

during human calcitonin administration (Woodhouse *et al.*, 1971; Bordier *et al.*, 1972) the latter is possible and could lead to a reduction in deformity. Whether or not the bone fragility can be reduced depends on its cause. If as previously suggested the disease process is a variant of fragilitas ossium (Eyring and Eisenberg, 1968) then a favourable result is unlikely. If, however, the fragility is due simply to the formation of structurally abnormal bone as in adult Paget's disease (Schmorl, 1932; Bordier *et al.*, 1972) successful treatment should prevent further fractures.

The histological findings in this case were similar to the other children previously reported (Eyring and Eisenberg, 1968; Thompson *et al.*, 1969) and confirm the increased bone turnover; active osteoclasts and active osteoblasts were greatly increased in number. The changes in the present patient were indistinguishable from those found in active adult Paget's disease (Schmorl, 1932). It is interesting to note that a similar patient with severe radiological changes had a normal serum alkaline phosphatase level, although osteoclasts and osteoblasts were abundant in the bone biopsy specimen (Bakwin and Elger, 1956). Loss of bone mass assessed radiologically has sometimes been reported but this was not observed in the present patient. Reduced bone mass would result from a relative increase in bone resorption over bone formation, a situation likely to be made worse or initiated by the gross restriction in physical activity that is frequently seen, and also by the occasional reported use of steroid medication (Eyring and Eisenberg, 1968).

There are many striking similarities between adult Paget's disease and the high turnover bone disease described in children; serum alkaline and serum acid phosphatase levels are raised, urine hydroxyproline excretion is increased, and a mosaic pattern is present in the bone biopsy samples. Because of this, and to simplify matters, we used the eponym "Paget's" disease to describe the present patient, although we are fully aware that there is no proof linking the two diseases processes.

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Addendum

After three months' treatment a further reduction in bone turnover occurred. Serum alkaline phosphatase fell from 187 to 95 K.A.U., and urine hydroxyproline fell from 687 to 327 mg a day. In spite of several hard falls no further fractures occurred. Occasional mild nausea was the only reported side effect of the injections.

References

- Bakwin, H., Elger, M. S. (1956). *Journal of Pediatrics*, 49, 558.
 Bordier, Ph., Woodhouse, N. J. Y., Joplin, G. F., and MacIntyre, I. (1972). *Journal of Bone and Joint Surgery*. In press.
 Caffey, J. (1961). *Pediatric X-ray Diagnosis*, 4th edn., p. 1042. Chicago, Year Book Medical Publishers.
 Choremis, C., Yannakos, D., Papadatos, C., and Baroutsou, E. (1958). *Helvetica Paediatrica Acta*, 13, 185.
 Dunnigan, M. G., and Gardner, M. D. (1965). *Scottish Medical Journal*, 10, 325.
 Eyring, E. J., and Eisenberg, E. (1968). *Journal of Bone and Joint Surgery*, 50A, 1099.
 Facon, I. G., Moreira, G., Uehlinger, E., and Giedion, A. (1964). *Helvetica Paediatrica Acta*, 19, 279.
 Fisher, M. T., Atkins, P. A., and Joplin, G. F. (1972). *Clinica Chimica Acta*, In press.
 Galante, L., Colston, K. W., Macauley, S. J., and MacIntyre, I. (1972). *Nature*, In press.
 Hartford, W. H. (1953). *Analytical Biochemistry*, 25, 290.
 Kivirikko, K. I., Laitinen, O., and Prockop, D. J. (1967). *Analytical Biochemistry*, 19, 249.
 MacIntyre, I. (1960). *Advances in Clinical Chemistry*, 4, 1.
 Marshall, W. C., and Moncrieff, A. A. (1962). *Proceedings of the Royal Society of Medicine*, 55, 238.
 Pappas, A. M., Miller, M. E., Anderson, M., and Green, W. T. (1971). *Clinical Orthopaedics and Related Research*, 74, 241.
 Schmorl, G. (1932). *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin*, 283, 694.
 Sieber, P., Riniker, B., Brugger, M., Kamber, B., and Rittel, W. (1970). *Helvetica Chimica Acta*, 53, 2135.
 Stimmerman, G. N. (1966). *American Journal of Pathology*, 48, 641.
 Swoboda, J. W. (1958). *Helvetica Paediatrica Acta*, 13, 292.
 Thalassinou, N. C., Leese, B., Latham, S. C., and Joplin, G. F. (1970). *Archives of Disease in Childhood*, 45, 269.
 Thompson, R. C., Gaull, G. E., Horwitz, S. J., and Schenk, R. K. (1969). *American Journal of Medicine*, 47, 209.
 Whitby, L. G., and Lang, D. (1960). *Journal of Clinical Investigation*, 39, 854.
 Woodhouse, N. J. Y., *et al.* (1971). *Lancet*, 2, 1139.
 Wootton, I. D. P. (editor) (1964). *Microanalysis in Medical Biochemistry*, New York, Grune and Stratton.

Pulmonary Aspiration after Fibre-endoscopy of the Upper Gastrointestinal Tract

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Summary

Pulmonary aspiration occurred in 16 out of 65 patients (24.6%) undergoing fibre-endoscopic examinations of the upper gastrointestinal tract under intravenous sedation, but it was rarely followed by serious complications. Aspiration was found to occur under sedation with diazepam alone, diazepam with atropine, and with chlormethiazole. The most important factors contributing to aspiration are the local pharyngeal

anaesthesia and the mechanical interference of the fibrescope with laryngeal closure and swallowing. The patient is also at risk of aspiration after completion of the procedure and should remain recumbent until the local anaesthesia has worn off.

Introduction

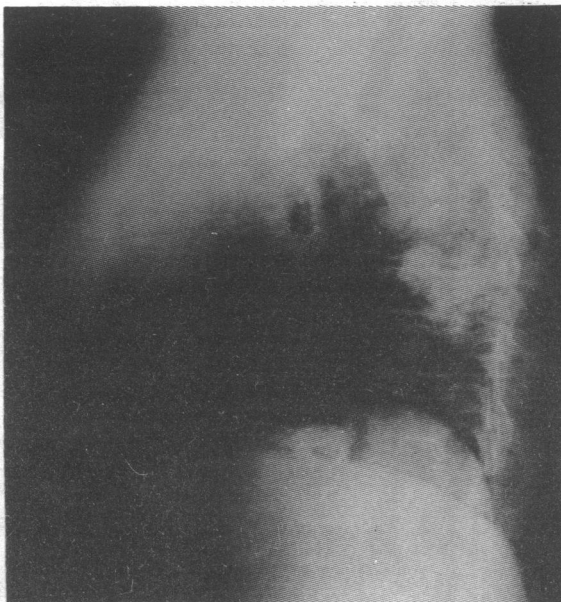
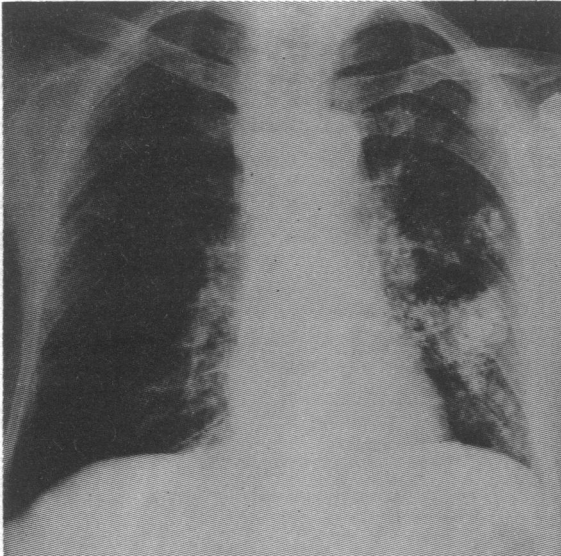
Fibre-endoscopic examination of the gastrointestinal tract under intravenous sedation is now widely practised. We have been concerned with the possible danger of aspiration into the lungs during this procedure, and we have looked at the potential factors involved in increasing the risk. These are the nature of the sedative agent, the dose of the agent used, local oropharyngeal anaesthesia, and the use of antisialagogues.

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Methods

Patients selected for gastroscopy had haemoglobin, prothrombin time, and platelet count checked, and usually had a barium-meal and chest x-ray examination beforehand. Details of the investigation were explained to them and their consent obtained. A history of allergy to iodine was sought, as this contra-indicated the subsequent use of Lipiodol (iodised oil viscous injection) in this study. Each patient was fasted for a minimum of four hours. In the hour before examination oropharyngeal and oesophageal anaesthesia was achieved by dissolving a benzocaine lozenge (100 mg) in the mouth and repeating at 30 minutes. When the patient was on



X-ray films showing extensive aspiration of Lipiodol into the left lung (posterior-anterior and left lateral).

the examination couch further local anaesthesia was obtained by spraying the back of the throat with an orange-flavoured Xylocaine spray (lignocaine hydrochloride).

The patients were divided into three groups according to the sedative regimen. One group received diazepam alone, a second group received chlormethiazole, and a third group received diazepam with atropine. The sedative agent was administered by slow intravenous injection of increments of the

agent until the patient was adequately sedated, as judged by the appearance of drowsiness, dysarthria, ptosis, hiccups, and nystagmus. The dose of diazepam required to reach this stage of sedation varied between 5 and 100 mg. The dose of chlormethiazole used varied between 300 and 2,480 mg. This variation of dosage of the sedative agent used and its relation to gastrointestinal fiberoptic examination has been discussed in detail elsewhere (Metreweli and Prout, 1972).

The patients were examined lying in the left lateral position, and the Olympus G.I.F.D. oesophagogastrobroscope or Olympus G.F.B. gastrofibroscope were introduced in the standard manner. Patients frequently coughed and gagged during this procedure but soon settled for the remainder of the examination. The examination period was 30-40 minutes.

Ten to 15 minutes after introduction of the fibroscope, and with the instrument held steady in position, 5 ml of Lipiodol Ultra-Fluid (iodised oil fluid injection) were introduced into the mouth by slow injection from a disposable syringe via a large-bore blunt plastic cannula (Luer filler needle, Pharmax Ltd.). The patient was requested to swallow this fluid as it was introduced. The end of the plastic cannula was placed on the tongue, projecting not more than 2 cm into the buccal cavity. This process was repeated between 30 and 40 minutes after intubation with the fibroscope still in situ.

At the end of the examination the patients were capable of rising from the couch and being taken by wheel chair to the radiographic department for a posterior-anterior and lateral chest film. The presence of chest symptoms or signs were sought the day after examination if the patient was an in-patient or at the subsequent visit in the case of outpatients. The results are summarized in the Table.

Frequency of Aspiration in Each Drug Group

Drug Group	Total No. of Patients	Total No. of Aspirations	Aspiration during Examination	Aspiration after Examination (see text)
Diazepam ..	31	9	5	4
Chlormethiazole	17	3	2	1
Diazepam + atropine	17	4	4	0
Total ..	65	16	11	5

Discussion

The results show that a surprising number of patients, 16 out of 65 (24.6%), aspirated small quantities of iodised oil during these examinations. Occasionally aspiration occurred into larger areas of lung (see Fig.). This implies that a similar number of patients aspirate small quantities of saliva and possibly some gastric juice during the examination.

None of the patients in this series, or indeed other patients under our care not included in this study, have so far developed unpleasant pulmonary sequelae, but these have been reported in a large combined series by Taylor, Cotton, Towey, and Gent (1972). Despite the small number of cases studied in this series it is none the less clear that this is not a specific effect of the sedative agent alone, as aspiration occurred in all three sedative groups.

Healy and Vickers (1971) concluded that for a period of five to 10 minutes after diazepam injection the patients undergoing dental treatment were able to aspirate foreign material into the trachea during the act of swallowing, but this was presumed to be as a result of impairment of the glottic closure reflex. None of their patients challenged at 10 minutes and later after diazepam injection showed evidence of aspiration. All of the present patients were, however, challenged 10 minutes after injection of diazepam—that is, in the period regarded as safe.

Diazepam encourages salivation (Dundee and Haslett, 1970), which might be a contributory factor towards aspiration, but the use of atropine as an antisialogogue did not protect against this hazard despite the fact that all patients in whom atropine

was used were noticeably drier. The quantity of intravenous sedative used does not appear to be significant, as those patients that aspirated had not had unusually high doses.

When we reviewed the radiographs of those patients who had aspirated, five out of 16 (31.3%) had evidence of aspiration into the right lower zone. It would be unlikely that aspiration would occur into this site while lying on the left side, and we therefore concluded that the patients had aspirated when sitting upright after the examination. Aspiration presumably occurred some 40 minutes after initial sedation. At this time the action of the sedatives is diminished but local anaesthesia is still prominent. Efficient oropharyngeal anaesthesia, however, is an essential prerequisite of gastro-intestinal fibre-endoscopic examination. Consequently we no longer allow patients to sit up after examination. They are instructed to stay horizontal until pharyngeal anaesthesia is no longer present.

Another factor contributing to the risk of aspiration is the mechanical interference with glottic closure and swallowing caused by the presence of the fibroscope. This and the effect of local anaesthesia are unavoidable.

We do not think that the nature of the intravenous sedative

used is of prime importance as has been suggested elsewhere (Taylor *et al.*, 1972) but is due to the unavoidable features inherent in this particular type of examination. We wish to draw attention to the fact that aspiration occurs more commonly than may have been suspected, although rarely followed by serious complications. None occurred in the present series. We therefore suggest that clinicians referring patients for endoscopy should be aware of the risk of pulmonary aspiration complicating the investigation.

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References

- Dundee, J. W., and Haslett, W. H. K. (1970). *British Journal of Anaesthesia*, **42**, 217.
 Healey, T. E. J., and Vickers, M.D. (1971). *Proceedings of the Royal Society of Medicine*, **64**, 85.
 Metreweli, C., and Prout, B. J. (1972). In press.
 Taylor, P. A., Cotton, P. B., Towey, R. M., and Gent, A. E. (1972). *British Medical Journal*, **1**, 666.

Rubella Vaccination and Termination of Pregnancy

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Summary

Six terminations of pregnancy have been carried out in Leicestershire since February 1970 because of rubella vaccine administered inadvertently during early unrecognized pregnancy. Any woman of child bearing age shown by serological tests to be susceptible to rubella should be offered vaccination, preceded and followed by adequate contraception.

Introduction

Circular 17/72 from the Department of Health and Social Security (1972) advises against routine rubella vaccination of women of childbearing age but recommends immunization for women in this age group who request protection, for women in the postpartum period, and for women at special risk of acquiring or transmitting rubella, provided in all cases that they are seronegative and are fully aware of the need to avoid pregnancy for at least two months after receiving the vaccine.

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Vaccination programmes are still in the early stages, but already experience in Leicestershire indicates that the safe administration of rubella vaccine is not as simple as might appear at first sight.

Preliminary Findings

Termination of pregnancy after rubella vaccination was considered necessary on six occasions in which the Public Health Laboratory in Leicester was involved between February 1970 and May 1972 (see Table). Three of the terminations (Cases 4, 5, and 6) were performed within 14 weeks in 1972. With the exception of the pregnancy of a 16-year-old unmarried girl (Case 2), all were "wanted" babies. Cases 1 and 3 were known to be seronegative before vaccination, and both women had been advised not to become pregnant for at least eight weeks. One started menstruation the day after vaccination but conceived within the next 14 days. Arrangements were made for termination at 11 weeks but spontaneous abortion occurred a week earlier. The products of conception did not contain rubella virus (MacDonald *et al.*, 1971).

Rubella vaccine was given to the remaining four women without previous estimation of their immune state. At least one woman is known not to have received any warning of the risks of pregnancy when immunized by a relief surgery nurse. In the case of the unmarried girl her doctor judged the risk of pregnancy to be negligible and advice therefore unnecessary. In four

Details of Patients inoculated with Rubella Vaccine during Pregnancy

Case No.	Age	Prevaccination Haemagglutination Inhibition Test	Last Menstrual Period	Date of Vaccination	Postvaccination Haemagglutination Inhibition Test	Termination
1	23	5 December 1969, <8	16 December 1969	15 December 1969	27 January 1970, + 80	28 February 1970
2	16		12 October 1970	2 November 1970	11 March 1971, + 128	11 March 1971
3	20	23 March 1971, <8 6 April 1971, <8	15 April 1971	22 April 1971	26 June 1971, + 256	7 July 1971
4	25		13 November 1971	19 November 1971	28 January 1972, + 32	7 February 1972
5	25		11 February 1972	19 February 1972		26 April 1972
6	27		18 February 1972	8 March 1972	28 April 1972, + 64	11 May 1972