his head, he can feel a popping sensation which can lead to headaches as described above.

Low Back Discomfort:

The patient states that he has sharp, non-radiating pain in the low lumbar region which is a needle-like sensation. He dates it back to the lumbar puncture done as a part of the myelogram procedure in December of 1985.

Other:

The patient states that he has difficulty sleeping at night. His arm discomfort results in repeated awakenings.

Past Medical History:

Right knee surgery for cartilage repair approximately ten years ago. Right rotator cuff injury with surgery some time in the early 1980's.

Medications:

None at the present time.

Family History:

Non-contributory.

Social History:

The patient currentl works as meter re der for CEI. He used to be a line mechanic. He states that he has missed-a total of about one year of work since his injury.

General Physical Examination:

A detailed general physical examination was not performed. The patient is a very large white male with a height of approximately 5', 11" and weight in excess of 250 lbs (not measured or- weighed). Blood pressure in the right arm utilizing a thigh cuff was 130/94. Auscultation of the heart and lungs revealed no significant abnormalities. All peripheral pulses were palpable.

Neurological Examination:

Mental Status: Alert, oriented X3 without evidence of cognitive dysfunction. Affect was somewhat blunted and mood appeared somewhat depressed.

Speech: Normal without evidence of dysphasia or' dysarthria.

Skull: Normocephalic without bruits.

C-Spine: Full range of motion; no bruits heard.

Cranial Nerves: - XII: The fields were full and the fundi benign. Extra-ocular motility was full with slight bilateral horizontal gaze nystagmus (physiologic nystagmus). Pupils were 4 mms, equal, round, and reactive to light without evidence of afferent pupillary defect. Facial motor function and sensation were normal. Hearing was intact bilaterally to clinical testing. Swallowing was normal. Soft palate elevated to the midline. Tongue was normal. Sternocleidomastoid and trapezius strength appeared normal.

Motor: The patient was extremely powerfully built. Individual muscle group testing revealed no evidence of weakness in the lower extremities os left upper extremity. Very careful testing *of* the right upper extremity did not reveal any definite weakness. At times, there was a slight grimace on his face when I checked individual muscles, but I still could not find evidence of weakness.

Coordination: No evidence of dysmetria or dysdiadochokinesis. Gait was normal. He was able to tandem walk.

Reflexes: ++ and symmetrical, lower extremities, with downgoing toes. Biceps and brachioradialis reflexes were + bilaterally and symmetrical. Triceps reflexes ++ bilaterally and symmetrical. No Hoffmann's signs.

Sensation: Pin, temperature, light touch, wibration, position, and stereognosis were evaluated. No abnormalities were found in the left upper extremity and both lower extremities. In the right upper extremity, there was some non-specific changes. To pinprick, there were variable changes over the dorsum of the right hand. At times, pin appreciation appeared decreased in the dorsolateral aspect of the hand (radial nerve/C5 distribution). At times, sensation appeared slightly decreased on the medial volar surface of the hand (ulnar nerve/C8 distribution). The findings were inconsistent and variable. Temperature appreciation appeared to be intact as did light touch. The vibration at times appeared slightly decreased over the right fifth metacarpo-phalangeal joint compared to the left. However, sensation was normal and symmetrical over the first metacarpo-phalangeal joint. Stereognosis was normal in the right hand as was position sense in the right fifth finger.

Summary:

The patient is a 41 year old, right-handed male who sustained an injury to his right upper extremity in July of 1985 when he slipped and attempted to break his fall by grabbing onto an object. From that point until the present time, he has had chronic headaches and neck pain with associated photophobia and orbital/periorbital soreness, right arm discomfort consisting of a combination of soreness and numbness aggravated by physical activity. He has also experienced popping sensations in his neck. He had a myelogram done 12/7/85 in an attempt to rule out a radiculopathy. The myelogram was terminated because of a seizure. Following the myelogram, he was confused for a period of time. He was followed up by a neurologist (Romeo Craciun, M.D.). The symptoms of confusion gradually resolved. Since the myelogram, he states that his headaches, neck discornfort, right upper extreinity symptomatology, have all worsened. He also has noted low back discomfort in the area of the needle insertion for the myelogram as well as difficulty sleeping at night.

He has missed approximately one year of work since the accident. He has not been able to return to his job as a line mechanic for CEI and now works as a meter reader for the same company.

In June of 1987, he had a repeat neurologic workup by Howard Tucker, M.D. An EEG was normal. A CT brain scan was unremarkable except for a few drops of residual myelographic contrast material. A CT neck scan was unremarkable except for artifacts created by his size.

A neurologic examination today failed to reveal any definite focal findings.

IMPRESSION:

1. Headaches, muscle-contraction type, etiology muscle tension.

2. Neck pain, etiology, muscle contraction/tension.

3. Low back pain, etiology muscle-contraction/tension.

4. Right arm pain; musculoskeletal pain syndrome/fibromyalgia. No evidence of radiculopathy.

5. Insomnia: etiology, rule out depression.

COMMENT:

I could not detect any specific abnormalities on my neurologic examination. I do believe the "common denominator" for most of the patient's discomfort is musculoskeletal rather than neurogenic. By this, I mean the pain in his head, neck, back, right shoulder, and right upper extremity are all more apt to be the result of muscle spasm than the result of underlying nerve injury. He has had extensive workups at several different times looking for an underlying neurologic process and one has not been uncovered. On the basis of his history, he may have had an EMG and nerve-conduction study of the right upper extremity at some point since his July of 1985 injury. If so, it would be important to review that data. If not, if there is still a question of a neurogenic process, then that is one test that could be performed which has a high yield for peripheral nervous system insult without subjecting the patient to any significant risk. I would be surprised if any significant insult is uncovered.

The low back discomfort the patient describes cannot be associated with a lumbar puncture. I have done probably in excess of a thousand lumbar punctures in my career, and I have never seen this to be a problem. There would be no easy pathophysiologic basis for the pain. I have seen some patients have a spinal tap and then because of tension, etc., develop paraspinous muscular pain. Perhaps that is the explanation for this patient's discomfort.

The sleep disturbance is somewhat more difficult to deal with. I do believe there are elements of depression. Insomnia is certainly a common somatic manifestation of depression. It is difficult for me to imagine how this patient would have insomnia based on his arm discomfort. Again, I have seen numerous patients with low-grade arm discomfort, and this generally does not keep them awake, particularly years after the insult.

There are two issues surrounding Mr. McIntosh, as I see it. The first issue is his ongoing symptomatology which I have already commented on. The second issue is the etiology of that symptomatology, particularly with reference to the myelogram performed on 12/7/85. As I understand it, the claim is being made that the myelogram is the major cause for the patient's symptomatology.

I have reviewed the reports regarding the myelogram, Dr. Craciun's neurologic examinations following the myelogram* and Dr. Howard Tucker's June 22, 1987 letter outlining his examination of the patient and his opinions about the myelogram.

Certainly, no one would question the role of the myelogram in evaluating this patient's symptomatology. There was a question of cervical radiculopathy and the myelogram is still an important tool in the evaluation of patients with suspected cervical radiculopathy.

Mr. Mcintosh presents a problem in the evaluation of cervical radiculopathy. The problem is his size. This is amply demonstrated by the CT neck scan ordered by Dr. Tucker. There were artifacts created by the patient's size that made interpretation difficult. The patient's myelogram was performed using the contrast material, metrizamide (Amipaque). Metrizamide is a water soluable contrast material. Its major problem is that it is not very "contrasty." By this, I mean that when diluted with cerebrospinal fluid, it can be difficult to see on a myelogram. This is particularly true for a cervical myelogram. This, coupled with the patient's size, led to difficulties at the time of the myelogram. The myelographers could 'not obtain images that were diagnostic. They next instilled Pantopaque through the myelogram needle. Pantopaque is a non-water soluable material that is much more "contrasty." After the material was instilled, the x-ray table was tilted so that the patient's head is lower than the low back region. 'This allows for gravity to move the contrast material towards the neck, since both metrizamide and Pantopaque are heavier (denser) than cerebrospinal fluid. At some point during the course of this procedure, the patient had what was described as a brief, generalized seizure. The procedure was aborted. Following the procedure, the patient was noted by Dr. Craciun to be confused. It was his presumption that the patient had an encephalopathy caused by the metrizamide and that this was the cause of the patient's seizure. Both are well known consequences of metrizamide. The patient's symptomatology gradually resolved. He has not had any further seizures and was never placed on anticonvulsant drugs.

The question, as I understand it, is whether or not the myelogram was poorly performed.

In Dr. Tucker's letter, he offers reasons why he feels that the *'myelogram technique used was a deviation of standard of care and is the approximate (sic) cause of his current symptoms."

He first of all challenges the 240 concentration of metrizamide. He states that this is a large amount. In actuality, it is not an amount; it is a concentration reflecting the dilution of the metrizamide. It is not a volume. Please find enclosed a dosage and reconstitution guide for metrizamide supplied by the manufacturer. As you can see, concentrations from 250 to 300 are

recommended by the company for a cervical myelogram. 240 pr 250 concentration appears to be the standard. That is what is used by radiologists at Mt. Sinai Medical Center. The concentration of 240 is therefore low, not high, and again, it does not reflect the amount of material inserted into the spinal column.

Dr. Tucker goes on to indicate that metrizamide was abandoned because of its toxicity and the marketing of newer, water soluable non-ionic contrast materials. He states that it is more expensive, but the hospital in which he works (he works in several so I don't which one he is referring to) elected to increase the expense for the benefit of the patient. This is really a side issue, as I see it. The suggestion is being made that the radiologists did not use newer materials available at the time of the patient's myelogram because of the expense. This is clearly incorrect. First of all, a?though new contrast materials were becoming available about that time, most hospitals did not use them in December of 1985. I contacted the myelographer, Dr. Christina Wirtz, to ask her when her group started using the newer contrast materials. She indicated that it was about February of 1986, approximatety three months' after the patient's myelogram. Mt. Sinai Medical Center where I work (which is one of Dr. Tucker's hospitals) also started using the newer non-ionic water sotuable contrast materials in February of 1986. I determined this by reviewing purchase orders for the Dept. of Radiology of Mt. Sinai Medical Center. Thus, Dr. Wirtz' group certainly was in keeping with the standards of the community, since they acted at the same time as the Dept. of Radiology at Mt. Sinai Medical Center. The expense is also a noti-issue. As I understand it, gram for gram, the new non-ionic materials are slightly more expensive. However, according to the radiologists at Mt. Sinai, because of the way metrizamide (Amipaque) is packaged, it actually can be more expensive than some of the newer materials. The reason for this is that metrizamide is packaged in a larger vial and a large percentage of the material has to be thrown after the myelogram. This is evidently not the case with some of the newer ionic materials. Also, to suggest that a radiologist would use expense as an issue for selecting less efficacious material is clearly unfair. In the case of these materials, the radiologists don't even pay for it.

With regard to patient safety, again, this would be a difficult issue in late 1985 and early 1986. it is clear that metrizamide produced toxicity. However, the toxicity was generally of short duration and reversible. Since the new, non-ionic materials were just coming on the market, it was not clear how toxic they might turn out to be. This is the reason many physicians don't jump to a new drug the moment it is introduced. A recent publication (see enclosed) indicate that the newer, non-ionic contrast materials can also produce neurologic toxicity (seizures). It is true, however, that they are less toxic than metriramide.

The next issue is the injection of Pantopaque following the injection of metrizamide. Dr. Tucker indicates that this is a deviation from the standard of practice. The radiologist at Mt Sinai Medical Center have used this technique in the past on many occasions. I know this to be true because I have had several patients in whom Pantopaque was instilled after metrizamide when adequate x-ray pictures could not be obtained with metrizamide alone. You have two choices: stop the metrizamide myelogram and wait to do a second Pantopaque myelogram, or combine the procedures. There are problems with both

approaches. Certainly as a clinician, I prefer combining the two procedures as was done in this case. It saves an enormous amount of cost since the patient has to be rehospitalized for a second myelogram. **Also,** the risk is quite low. Nonetheless, the fact that Pantopaque is instilled into the back after metrizamide, would increase the risk slightly of seizures since one would have to presume that the metrizamide would be "pushed" into the cranial vault more quickly than would ordinarily be the case. It must be remembered that all the metrizamide administered in a myelogram will enter the cranial vault because the route of egress **of** the metrizamide is through the arachnoid granulations in the superior sagittal sinus. The only difference is that by instilling Pantopaque, it **will** expedite the motion of the metrizarnide into the intracranial cavity.

The next issue is arachnoiditis. Yes, Pantopaque can cause arachnoiditis. Probably metrizamide can also as can surgery on the spine. Isolated arachnoiditis from Pantopaque In the absence of surgery is rare. There is nothing in this patient to suggest that he has arachnoiditis. To suggest that the patient's headaches are due to arachnoiditis, in my opinion, is absolutely inappropriate. The headaches are typical muscle-contraction headaches without evidence of arachnoiditis. Arachnoiditis can certainly produce radicular symptoms. If the claim is being made that this patient has arachnoiditis, then it must be documented, since there *is* in my mind nothing to suggest its presence. Dr. Craciun in his evaluation did not make this diagnosis, either.

In summary, with regard to the myelogram, there is no question that the patient had a metrizamide encephalopathy. This is not rare. I myself have had several patients who developed these symptoms during the time that metrizamide **was** in use. However, there **is** not a shred of evidence to suggest that the myelogram performed was not **up** to the standards of the community.

If you have any additional questions or comments after reviewing this information, please **do** not hesitate to contact me.

Respectfully,

Michael Devereaux, MD

Michael W. Devereaux, M.D.
Chief, Division of Neurology

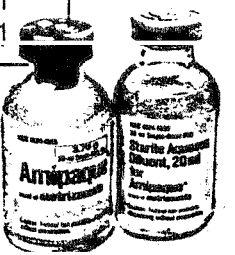
MWD:sb
5/24/88

AMIPAQUE
brand of metrizamide

Dosage and Reconstitution Guide

Procedure	Amipaque Concentration, mgI/ml	Usual Dose of Reconstituted Solution, ml	Maximum Dose, mgI	Volume of Diluent to Achieve Desired Concentration, ml			
				3.75 g vial		6.75 g vial	
				Diluent	End Volume*	Diluent	End Volume*
Lumbar myelography	170	10-15	2850	8.9	10.6	16.1	19.2
	180			8.3	10.0	15.0	18.1
	190			7.8	9.5	14.0	17.1
Thoracic myelography	220	12	2640	6.5	8.2	11.7	14.8
Cervical myelography (via lumbar injection)	250	10	3000	5.5	7.2	10.0	13.1
	260			5.2	6.9	9.4	12.5
	270			5.0	6.7	9.0	12.1
	280			4.7	6.4	8.5	11.6
	290			4.5	6.2	8.1	11.2
	300			4.3	6.0	7.8	10.9
Cervical myelography (via lateral cervical injection)	220	10	2200	6.5	8.2	11.7	14.8
Total columnar myelography	250	10	2800	5.5	7.2	10.0	13.1
	260			5.2	6.9	9.4	12.5
	270			5.0	6.7	9.0	12.1
	280			4.7	6.4	8.5	11.6
Cisternography (via lumbar injection)	170	4-6	1140	8.9	10.6	16.1	19.2
	180			8.3	10.0	15.0	18.1
	190			7.8	9.5	14.0	17.1

nd volume of solution is achieved when diluent is added to Amipaque lyophil It will be greater than the volume of added diluent by 1 7 ml lor Ihe 3 75 g vial and by 1 ml lor Ihe 6 75 g vial Administer only the volume recommended in the "usual dose ' column



Directions for Preparation of Amipaque Solution:

1. Select iodine concentration recommended for particular procedure (columns 1 and 2)
2. Employing sterile technique. withdraw required amount of diluent to obiain that concentration (Example Io obtain 170 mgI/ml concentration, add 16 1 ml of diluent to 6.75 g vial)Use a small (22-gauge) needle to prevent coring
3. Still using small needle, inject diluent into lyophil vial of Amipaque.
4. Leaving syringe and needle in place. gently swirl (do not shake) vial until contents are completely dissolved (approximately 3 to 10 minutes) Solution should be clear and colorless to slightly yellow Do not use if undissolved particulate matter or bubbles are present
5. "End volume" will exceed amount required Io achieve desired dose Wilhdraw only as much as is recommended (see **DOSAGE** TABLE)
6. Detach syringe from vial and attach it to the myelographic **injection** unit
7. Use Amipaque solution immediately Discard unused portion

See other side *for important* product *information* concerning warnings, adverse reactions. patient *selection, precautionary* recommendations. *and* directions *for use*

Winthrop

Seizures Following Myelography with Iopamidol

Allan I. Levey, MD, PhD,* Howard Weiss, MD,*
Robin Yu, MD,‡ Henry Wang, MD,§
and Allan Krumholz, MD*†

Iopamidol, a water-soluble contrast medium, has been rarely associated with seizures. We describe 3 patients (from a series of 785) who had generalized tonic-clonic seizures after iopamidol myelography. Two of the patients underwent lumbar and one cervical myelography. There was a history of seizures in 2 patients, and the dose of iopamidol used in the patients who convulsed was high, ranging from 3,000 to 4,500 mg iodine. Despite the reported low incidence of complications with iopamidol, seizures may occur, especially in patients with previous seizures and also in those receiving higher doses of iopamidol.

Levey AI, Weiss H, Yu R, Wang H, Krumholz A. Seizures following myelography with iopamidol. Ann Neurol 1988;23:397–399

Radiological contrast media introduced intrathecally can have a variety of adverse effects on the nervous system [1]. Nonionic water-soluble agents widely used in myelography, such as merrizamide, have been observed to cause meningeal reactions, encephalopathy, and seizures. Iopamidol is a newer nonionic water-soluble medium that has become popular because it provides high contrast, yet its central neurotoxic effects are less frequent and less serious [2–4]. There have been several reports of patients with meningeal reactions after iopamidol myelograms [5–8], but only 2 cases of seizures have been noted [6, 9]. Here we describe 3 patients who had seizures after myelography with iopamidol.

Case Reports

Patient 1

A 46-year-old woman was admitted to the hospital in August 1986 for lumbar myelography to evaluate severe low back pain of four months' duration. Her history was notable for alcohol abuse and migraine headaches. Her only medication was an occasional analgesic for headaches. On one occasion 2 years before admission the patient had a single generalized seizure after consumption of a six-pack of beer. Anticonvulsant therapy was not recommended, and subsequently she discontinued alcohol and had no further seizures. The patient underwent lumbar myelogram with 15 ml of iopamidol (200 mg iodine per milliliter), which revealed a filling defect on the right side of the L5-S1 interspace. The cerebrospinal fluid contained no white blood cells and a protein concentration of 32 mg/dl. The evening after the myelogram she had a headache, for which she received 50 mg of meperidine and 50 mg of hydroxyzine. The following morning she was noted to be intermittently confused and agitated, and rhen she had several generalized convulsions of approximately 2 minutes' duration. Phenytoin therapy was initiated. The general and neurological examinations were normal except for mild postictal confusion, which rapidly cleared. Laboratory data including complete blood count, electrolytes, and ocher blood studies were normal. A head computed tomographic (CT) scan showed small compressed lateral ventricles, loss of the normal interhemispheric fissure and conical sulci, and decreased attenuation of the white matter, consistent with generalized cerebral edema. An electroencephalographic (EEG) tracing obtained rhe same day was very abnormal, with long runs of anterior maximum 1- to 3-Hz spike and wave discharges; these were at times biiaterally synchronous, and at other rimes localized to the right frontal region. There were also funs of anterior 2- to 3-Hz slow waves lasting 1 to 2 seconds. Therewere no behavioral abnormalities associated with the recording. An EEG several days later showed some paroxysmal activity in the frontal regions, and the patient was discharged on phenytoin in good condition. Three months later the patient had 2 further generalized seizures, at which time her serum phenytoin level was zero. Since then, she has maintained therapeutic levels of phenytoin arid has had no seizures.

Patient 2

A 53-year-old man was admitred to the hospital in January 1987 for cervical myelography with lumbar puncture. He had suffered head and neck trauma in an automobile accident several years earlier and had since experienced chronic neck pain. For the previous 6 months he had noted pain and weakness in both arms. The pain worsened acutely 10 days before admission while he was golfing, and there was associated numbness on the left side of his body. His medical history was unremarkable, he took no medications, and there was no history of seizures or other neurological disease. The patient underwent lumbar puncture and cervical run-up myelography with 15 ml of iopamidol (300 mg iodine per milliliter), which revealed ventral extradural defects at C5-6 and C6-7. The cerebrospinal fluid contained no white blood cells, and the protein concentration was 39 mg/dl. Approximately 1 hour after the procedure the patient had a generalized tonic-clonic seizure lasting 1 minute. He was treated initially with diazepam and later discharged without anticonvulsant medication. No further seizure activity has been noted.

Patient 3

A 55-year-old man was admitted to the hospital in October 1986 for lumbar myelogram. Ne had suffered chronic lower back pain that increased for 1 year, and a burning pain that radiated into his groin. Electrical studies were reportedly

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consistent with bilateral lumbosacral radiculopathy, and a CT scan showed multilevel spinal stenosis. The medical history was notable for hypertension and a poorly described seizure disorder for which he previously took phenytoin and phenobarbital. He had not taken any medications for 10 years, and his last seizure had been 6 years earlier.

Neurological examination was normal, with positive straight leg raising signs bilaterally. The patient underwent lumbar myelogram via puncture at L3-4 with injection of 15 ml of iopamidol (200 mg iodine per milliliter), which revealed central canal stenosis from L2-L5. Cerebrospinal fluid was not obtainable. Approximately 5 hours after the procedure the patient had a generalized convulsion lasting 1 minute. Phenytoin therapy was initiated. On neurological examination, the patient was noted to be fatigued and diffusely weak, with bilateral ankle clonus and equivocal plantar responses. Laboratory data including electrolytes 2nd arterial blood gas were normal. A head CT scan 30 hours later showed residual contrast within the subarachnoid space of the cerebral sulci and basal cistern. There was no contrast within the ventricles, and the scan was otherwise normal. An EEG 3 days later was within the normal limits of variability; there were no seizure discharges or localizing signs. He later underwent decompressive laminectomy without complications and was discharged without anticonvulsant therapy.

Discussion

Iopamidol has been found to be epileptogenic in animals [10]; however, seizures have been rarely noted in clinical trials. Bassi and coworkers [6] reported a series of 1,138 patients, in whom only 1 was noted with "convulsions." They did not specify the dose of contrast medium used or which spinal segment was analyzed; however, higher doses (greater than 4,070 mg iodine) and cervical injections generally resulted in higher rates of complications. One other patient who had a generalized seizure after a high-dose (6,000 mg iodine) iopamidol myelogram has been reported [9]. This patient had recently had a metrizamide myelogram as well. Macpherson and associates [11] found that 7 of 40 patients (23%) had focal and generalized sharp waves on EEG after cervical myelogram with iopamidol, but none of their patients developed seizures. They also found no relationship between the EEG changes and the density of contrast reaching either the ambient ciscern or cortical sulci (although they did not exceed a dose of 3,000 mg iodine). Therefore, they suggested that individual sensitivity to iopamidol was an important factor. In other studies, there have been no seizures noted in series of 100 [12], 80 [5], 65 [2], 30 [3], 36 [4], and 21 patients [7].

We reviewed the experience with iopamidol at the Johns Hopkins Medical Institutions. The 3 patients reported here were from a total of 627 patients at Sinai Hospital; no seizures have occurred in 156 consecutive patients at Johns Hopkins Hospital. Two of the patients (1 and 3) likely had preexisting seizure disorders that were aggravated by the iopamidol. Also, in 1 of these patients an antihistamine and narcotic may have lowered the seizure threshold. In Patient 1, confusion and diffuse cerebral edema seen on CT scan after myelography were also consistent with a toxic encephalopathy. Patient 2 had no known predisposition to seizures before the myelogram, and has not had seizures since then. It is important to note that this patient received 4,500 mg of iodine, which is the highest dose recommended by the manufacrurer.

Little is known of the mechanism of seizure production by iopamidol. Most neurotoxic effects of water-soluble contrast agents are thought to be caused by direct effects on the brain [1]. The findings of focal and generalized sharp waves on EEG after iopamidoi myelography [11] suggest that the epileptogenic effects may be mediated by either cortical or brainstem irritation. Although metrizamide neurotoxicity has been related to competitive inhibition of brain hexokinase [1], this is probably not the mechanism of iopamidol neurotoxicity because the iopamidol molecule does not contain the glucosamine moiety in metrizamide that acts as a glucose analogue inhibiting hexokinase.

Despite the relatively low incidence of serious complications, physicians might expect to see occasional seizures after iopamidol myelography because of its popularity and frequent use. The occurrence of seizures is probably related to individual sensitivity; it is unpredictable and less likely than with metrizamide. However, a history of seizures, the use of high doses of iopamidol, and the concurrent administration of drugs that lower the seizure threshold might all contribute to a higher risk of seizures after iopamidol myelography.

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