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CLINICAL AND BIOCHEMICAL STUDY OF ACCIDENTS IN PERIDUROGRAPHY*

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ABSTRACT

Since the experiences of severe side effects of peridurographic examination have been reported, this procedure has been used less frequently in spite of its easy to get. The most remarkable symptoms of accidents were clonic convulsion, disturbances of speech and consciousness, headache, hyperperspiration and myalgia. Physical examinations revealed always increase of tendon reflex and sometimes pathologic reflex.

The accidents could be caused by intraspinal administration of water-soluble contrast medium (Diatrizoate), and also there is a report that there was an accident only when contrast medium was injected in the cranial portion of the subarachnoid space. Contrast medium permeates through the dura mater. Its permeability rate was about 0.4% in the patient with normal meninges.

Since some agents which affect carbohydrate metabolism was found to cause acute convulsion, and decrease of ATP production or ATP utilization was considered to have close relation to consciousness, the effects of the contrast medium on hexokinase activity and mitochondrial respiration of rat brain were examined, and noticeable inhibitory effects were found. The inhibitory effect on D-amino acid oxidase was also observed.

The medium had no effects on the succinic dehydrogenase activity, but it had remarkable effects on the state 3 respiration, and decrease of P : O ratio indicated decrease of ATP production. These results suggest that the water-soluble contrast medium, which is injected in the subarachnoid space, stimulates the cerebral cortex and produces the metabolic disturbances of the brain which might have some relation to development of the accidents.

INTRODUCTION

Many patients, who are suffering from pains in the low back and lower extremities due to lumbar disc hernia, visit the orthopedic clinic, and much effort has been made to diagnose it, especially in determining its level and localization. Regarding level and localization of the ruptured disc, neurological findings are the most important aid for diagnosis. Myelography, nucleography and peridurography are also helpful for examinations.

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Recently, myelographic examination is used the most in this country. Bosworth, Kirita and Dotani, however, pointed out its side effects, *i.e.* long lasting pain due to adhesion, oleoma formation, secondary inflammtion and so on, which result from oily contrast medium which remain for a long time. Lately, relatively easily removable contrast medium (ex. myodil) began to be used widely, but it is difficult to remove it completely.

At nucleographic examination, it is advisable to visualize degeneration of the nucleus pulposus and to determine the level of degenerated disc. However, when transdural approach is done, complaint of headache and nape rigidity are frequently made. In addition, it can be thought that nucleographic examination causes degeneration of the disc, so its use shoud be restricted only in special cases[1].

Symptoms due to disc hernia are originally caused by pressure in the extradural space, and secondary inflammation associated with adhesion is seen. This is the reason why peridurographic examination is helpful to examine extradural condition.

Since peridurographic examination had been performed by Sicard and Forestier in 1921, it has been reported in this country by Azuma, Maeda, Iwahara and Yokoyama[2]. Recently, it has been recognized as clinically useful examination for lumbar disc hernia and is reported in detailed studies of Mori[3], Yamamura[4] and Hoshino[5]. However, it is not used so widely now, because the rare, but unfavorable side effects develop unexpectedly or is due to intradural injection of the water-soluble contrast medium by technical mistake.

In 1942, Pendergrass, *et al.*[6] reported on the cases of death and unfavorable sequelae following intradural injection of water-soluble contrast medium. Mori[3] (1958) and Nozaki[7] (1964) reported their experiences of accidents following peridurographic examination carried out a few days after lumbar puncture.

Recently, Mori[8] reported detailed studies of histological changes of brain caused by contrast media. According to him, there are no established theories as to what kinds of biochemical disturbances cause such histopathological changes and clinical symptoms.

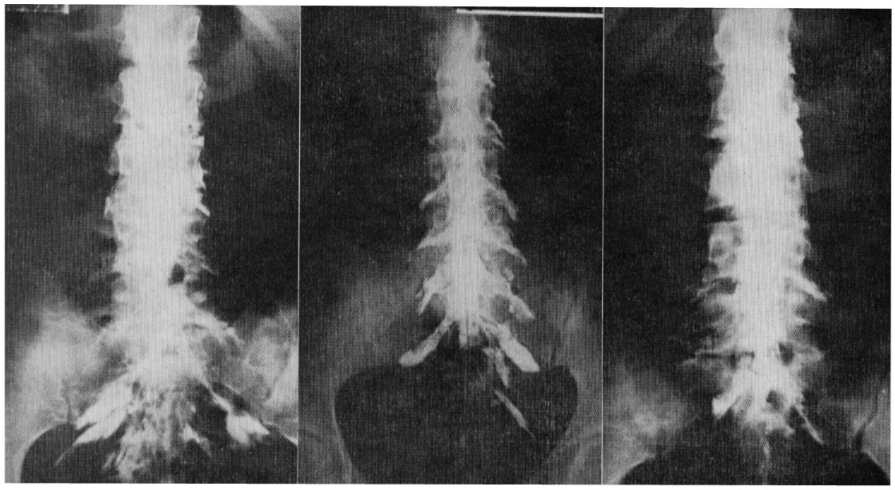
At the Orthopaedic Clinics of Nagoya University and its affiliated hospitals, peridurographic examination has been used as routine examination for lumbar disc hernia since Mori's study in 1958 was reported.

The author reports on the collected six cases and biochemical study of the effects of water-soluble contrast medium on mitochondrial respiration, hexokinase activity, etc. of the brain in order to report the causes of development of accidents.

CLINICAL STUDY

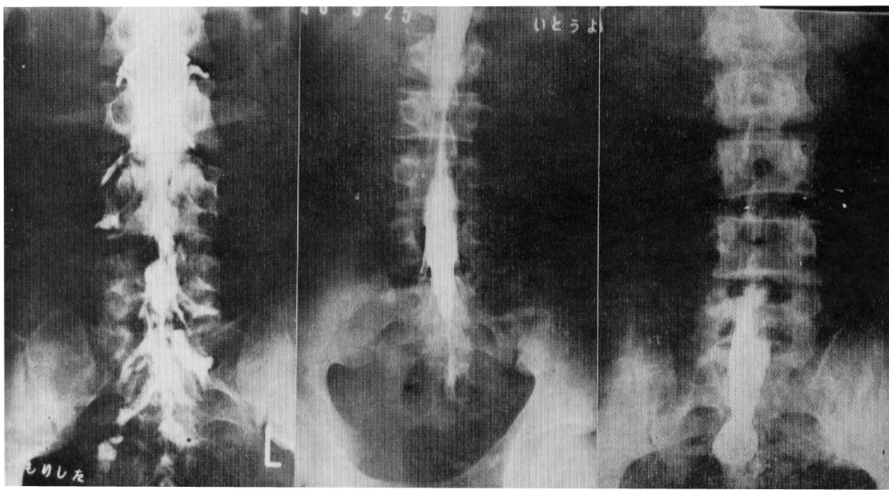
Case report and analysis of symptoms

Lumbar disc lesion was diagnosed in every case, and 12–20 ml of 76%



Case 1 Case 2 Case 3

FIG. 1



Case 4 Case 5 Case 6

FIG. 2

Urografin (Sodium and Methylglucamine Diatrizoate) was used as contrast medium for peridurographic examinations (Table 1).

X-Ray examination of peridurograms was used in four cases and myelograms in two cases. Cyst-like enlargement of caudal sac of the dura was reported in case 6, and it is supposed that it was one of causes of accidents (Fig. 1 and 2).

The onsets of symptoms of reaction were one to three hours after examinations except case 5 in which injection was made intraspinally by technical failure. All cases were healed perfectly without any sequelae except case 2 who died nine hours after the onset of symptoms of reaction.

TABLE 1. Summary of Cases

Case No. Sex and Age	Clinical Diagnosis	Contrast Medium	Onset of Symptoms	X-Ray Findings	Prognosis
1 Female 18	Lumbar disc lesion	Urografin 76% 13 ml	3 hrs.	Peridurogram	Complete cure
2 Female 21	〃	Urografin 76% 20 ml	2 hrs.	Peridurogram	Death
3 Female 15	〃	Urografin 76% 12 ml	2.5 hrs.	Peridurogram	Complete cure
4 Male 22	〃	Urografin 76% 12 ml	1.5 hrs.	Peridurogram	Complete cure
5 Male 18	〃	Urografin 76% 15 ml	10-15 min.	Myelogram	Complete cure
6 Male 33	〃	Urografin 76% 20 ml	1 hr.	Myelogram	Complete cure

TABLE 2. Analysis of Symptoms

Case→ Symptoms ↓	1	2	3	4	5	6
Clonic Convulsion	+	+	+	+	+	+
Headache	+	+	+	+	+	+
Impairment of Consciousness	−	+	−	−	+	+
Dysarthria	−	+	−	−	+	+
Hyperperspiration	+	+	+	+	+	+
Vomiting	−	+	−	−	−	+
Myalgia	+	?	+	+	+	+
Flush of face	+	+	−	−	+	+
Duration of Convulsion	6 hrs.	9 hrs.	5 hrs.	7 hrs.	18 hrs.	24 hrs.

Symptoms (Table 2)

1. Convulsion is one of the most important symptoms and is clonic in nature. There were several clonic convulsion of several seconds duration repeatedly for more than twenty hours. Since clonic convulsion is severe, and its repetition causes increase of metabolism and difficulty in respiration, it is necessary to administer anticonvulsives quickly.

2. Headache is severe and long lasting. Patients frequently complain of difficulty in lifting their head up for several days on account of severe headache.

3. Disturbances of consciousness. In mild cases it does not develop, but in almost all cases it does in various degrees ranging from slight to comatose.

4. Speech disturbances develop with convulsion and cloudiness of consciousness. It is supposed that disturbances result from complicated interaction among decrease of cerebral blood flow, disturbances of brain metabolism due to convulsion and cortical irritation and impairment of brain metabolism caused by contrast medium.

5. Hyperperspiration is seen in all cases. It is thought that it develops in order to compensate for fever and increased metabolism which result from repeated convulsion. However, effects of contrast medium on the autonomic nervous system can be considered, because flush of face, miosis etc. are noted. Effects on the autonomic nervous system may be due to direct chemical irritation to the brainstem and impairment of brain metabolism by contrast medium and response to convulsion.

6. Vomiting is observed in some cases.

7. Myalgia. All recovered patients complain of severe myalgia following repeated convulsion, especially in the extremities.

Physical findings

1. Increase of tendon reflex. Pathologic reflexes, Babinki's etc. are sometimes noted.
2. Increased pulse rate, weak in nature.
3. Normal or high blood pressure.
4. Fever
5. Miosis
6. Flush of face

CSF examination

1. Increase of pressure
2. Increase of protein concentration
3. Pleocytosis

ETIOLOGIC FACTORS

Several etiologic factors are presented[6];

1. Hypersensitivity to Iod-containing drug

According to this opinion, accidents result from hypersensitivity to the Iod-containing contrast medium. Sensitivity test was performed in all cases and showed nothing positive and also symptoms of these accidents differ from those of anaphylactoid reaction resulting from hypersensitivity, *e.g.* a) delayed onset, one to three hours after examination, b) normal or rather high blood pressure, c) flushing of the face and d) no urticaria, itching and iodacne.

It is the author's opinion that the accidents have no relation to hypersensitivity to the drug.

2. Rapid increase of intracranial pressure

Increase of intracranial pressure causes convulsion occasionally, but even when 15–20 ml of physiologic saline is injected in the subarachnoid space, convulsion is not produced. In addition, there are cases with convulsion in which contrast medium was injected in the extradural space. These reasons are why the rapid increase of intracranial pressure is not thought to be important etiologic factor.

3. Changes of osmopresrure of CSF

Even when 20 ml of hypertonic saline is injected intradurally, convulsion is not elicited, moreover, contrast medium injected in the extradural space does not cause significant changes of osmopressure of cerebrospinal fluid.

4. Chemical irritation to cerebral cortex and meninges

In some cases, so-called meningeal irritation signs (meningeal reaction) are observed and besides, histopathological studies reported degeneration of nerve cells, edema and swelling of choroid plexus and hemorrhage. For the previously mentioned reasons, it can be thought that cerebral cortex and meninges, directly in contact with cerebrospinal fluid, become irritated by contrast medium.

5. Inhibition of brain metabolism

On experimental studies of convulsions, the agents having effects on carbohydrate metabolism, *e.g.* fluoroacetate, insulin etc., are used occasionally for evoking convulsion.

Study of action mechanisms of anesthetics on general anesthesia and consciousness indicates that these have close relation to inhibition of ATP production or ATP utilization. For the above reasons, the author performed the biochemical experiments, especially about effects of water-soulble contrast medium on the hexokinase activity and mitochondrial respiration. According to the results of experiments, the author feels that metabolic inhibition is one of the important etiologic factors.

PERMEABILITY OF THE DURA MATER

In both clinical and experimental cases, when contrast medium was injected

in the subarachnoid space, accidents developed. In the cases in which contrast medium was injected in the extradurl space as well as intraspinal space, the X-Ray examination revealed peridurographic findings of severe accidents development. The study that extradural space is connected with intradural space by lymphatic vessels is also reported. It is considered, therefore, that contrast medium may be permeable through the dura mater.

The author performed experiment to investigate permeability of the dura mater as follows:

15 ml of Iothalamate labelled with ^{131}I (supplied by the Daiichi Kagaku) was injected in the extradural space in five cases and then cerebrospinal fluid was obtained by lumbar puncture two hours after injection. Radioactivities of CSF and original Iothalamate were counted by Well-type scintilation counter.

Permeability rate was calculated as follows:

$$\frac{\text{Total counts of CSF}}{\text{Total counts of Iothalamate injected}} \times 100.$$

Permeability rates were 0.3, 0.4, 0.46, 0.48 and 4.0 per cent respectively.

The above results suggest that some contrast medium injected in the extradural space may permeate into subarachnoid space through the dura mater and also if there are some factors that increase permeability of meninges, *e.g.* inflammation, lesion of the dura etc., sufficient volume of contrast media which can cause accidents may permeate through the dura mater.

At the same time, electrophoresis of the cerebrospinal fluid by cellulose acetate stripes was done to determine the Iothalamate boung with α-globulin component.

EXPERIMENTAL STUDY

The most prominent symptoms of accidents in peridurographic examination are severe clonic convulsion and disturbances of speech and consciousness. It is very interesting to determine what kind of metabolic disturbances in brain can cause such symptoms. In experimental study electric stimulation is used most frequently as a trigger to produce acute convulsion. Several chemical substances are sometimes used too; strychnine and picrotoxin which stimulate all parts of the central nervous system and fluoroacetate, 2-deoxyglucose and insuline which affect carbohydrate metabolism[9].

Insulin is polypeptide hormone involved in the regulation of metabolism, especially carbohydrate metabolism, and hexokinase reaction (phosphorylation of glucose) is affected by insulin[10]. Therefore, it is suggested that disturbances of carbohydrate metabolism may be one of the etiologic factors inducing convulsion.

Recent studies on action mechanism of anesthetics have indicated the

evidence that decrease of ATP production due to inhibition of mitochondrial respiration or disturbances of ATP utilization have close relation to anesthesia and consciousness[11]. Because of the above reasons, the author investigated the effects of the water-soluble contrast media on mitochondrial respiration, hexokinase activity of brain and other metabolic systems.

Materials and methods

Preparation of mitochondria[12]

SD strain rats, body weight ranging from 200 to 300 g, were used. The medium for the preparation of liver mitochondria contained 0.21 M mannitol, 0.07 M sucrose, 0.1 mM EDTA and M trisbuffer (pH 7.4). The whole brain was gently homogenized in 0.25 M sucrose containing 0.1 mM EDTA and M tris-buffer (pH 7.4). Medium was centrifuged at 600× g for 10 min. to remove cell debris. The supernatant was centrifuged at 10,000× g for 10 min. The sediment was washed with the above solution, suspended and used as the mitochondrial fraction.

Preparation of homogenates for hexokinase activity

Whole brain was homogenized in ice-cold 0.12 M potassium phosphate buffer, pH 7.8, containing 0.15 M KF (5 ml/g tissue) according to Long[13]. The homogenate contained 0.1 M phosphate and 0.125 M fluoride.

Assay of oxidative phosphorylation

Mitochondrial respiration was measured at 20°C by an oxygen electrode apparatus with an automatic recorder (Beckman Oxygen Sensor connected with Electronic Polyrecorder Model EPR-2 TB). The reaction medium contained 0.3 M mannitol, 10 mM KCl, 2.5 mM $MgCl_2$, 0.25 mM EDTA and 10 mM potassium phosphate buffer, pH 7.4. Respiratory control ratio was directly obtained from the records. P:O ratio was calculated according to Hagihara[14].

Assay of hexokinase activity

The reaction medium (total 1.0 ml) contained 0.15 M $MgCl_2$ (0.1 ml), 0.4 M glucose (0.1 ml), 1.0 M ATP (0.1 ml), homogenate (0.1 ml) H_2O and various concentration of Iothalamate. After incubation at 30°C for 10 min. 1.0 ml of 0.3 N $Ba(OH)_2$ was added in order to stop enzyme activity and then 5% $ZnSO_4$ (1.0 ml) was added to precipitate the protein. After centrifuged for 5 min., the almost clear supernatant was filtered through Toyo No. 7 filter paper. 0.3 ml of the filtrate was taken for glucose determination by using β-D-glucose oxidase[15].

Assay of D-*amino acid oxidase*

D-amino acid oxidase was prepared from hog kidney and purified according to Yagi *et al.*[16]. Reaction medium contained 0.1 mg D-amino acid oxidase (0.02 ml), 1.0 M D, L-alanine (0.5 ml), FAD (5×10^{-5} M) and 1/60 M pyro-

phosphate buffer (pH 8.3), total 5.0 ml. Activity of D-amino acid oxidase was measured at 20°C by Beckman Oxygen Sensor with electronic polyrecorder.

Sodium and Methylglucamine *Diatrizoate* (Urografin) and Methylglucamine *Iothalamate* (Conray) were used as water-soluble contrast media.

RESULTS

Effects of contrast media on mitochondrial respiration

Addition of contrast media, varying from 6.5 mM to 30.9 mM, showed no effects on the succinate respiration, state 4 respiration, but showed effects on state 3 respiration (Fig. 3). In the absence of contrast medium, respiratory control ratio was 6.7 and P:O ratio was 1.75.

Effects on state 3 respiration in various concentration of contrast media (Fig. 4)

Inhibitions of O_2 uptake in 6.5, 12.8, 18.9, 24.9 and 30.7 mM of Diatrizoate were 30.4, 66.3, 79.3, 95.7 and 100 per cent respectively, and respiratory control ratios in same concentration were 5.0, 2.94, 2.2, 1.25 and 1.0 (Fig. 5). Inhibitions of O_2 uptake in 6.9, 16.5, and 30.9 mM of Iothalamate were 25.0, 58.7 and 98.9 per cent.

Effects of Diatrizoate on state 3 respiration were almost identical with

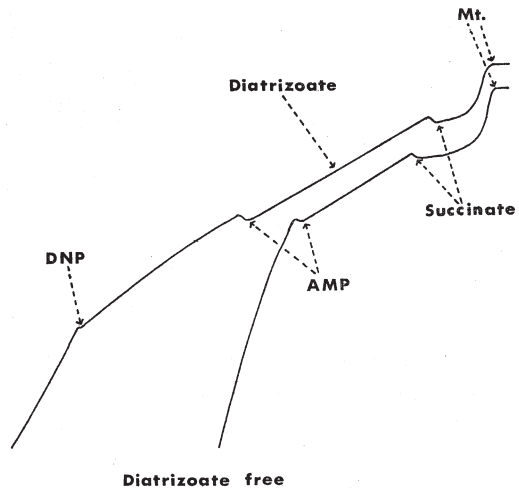


FIG. 3. Effect of the water-soluble contrats medium (Diatrizoate) on the state 3 respiration.

The oxygen uptake was measured polarographically in the medium containing 0.3 M mannitol, 10 mM KCl, 0.25 mM EDTA, 2.5 mM $MgCl_2$ and 10 mM potassium phosphate buffer (pH 7.4). Protein concentration of mitochondria was 1.0 mg/ml. Concentrations of succinate and AMP added were 5 mM and 60 μM respectively. Concentrations of Diatrizoate and DNP were 30.7 mM and 10 mM respectively.

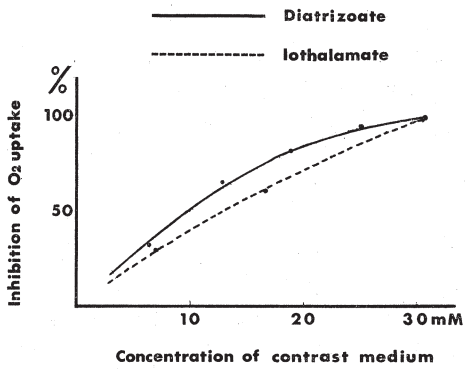


FIG. 4. Effects on the state 3 respiration in various concentration of Diatrizoate and Iothalamate.

Experimental conditions were as in Fig. 3. Mitochondrial concentration was 1.0 mg protein/ml. The solid line indicates the effect of Diatrizoate and the dotted line reprsents that of Iothalamate.

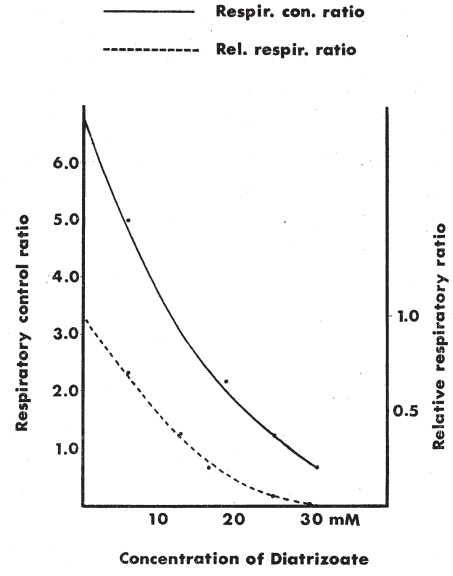


FIG. 5. Effect of contrast medium on respiratory control ratio.

Experimental condition were as in Fig. 3. Mitochondrial concentration was 1.0 mg protein/ml. Relative respiratory ratio means the ratio of the respiration rate in the presence of contrast medium to that in the absence of contrast medium. The solid line indicates respiratory control ratio and the dotted line represents the relative respiratory ratio at state 3.

those in same concentration of Iothalamate.

P:O ratios in various concentration of Iothalamate, 14.8, 44.5 and 74.2 mM, were 1.63, 1.42 and 1.33 respectively (2 mg protein/ml).

Release of inhibition

Inhibition of O_2 uptake was released by addition of serum and DNP (dinitrophenol), however, not released by addition of bovine albumin, FAD and cytochrome C.

Effects of contrast medium on hexokinase activity

By addition of Iothalamate, hexokinase activity was inhibited. Activities in 69, 138 and 207 mM of Iothalamate were 56.7, 35.8 and 32.8 per cent respectively as shown on Fig. 6.

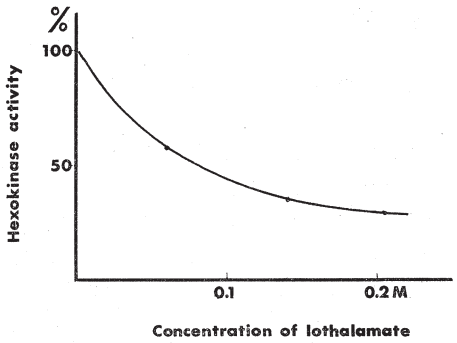


FIG. 6

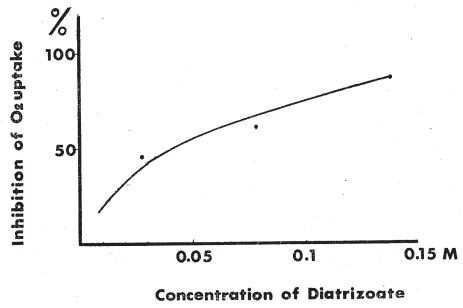


FIG. 7

FIG. 6. Effect of contrast medium on hexokinase activity of brain.

Reaction medium contained 0.15 M $MgCl_2$ (final 5×10^{-3} M), 0.1 ml of 1.0 M ATP and 0.4 ml of homogenate. Inhibition rate means the ratio of dosis of glucose consumption in the presence of Diatrizoate to that in the absence of it.

FIG. 7. Effect of Diatrizoate on D-amino acid oxidase.

The oxygen uptake was measured polarographically in the medium containing 0.1 mg D-amino acid oxidase, 1.0 M D, L-alanine (0.5 ml), FAD (5×10 M) and 1/60 M pyrophosphate buffer (pH 8.3), total 5.0 ml.

(Glucose contents in reaction mixture were measured by using β-D-glucose oxidase, because contrast medium has no effects on β-D-glucose oxidase activity.)

Effects on D-*amino acid oxidase activity* (Fig. 7)

D-amino acid oxidase activity was inhibited by addition of Diatrizoate and inhibitions in 27.5, 81.0 and 131 mM were 47.5, 58.3 and 77.7 per cent respectively. This inhibition was not competitive inhibition with substrate (D, L-alanine).

DISCUSSION

There have been reports on the accidents in the peridurographic examination or those following intradural administration of water-soluble contrast medium by technical mistake. In these reports the danger of peridurography has been emphasized too much, so this procedure has been used less frequently in spite of its easy to use.

There exists a histopathological study by Mori, but little work has been done to study biochemical mechanism of the accidents. In 1942, Pendergrass *et al.*[6] reported 2 cases, one is a child with internal hydrocephalus and large ventricles, who died shortly after the injection of Uroselectan into the ventricular system, and the other died following injection of 35 per cent diodrast intraspinally, but there are no further details.

Mori[3] (1958) reported a case of one who died with severe convulsion and coma following peridurographic examination with 15 ml of 76% Diatrizoate a few days after lumbar puncture, and he emphasized that this procedure be

avoided when meninges are injured. In the same work, he reported on the effects of the water-soluble contrast medium on the spinal cord of a rabbit in which there were edematous softening of the spinal cord and degeneration and necrosis of nerve cells.

In 1964, Ishigaki *et al.*[17] reported on experience in treatment of 6 cases out of which 3 cases died following intraspinal administration of contrast medium by mistake and presented the term "aseptic meningeal reaction". Hatanaka[18], however, stated that since liquor-brain barrier is almost freely passable quite unlike blood-brain barrier, it should be considered that the contrast medium, injected intraspinally, stimulates and injures not only the meninges, but also the central nervous system. According to the above reasons, he presented the term "the reaction of the brain and spinal cord by irritation due to contrast medium injected intraspinally".

Mori[8] (1966) reported on the histopathological study of the effects of the contrast media on the central nervous system of a mouse based upon his experiences of 3 cases that were injected in the subarachnoid space by technical failure or accident. He attached importance to its effect on the brain.

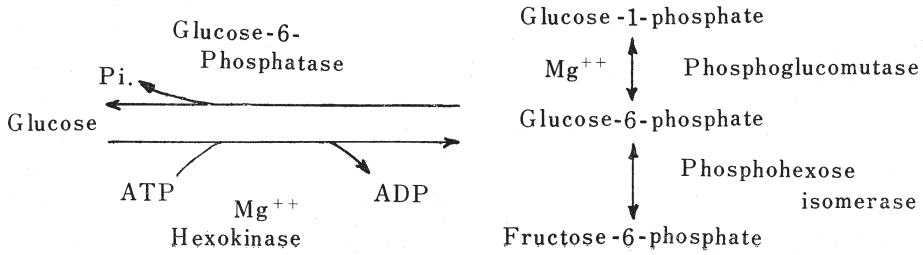
The author reports on 6 cases and the effects of contrast medium on the brain metabolism, especially carbohydrate metabolism, mitochondrial respiration and others.

Importance of carbohydrate metabolism in the brain is so well-known that it is not necessary to write about it in detail. Since the cerebral respiratory quotient is almost 1.0 (0.95 ± 0.1)[19], it is obvious that the brain principally gets its energy from carbohydrate. Therefore, when carbohydrate metaboism is disturbed, cerebral functions are markedly impaired.

Tendency and threshold of convulsion are influenced by various physical conditions; hypocalcemia and hypoglycemia are apt to promote convulsion and some of these are used in order to evoke convulsion[20].

It is well-known that the epileptic convulsion develops in hypoglycemia caused by insulin; therefore, it is considered that inhibition of glucose metabolism is possibly one of the etiologic factors of development of convulsion.

Insulin affects the hexokinase reaction which regulates the first step of the carbohydrate metabolism, and hexokinase acts for phosphorylation of glucose to glucose-6-phosphate under existence of ATP and Mg^{++}.



Actually, hexokinase activity of rat brain shows very high value which is almost double that of any other tissues and this indicates the importance of carbohydrate metabolism of the brain[13].

Inhibition of hexokinase activity by the contrast medium induces decrease of utilization of glucose in the brain. This is a kind of hypoglycemia-like condition in the nerve cells. In addition, contrast medium stimulates chemically the cerebral cortex. These conditions may have a tendency to cause convulsion. It is considered that, since impairment of carbohydrate metabolism affects energy metabolism, disturbance of consciousness is extended further.

The steps, which nerve cells of brain are damaged by metabolic disturbances, depend upon the metabolic rates at respective parts of the central nervous system[21]. Therefore, cerebral symptoms in hypoglycemia are divided into five phases; 1) cortical phase, 2) subcorticodiencephalic phase, 3) mesencephalic phase, 4) premyelencephalic phase and 5) myelencephalic phase. The more newly developed cortex of brain, the higher the metabolic rates become, but on the contrary, the olderly developed, the lower.

According to above classification, symptoms derived from dysfunction of the cerebral cortex—convulsion, disorientation, disturbances of consciousness and speech, etc.—start at first, then the myelencephalic symptoms—shallow respiration, miosis, hyperperspiration, coma, etc.—develop last[21].

Terplan reported the remarkable swelling of the brain, widely disseminated degeneration of cerebral cortex, hemorrhage and perivascular cell infiltration in the brain of a diabetic patient who died of hypoglycemia by an overdose of insulin. These are similar to Mori's report of histopathological findings in the central nervous system due to contrast medium.

Once seizure develops, it is followed by decrease of cerebral blood flow, metabolic changes of the brain, acidosis, dehydration, electrolyte imbalance and increase of lactic acid in serum by longlasting severe convulsion[20]. In addition, response of autonomic nervous system and thalamus-endocrine system are mobilized.

Recent study on mechanism of anesthesia has indicated that anesthesia and consciousness have close relation to decrease of ATP production which results from inhibition of the oxidative phosphorylation of brain and to a decrease of ATP utilization by anesthetics.

PREVENTION AND TREATMENT OF ACCIDENTS

Water-soluble contrast medium inhibits the mitochondrial respiration of the nerve cell and decrease of P:O ratio indicates a decrease of ATP production. It is considered that such impairment of energy metabolism of the brain can bring about cloudiness. Cerebral hypofunction, which results from disturbances of carbohydrate metabolism, decrease of cerebral blood flow and

changes of brain metabolism due to severe convulsion, make cloudy consciousness deeper.

Although the role of D-amino acid oxidase *in vivo* is not clear, it can be considered from the inhibitory effect of the contrast medium on this enzyme that the medium has effects on flavoproteins of metabolic systems which may result in an inhibition of mitochondrial respiration.

When contrast medium is injected intraspinally, accident is caused without exception. However, even when it is injected in the extradural space, if there is increase of permeability of the dura mater, it may permeate enough to cause severe accidents.

If 2–3 ml of contrast medium is injected in the subarachnoid space, it may cause the accidents. In the patient who has normal permeability of the dura, 20 ml of medium that is injected extradurally is not enough to cause the accidents.

Prevention

1. Use of short needle
2. Determination of "No outflow of cerebrospinal fluid"
3. Use of roentgenoscope (Roentgen-TV)
4. Avoidance of peridurographic examination when the dura mater is injured.
5. Pay attention to anatomic malformation of the dura mater.

Short needle, gauge No. 22, was used. However, when there is an anatomic malformation of the dura, it can reach to the dura. Even if the needle reaches in the subarachnoid space, there is not always an outflow of cerebrospinal fluid. If Roentgen TV is used, immediate management can be performed even when the contrast medium is injected intraspinally. But when there is an increase of permeability of the dura, some volume of contrast medium may permeate to cause accidents.

Mori and Nozaki reported their experience of accidents following peridurographic examination carried out a few days after lumbar puncture and emphasized the avoidance of this procedure when the dura is injured.

Treatment

1. Anticonvulsives should be administered immediately.

Convulsion causes decrease of cerebral blood flow and increase of energy consumption, and moreover, accumulation of metabolic intermediates, and metabolic disturbances of the brain results. All the above conditions causes further cerebral hypofunction. These are the reasons why convulsion should be stopped as soon as possible.

2. Removal of contrast medium with CSF and wash with physiological saline. These should be done immediately, under general anesthesia if necessary.
3. Administer glucocorticoids or its derivatives intraspinally and intrave-

nously for prevntion of aseptic meningeal reaction due to direct chemical irritation.

4. O-inhalation

5. Control of respiration

In longterm cases, muscle relaxants should be administered, and sometimes it is necessary to treat the patient under general anesthesia with intubation.

6. Correction of electrolyte imbalance.

Electrolyte imbalance following general hyperperspiration and acidosis due to increase of serum lactic acid resulting from repetition of severe convulsion should be corrected by intravenous infusion of a suitable solution.

7. Protection of heart, liver, kidney, etc.

SUMMARY AND CONCLUSION

1. Accidents in peridurography are caused by intraspinal administration of the water-soluble contrast medium. However, even when it is injected extradurally, if there is increase of permeability of the dura mater, it may permeate enough to develop severe accidents.

2. It may be considered that the cause of convulsion is related to disturbance of carbohydrate metabolism and due to direct irritation of the cerebral cortex by the contrast medium.

3. It may be considered that disturbance of mitochondrial respiration causes the cloudy consciousness.

4. The inhibitory effect of the contrast medium on D-amino acid oxidase (one of flavoproteins) was observed.

5. Permeability rate of Iothalamate through the dura mater is about 0.3–0.5%.

6. The author studied the etiologic factors, prevention and treatment of the accidents in peridurographic examination based upon the collected six cases.

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