BISMUTH EDTA COMPLEX

N. SAPEIKA, B.A., M.D., PH.D.

Department of Physiology and Pharmacology, University of Cape Town

The water-soluble stable chelated compound, lead ethylenediamine tetraacetic acid (lead EDTA complex), has been shown experimentally to have value as a contrast medium for oral and parenteral administration.[1, 2, 3] The less soluble lead calcium EDTA complex also produces good shadows of the alimentary canal, but by intravenous injection it does not produce shadows of the kidneys.[4]

It was considered desirable to investigate other metallic complexes of related type for possible radiographic use. Since certain bismuth compounds have been used in diagnostic radiology, it was of interest to study the bismuth complex of ethylenediamine tetraacetic acid. The atomic weight of bismuth is 209, as compared with that of lead, which is 207. The bismuth compounds used in the past proved toxic and have been superseded by other radiopaque compounds. Since the complexes formed by ethylenediamine tetraacetic acid with divalent and trivalent metals are stated to be generally stable, soluble, unhydrolysed compounds, in which the metal is bound in a form which is inactive, it was considered that this type of chelated bismuth compound might prove of more value. A supply of the bismuth complex was prepared by the Geigy Company, and some of its properties are reported here.

Experimental Results

Bismuth EDTA complex proved to be less soluble than the lead complexes previously investigated. The highest concentration prepared in warm Locke's solution was a 2.5% solution, and this was used throughout the investigation. The pH value of this solution was 2.18.

Radiography. The solution was administered orally through a stomach tube to adult albino rats, which were subsequently anaesthetized for radiography. A shadow of the gastro-intestinal tract was obtained, not of very

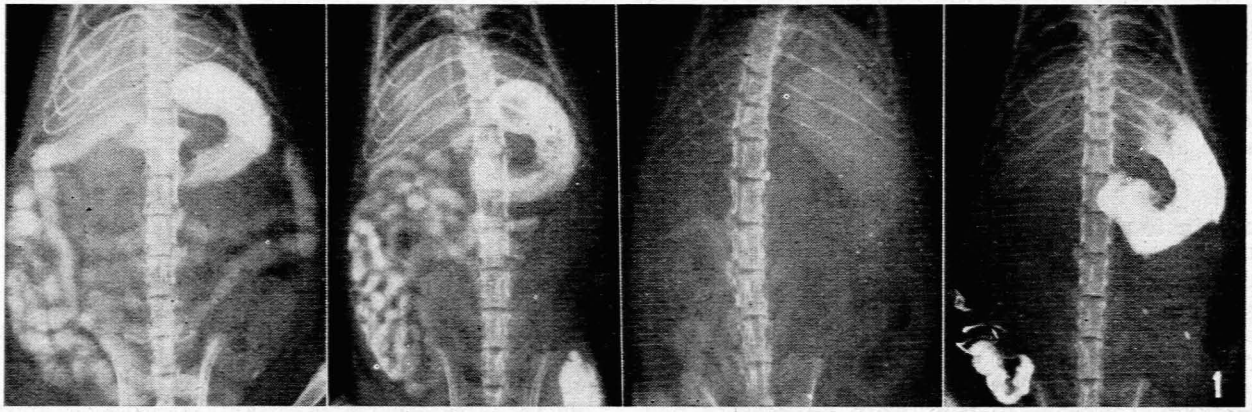

Fig. 1. Radiographs of alimentary canal (rat) to show relative densities of solutions of contrast media 1 hour after administration. Left to rght: lead EDTA 25% (1 ml.); lead calcium EDTA 15 % (1 ml.); bismuth EDTA 2·5% (2 ml.); emulsion of barium sulphate 1 ml.

dense degree and provided 2 ml. or more of the solution was administered (Fig. 1).

The intravenous injection of 2 ml. of the solution failed to produce shadows of the renal calyces and pelves in rats.

Toxicity. No ill effects were observed clinically in rats to which 2 ml. doses were administered orally. Rats which received 1—2 ml. of the solution intravenously during anaesthesia for urographic studies made good recovery. Intraperitoneal injection of large doses (5 ml.) produced death within 12 hours of administration.

Intravenous injection of 0.25—1 ml. per kg. bodyweight in anaesthetized cats produced depression of auricular and ventricular contractions and disturbances of conduction of longer or shorter duration, depending on the dose administered; there was some decrease in the blood pressure and marked fluctuations at the lower and the higher levels until the return to normal. The effects recurred with repeated doses. Atropine did not prevent the effects. Recovery ultimately occurred from each dose. The heart was not arrested. The changes, due to a direct action of the complex on the myocardium, were demonstrated on kymographic and electrocardiographic tracings (Figs, 2 and 3.). The latter showed bizarre changes in the complexes. Intestinal volume recording revealed no significant change in the size of the blood vessels.

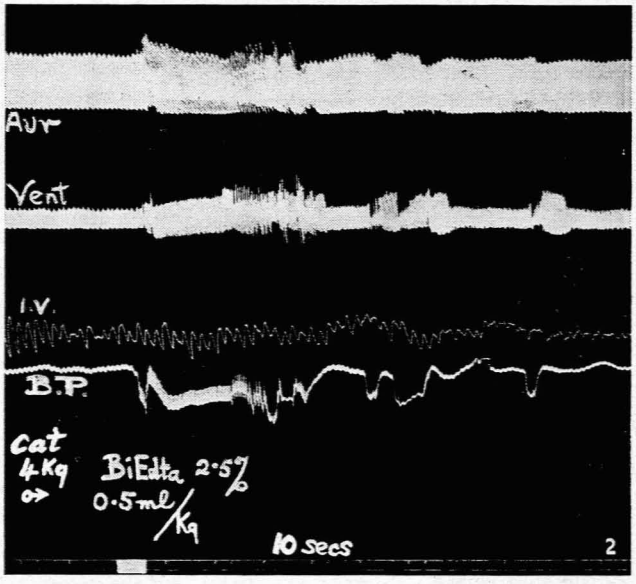

Fig. 2. Cat 4 kg. Effect of bismuth EDTA 2·5% (0·5 ml. per kg.) on auricular and ventricular contractions, intestinal volume, and blood pressure.

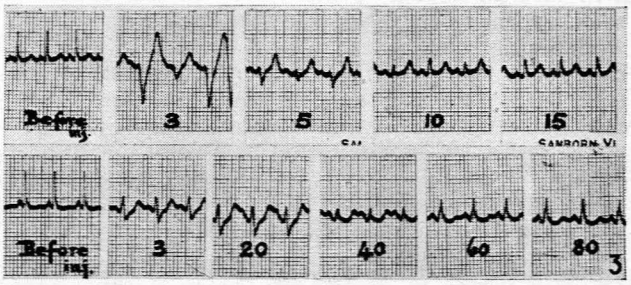

Fig. 3. Electrocardiographic changes produced in cats by bismuth EDTA complex 2·5% solution.
Upper tracing: before injection and 3, 5, 10, 15 minutes after injection of 0·25 ml. per kg.
Lower tracing: before injection and 3, 20, 40, 60, 80 minutes after injection of 1·0 ml. per kg.

The contractions of isolated segments of the small intestine of the cat are not affected even by high concentrations (1 in 2,000).

Discussion

Oral administration of a solution of 2.5% bismuth EDTA complex produces a shadow of the stomach and intestine much less dense than that produced by the more soluble lead complexes. A greater density of shadow would be obtained if a suspension of the complex were used. Before barium sulphate replaced insoluble bismuth salts as a diagnostic aid in gastro-enterology, bismuth subcarbonate was administered in suspension in doses of 50 g.

Intravenous injection of the bismuth complex was

unsatisfactory for urography. This is again due to the relatively low solubility of the compound and the low concentration and dose that can be injected. Lead calcium EDTA also failed in this respect presumably for the same reason. On the other hand the very soluble lead sodium EDTA proved satisfactory for intravenous urography. The bismuth complex produced marked changes in the heart action, but recovery occurred even when the kymographic and electrocardiographic records suggested profound changes in myocardial activity. The myocardial changes may be due to altered (intracellular) electrolyte ratio as suggested for lead EDTA complex.[2, 3] They are presumably not due to the action of bismuth, which is apparently firmly chelated and unionized in the EDTA complex. It is interesting for comparison that intravenous injection of the usual soluble bismuth preparations leads to dangerous and even fatal (flocculation) shock due to the formation of insoluble compounds. The fall of blood pressure produced by such soluble bismuth salts generally recovers promptly; it is chiefly cardiac, due to disturbed conduction and heart block.[5] The kidneys, liver and other organs may also be affected by these soluble bismuth salts. Such effects have not been studied as far as bismuth EDTA complex is concerned.

SUMMARY

Bismuth EDTA complex in 2.5% solution gives a shadow of the stomach and intestines. A larger dose must be administered than with the more soluble lead complexes and the shadow is not so dense. By intravenous injection it is not satisfactory for urography. It produces depression of the heart and striking electrocardiographic changes, from which recovery occurs.

The bismuth complex was supplied as 'Sequestrol-bismuth complex NA' by the Geigy Company Ltd., Rhodes, Middleton, Manchester, to whom grateful acknowledgment is made. Expenses were partly defrayed by a grant from the C. L. Herman Research Fund. Mr. J. W. Bates assisted in the investigation. Dr. B. Isaacson recorded the electrocardiograms.

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