well. Three days after operation there was a sudden onset of severe vomiting and diarrhoea. The child's condition rapidly became worse, and unconsciousness supervened the following day. On readmission (five days after operation) the temperature was 103°, pulse rate 160, and respirations 32. The patient was very drowsy, but could be roused; his colour was good. There were scattered rhonchi throughout both lungs, a patch of tubular breathing, and crepitations at left base. The temperature remained at 103° to 104°; delirium and unconsciousness supervened, death taking place two days after admission—that is, one week after tonsillectomy. No blood culture or post-mortem was performed, but the clinical picture was one of septicaemia.

Case 11.—A female, aged 9 years, had tonsils and adenoids removed, guillotine method, on October 7th, 1931. She was discharged from hospital after twenty-four hours apparently well. On arrival home she was seen by the family doctor, who found her not at all well, with a temperature of 101°. The child continued very ill; the throat was dirty, and the temperature ranged from 101° to 103°. On October 10th there was severe epistaxis. The following day the patient was still very ill; her expression was anxious, and her breath very offensive. There was sordes on the lips and teeth, and the throat was very dirty and sloughy. The cervical glands were enlarged and tender, and blood oozed from the nasopharynx. She was admitted to a nursing home, when the temperature was 102°, pulse rate 144, and respirations 28. A throat swab showed the presence of streptococci and staphylococci. In the morning of October 12th the patient's condition slightly improved, but in the evening there was another severe epistaxis, and she became semi-conscious. A post-nasal plug was introduced to control haemorrhage, and anti-streptococcal serum was given. The child died that evening. No blood culture was obtained.

Although the post-nasal haemorrhage was probably contributory, the fatal result in this case, in view of the high pyrexia and general picture, was considered to be due to septicaemia.

I desire to express my thanks to my colleagues in charge of the ear, nose, and throat departments for allowing me to see and record these cases.

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M. Gundel and F. Müller-Voigt (*Deut. med. Woch.*, November 2nd, 1934, p. 1664) give an account of a hurricane campaign of diphtheria immunization in the town of Duisburg-Hamborn. With a population of 440,000 it has suffered more and more from diphtheria since 1928. In that year there were 1,438 cases and 112 deaths. In 1933 the cases rose to 2,090 and the deaths to 126. In 1934, up to September, there were as many as 2,214 cases and 160 deaths. Artificial immunization of the children seemed, therefore, urgently indicated, and within the space of six days first injections were given to 23,000 of the 38,562 children between the ages of 1 and 5, and to 57,034 of the 64,450 school children between the ages of 6 and 14. The material used was formol-toxoid and toxin-antitoxin, and the immunization was effected by three injections. In the absence of legislative measures wherewith to enforce this undertaking, the authors achieved rapid, wholesale immunization of the town's juvenile population by means of systematic educational propaganda and a well-organized campaign, which required the co-operation of more than a hundred doctors and over 3,000 other workers, about 1,700 of whom were school teachers. The propaganda included articles in the Press, and addresses. It was found much easier to deal with the school child than with the pre-school child, as the former could be shepherded by their teachers, whereas the latter required extraction from their homes, a process which could not be achieved by simply inserting notices in the Press. The rate at which the school children were inoculated, after some practice had been acquired, was 140 to 150 per hour; the rate was considerably slower for the pre-school children.

ACUTE IODISM FOLLOWING LIPIODOL BRONCHOGRAPHY

BY

J. G. SCADDING, M.D., M.R.C.P.

RESIDENT MEDICAL OFFICER, BROMPTON HOSPITAL

The use of lipiodol for bronchography has now become so much a part of the routine investigation of non-tuberculous chest diseases that the occurrence of any severe complication appears worthy of record.

Lipiodol consists of poppy-seed oil in which 40 per cent. of iodine is held in chemical combination with the unsaturated fats. The possibility of the production of toxic symptoms in patients with an idiosyncrasy for iodine is obvious. However, severe symptoms from this cause appear to be rare, owing to the close chemical combination in which the iodine is held. Sicard and Forestier¹ state that they have encountered only transient iodism of benign type. A report² of the Council of the American Medical Association on the dangers of the injection of iodized oils makes no mention of the possibility of dangerous toxic symptoms. Firth³ describes a personal experience of troublesome but not serious symptoms from iodine sensitivity following endotracheal introduction of chloriodized peanut oil; in addition to coryza, lachrymation, and an urticarial rash, he had a transient parotitis and severe frontal headache, all passing off within a week. Carmichael⁴ records two considerably more severe cases after lipiodol, characterized by vomiting, diarrhoea, conjunctivitis, and a haemorrhagic, urticarial, and bullous rash. Both cases improved rapidly within a week. O'Donovan⁵ reports a case in which death occurred six weeks after lipiodol injection, accelerated by the aggravation of a previously existing papulo-pustular rash.

The two cases described in this communication, one of which proved fatal, occurred recently at the Brompton Hospital. Over 2,900 lipiodol examinations have been performed at this hospital without a previous serious accident from iodine sensitivity. A transient coryza with lachrymation and possibly a mild urticarial or erythematous rash, all passing off within a few days, have been observed not infrequently. In a few cases more severe rashes—appearing rather later, up to a week or ten days after the injection—have occurred. These tend to be of an acute and irritant urticarial type. Headaches have followed the injection in rare instances, and in one case frontal headache was severe enough to cause suspicion of acute glaucoma. I have been unable to find any previous record in the literature of a fatality directly due to acute iodism consequent on the diagnostic use of lipiodol.

Case I

A man, aged 46, was admitted to the Brompton Hospital in August, 1933. He was referred from a sanatorium, where doubt about the original diagnosis of pulmonary tuberculosis had arisen on account of atypical x-ray appearances and persistently negative sputum examinations. The differential diagnosis appeared to rest between chronic lung abscess and neoplasm. His general condition was poor, and he had lost 3 st. in weight.

On August 22nd I introduced 20 c.cm. of lipiodol by the subcuticoid route. The film taken after this showed a good outline of the bronchi, with a probable chronic bronchiectatic abscess of the right upper lobe; there was no lipiodol in the stomach. Six hours later he had developed marked coryza, with nose-bleeding, salivation, and injection of the conjunctivae. The following day he was obviously weaker; the pulse was rapid and of poor volume, and the temperature was rising; the nose-bleeding continued. Scattered petechiae had appeared, especially on the dorsum of the hands and

forehead; the conjunctivae had become grossly oedematous, and haemorrhages had occurred into them; the tongue was swollen, and there was a large submucous haemorrhage in it. The submaxillary glands had become very swollen and tense.

On the next day, August 24th, all the symptoms were more severe; the blood pressure was reduced to 85/60. An urticarial element was evident in the rash, which had become more widespread; subcutaneous haemorrhages were seen over the pressure points, especially the right elbow and the sacrum. There was marked dyspnoea, and scattered moist rales were audible over both lungs. There was great difficulty in swallowing on account of the grossly swollen tongue, but no evidence of oedema of the glottis sufficient to cause obstruction. Bleeding from the nose and gums continued; the patient was unable to open the oedematous and haemorrhagic eyelids. He ultimately died, from exhaustion and pulmonary oedema, fifty-four hours after the lipiodol injection.

The treatment in this case consisted of the administration of a saline purge at the onset of symptoms; adrenaline locally to the swollen tongue and fauces failed to reduce the oedema; atropine was given to check excessive bronchial secretion; and sodium thiosulphate, 0.5 gram intravenously, produced no improvement.

Post-mortem Examination.—This was performed by Sir Bernard Spilsbury, and the following is a summary of the relevant pathological changes. External appearances: numerous large petechiae in skin of face, with larger haemorrhages in skin of upper eyelids and in conjunctivae. Numerous petechiae in skin of hands and feet, a few on rest of limbs and trunk. A group of large haemorrhages with ulceration over back of right elbow and over sacrum. Raised red nodule over trachea; no septic change found on incision. Heart: pericardial cavity obliterated by fine old adhesions. Extensive haemorrhages into visceral pericardium, chiefly over left ventricle. Heart somewhat enlarged and dilated. Small haemorrhages in myocardium, and one in endocardium. Microscopically, slight fatty degeneration and some brown atrophy of the muscle. Air passages congested, large petechiae in mucosa of trachea, becoming confluent in larynx. Oedema of ary-epiglottidean folds, especially on right side. Lungs: very dense adhesions over upper part of right lung; marked bronchiectasis, with fibrosis of upper half of right upper lobe, with a large cavity in lower part of lobe. Lower parts of both lungs congested and oedematous. Liver: small haemorrhages into substance. Kidneys: cloudy swelling and congestion. Intestines: haemorrhages in mucous membrane of middle third of small intestine. Tongue: haemorrhage in left side of tip, forming a small nodule. Submaxillary glands: enlarged, with haemorrhages beneath capsule and between lobules.

Case II

The patient, a woman aged 59, had been attending the hospital for some years. In 1930 a lipiodol examination was performed, and showed bilateral basal cylindrical bronchiectasis. She had been treated on frequent occasions with medicines containing potassium iodide, though the dosage did not exceed 15 grains daily; neither the lipiodol nor the iodide had caused toxic symptoms. A second lipiodol examination was performed on June 29th, 1934, 20 c.cm. being introduced by the crico-thyroid route, the patient subsequently returning home. The *x*-ray film showed more advanced bilateral bronchiectasis.

She was admitted to hospital on the following evening, June 30th, acute symptoms having appeared about six hours after the injection. On admission she had an urticarial rash with large purpuric patches over both olecranon, and just below the knees. There was gross painful swelling of both forearms, round both elbows, and behind the knees, the appearances resembling those of cellulitis. The face was puffy, the conjunctivae grossly swollen, with purpuric patches in them and in the eyelids. There were a few purpuric spots on the tongue, and one on the upper lip. The chest was full of bubbling rales and rhonchi; cough was difficult. There was some dysphagia.

On July 2nd all symptoms were more severe. The brawny swellings on the forearms were extremely painful. The patient was unable to swallow even fluids, but there was no respiratory

obstruction in the larynx; adrenaline locally failed to reduce the swelling sufficiently to render swallowing possible. The pulse was of very poor volume. The urinary output was scanty, and there was a cloud of albuminuria; the patient was rapidly becoming weaker.

It was thought that the lack of circulating fluid owing to deficient intake and to withdrawal of fluid into the oedematous tissues was the chief cause of the asthenia; 25 oz. of hypertonic (1.8 per cent.) saline with 5 per cent. glucose was therefore given intravenously. In spite of a rigor, very definite improvement followed within a few hours; the patient was able to swallow fluids freely, and the pulse became stronger. During the next few days steady improvement continued. The brawny oedema of the limbs persisted for a week, and the purpuric areas on the elbows, knees, eyelids, and upper lip ulcerated and healed under scabs. A purulent infection of the oedematous conjunctivae occurred, but cleared up without complications. The patient was not fit to leave her bed for four weeks, but eventually made a good recovery.

Discussion

There can be no doubt that the toxic symptoms in these two cases were due to hypersensitivity to iodine. The fact that the second patient had already had a lipiodol injection, and had been treated with potassium iodide medicinally without ill effect, shows that testing for sensitivity by a dose of potassium iodide is of little value. It also suggests the possibility of the symptoms having been due to an abnormal sensitivity to the poppy-seed oil component of the lipiodol. This appears to be negated by the close similarity of the symptoms to those known to be produced by iodine sensitivity. A case presenting very similar symptoms, though without the haemorrhagic rash, after a single dose of 25 grains of potassium iodide, has been reported by Snell and Savin.⁶ There can be no question of impurities in the lipiodol, as in both cases it was perfectly clear, and other injections with the same batch gave rise to no ill effects.

The accidental introduction of lipiodol into the stomach is generally considered to be a necessary antecedent of toxic symptoms. In neither of these cases was there lipiodol in the stomach when the *x*-ray film was taken, but it is possible that, in spite of instructions to the contrary, the patients swallowed some after coughing it up. Sicard and Forestier,⁷ however, have shown that, judging the rate of absorption of lipiodol by the rate of elimination of iodine in the urine, the rates of absorption from the lungs and from the gut do not differ so much as might be expected. For instance, they found that if lipiodol is administered in capsules by the mouth 34 per cent. of the iodine is excreted by the kidneys within five days; if introduced into the bronchi, 20 to 23 per cent. is thus excreted.

It appears, therefore, that the greatest care in testing for sensitivity to iodine and in avoiding the introduction of lipiodol into the alimentary tract will not always prevent the occurrence of serious symptoms from iodism after the diagnostic use of lipiodol. It is suggested that in the fortunately rare event of such symptoms being severe, the use of intravenous hypertonic saline is a theoretically rational and practically useful measure.

I am indebted to Mr. Tudor Edwards and Dr. A. L. Punch for permission to report these cases, and to Sir Bernard Spilsbury for allowing me to use his post-mortem record.

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