

tion as long as 11 weeks after implantation the cellophane was readily located encapsulated in a thin membranous envelope; it showed no evidence of disintegration or resorption. Lowry⁸ reported a tendency of certain cellophane films which he studied to be absorbed. In the studies of Oppenheimer *et al.*⁹ the regenerated cellulose which they implanted was unabsorbed over a period of 11 months or more.⁹

In addition to the gross observations which are recorded here, specimens of the implant areas were fixed and submitted for histologic examination; the results of the histologic readings will be reported in detail in another paper. Since the properties of water insoluble gelatin film suggested that it might have clinical utility wherever an absorbable membrane is indicated, this possibility is being independently investigated in several surgical research laboratories.

⁸ Lowry, M. L., *Arch. Surg.*, 1946, **52**, 160.

⁹ Oppenheimer, B. S., personal communication, November 1948.

Summary. The preparation and properties of gelatin films, which resisted water solution in varying degrees, have been described.

These films, although water insoluble, have been shown to be digested in different lengths of time when subjected to proteolytic enzymes *in vitro* in a standardized assay.

Some of the altered gelatin films were implanted into muscle areas of albino rats. Upon visual inspection they were found to be absorbed at the recorded intervals, with no evidence of untoward tissue reaction. The data indicate that the biologic absorption time can be roughly predicted from *in vitro* digestion results; as the *in vitro* times become greatly prolonged, however, a comparable resistance to biologic absorption is not seen.

Cellophane implants were not absorbed but at the eleventh week were encapsulated in a thin membranous capsule.

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17109. Sodium Acetate as a Source of Fixed Base.*

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Recent studies have shown that acetic acid is an extremely rapidly oxidized product of the intermediary metabolism of both carbohydrate and fat.¹ From the large turnover of acetate in the normal metabolic processes of the body, it is obvious that sodium acetate should serve as a rapidly available source of fixed base. Using the change of serum CO₂ content as an index of the presumptive rate of oxidation of the acetate ion, studies were performed in dogs and in man to define the usefulness of sodium acetate as a source of fixed base.

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¹ Bloch, K., *Physiol. Rev.*, 1947, **27**, 574.

Procedure and results. Dogs, anesthetized with pentobarbital, were infused intravenously with a solution of 1/6 molar sodium acetate, the total amount administered being 15 mEq per kg of body weight. Blood specimens were taken under oil at intervals of 15 minutes or longer, and serum CO₂ was determined by the manometric method of van Slyke. Studies on 8 dogs yielded uniform results and showed a rapid rise in CO₂ content. The observations from 5 experiments with similar rates of infusion are given in Table I. Within 15 minutes after starting the sodium acetate infusion the Serum CO₂ showed a prompt elevation and continued to rise during the infusion, leveling off in the afterperiod without further significant change. Infusion of the same

TABLE I.
Effect of Sodium Acetate Infusion on Serum CO₂ Content in the Dog.

Dog	A	B	C	D	E	Avg
Duration of infusion (min.)	75	75	55	65	60	66
Time after starting infusion (min.)	Serum CO ₂ volumes %					
0	51.5	51.0	53.7	56.2	52.4	53.0
15	60.4	62.4	64.8	68.7	64.1	64.1
30	74.1	75.0	82.0	80.2	75.6	79.4
60	88.8	89.3	92.6	99.8	99.2	93.9
120	97.0	97.1	100.2	105.8	102.2	100.5
180	97.0	98.1	104.1	107.4	102.1	101.7
240	—	98.8	104.0	106.8	102.0	102.9

quantity of sodium acetate twice as quickly promoted a rise which was less marked, thus suggesting that the renal threshold for acetate had been exceeded. Because of the reported vasodilator action of acetate,² blood pressures and electrocardiograms were taken, but no changes or abnormalities were noted with the doses employed.

Solutions of 1/6 molar sodium acetate were prepared and autoclaved in the routine manner for use in patients. Normal adult subjects and patients with renal acidosis were studied in the fasting state. Infusions of 1 liter were given within a one hour period. The average dosage, uncorrected for differences in weight of patients, was 2.8 mEq per kg of body weight, approximately one-fifth of the amount given per kg to the dogs. No attempt was made to define the upper limit of tolerance in human subjects. The amounts used satisfy reasonable clinical requirements. Blood pressures and pulse rates were determined at frequent intervals and no significant changes were noted, nor were any subjective symptoms or other evidence of toxicity observed. The results of the serum analyses are shown in Fig. 1. The rapid rise of serum CO₂ was evident within 15 minutes and the rise continued progressively. Except in 2 subjects, there was no further increase in serum CO₂ after termination of the infusion. The data have been presented without correction for body weight, body water or renal excretion, and although small variations could be accounted for by these factors, it is evident that acetate is rapidly metabolized with the re-

lease of fixed base. Three subjects were given one liter of 1/6 molar sodium bicarbonate in one hour as a control study. As seen in Fig. 1, the rate of increase in serum CO₂ content was essentially the same for the sodium bicarbonate infusion as it was for the sodium acetate, indicating, within the limits of the methodology employed, that there was an almost instantaneous utilization of the acetate. In 3 patients the urine became sharply alkaline fol-

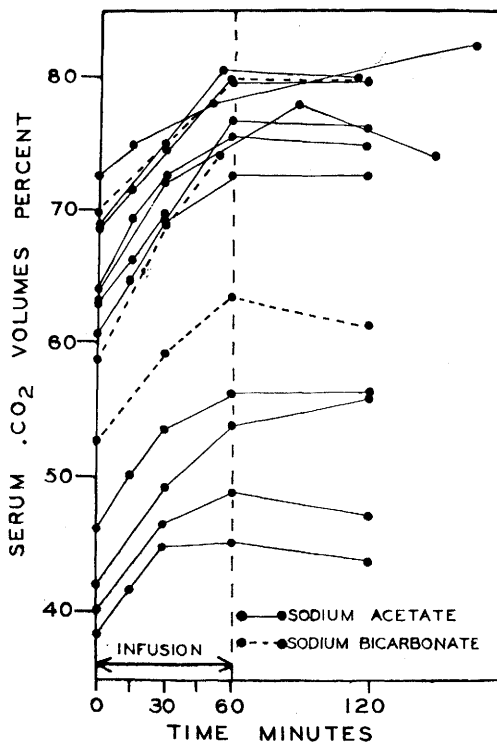


Fig. 1.

Comparison of effect of sodium acetate and sodium bicarbonate infusions on serum CO₂ content in man.

² Bauer, W., and Richards, D. W., Jr., *J. Physiol.*, 1928, **66**, 371.

lowing the infusion of the sodium acetate.

Discussion. Sodium acetate affords a readily procurable and inexpensive source of fixed base, as rapidly and as completely available as sodium bicarbonate. Solutions are easily prepared, easily sterilized, and indefinitely stable. The pH of 5 different lots of sodium acetate made up in 1/6 molar concentration was found to vary from 7.6 to 8.0. We believe that the use of sodium acetate solutions is indicated in rapid parenteral alkalization and should be useful in the therapy of most types of metabolic acidosis. However, we wish to emphasize that because the metabolism of acetate has not been specifically defined as to its possible effect on ketone body production in diabetic acidosis, we have not used it to date in this condition.

These studies have not revealed previously

undescribed properties of sodium acetate. Indeed the salt has been recommended in standard textbooks^{3,4} as a source of fixed base, but its clinical use has been limited. The present observations demonstrate the rapid catabolism of acetate and emphasize certain practical advantages which it possesses for clinical use.

Summary. Studies in dogs and in man demonstrate that sodium acetate is an easily prepared and a rapidly available non-toxic source of fixed base suitable for parenteral administration when alkalization is indicated.

³ Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics*, The Macmillan Company, New York, 1941.

⁴ Sollmann, T., *A Manual of Pharmacology*, W. B. Saunders Company, Philadelphia, 1948.

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17110. A Method for Assay of Serum Proteolytic Activity.*

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That blood contains an inactive precursor (plasminogen) which can be activated to form a proteolytic enzyme (plasmin) has been established.¹⁻⁷ Study of variations in this enzyme have largely been on the basis of its fibrinolytic properties. Using a method of

preparation outlined by Milstone,⁶ we have been able to obtain from serum a plasminogen-containing fraction with consistent and reproducible activation in humans and dogs.

Reagents and Materials. 1. *Streptokinase*—the filtrate of a 24-hour culture of Group A, Type 11, Beta hemolytic streptococci, grown in beef heart infusion broth with 0.05% added dextrose.

2. *Protamine Sulphate*[§]—a solution of protamine sulphate in veronal buffer, 2 mg per ml.

3. *Veronal Buffer*—pH 7.35⁸

4. *Acetic acid—distilled water mixture*—19 volumes of distilled water plus 0.32 volumes of 1% acetic acid.

⁷ Ferguson, J. H., Travis, B. L., and Gerheim, O. B., *Proc. Soc. Exp. Biol. and Med.*, 1947, **64**, 285.

[§] Eli Lilly and Company, Indianapolis, Ind.

⁸ Clark, D. G. C., Clifton, E. E., and Newton, B. L., *Proc. Soc. Exp. Biol. and Med.*, 1948, **69**, 276.

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[‡] Senior Fellow, American Cancer Society, as recommended by the Committee on Growth of the National Research Council.

¹ Christensen, L. R., and MacLeod, C. M., *J. Gen. Physiol.*, 1945, **28**, 559.

² Christensen, L. R., *J. Gen. Physiol.*, 1946, **30**, 149.

³ Ratnoff, O. D., *J. Exp. Med.*, 1948, **88**, 401.

⁴ Delezenne, C., and Pozerski, E., *Compt. rend. Soc. Biol.*, 1903, **55**, 690.

⁵ Kaplan, M. H., Tagnon, J. H., Davidson, C. S., and Taylor, F. H. L., *J. Clin. Invest.*, 1942, **21**, 533.

⁶ Milstone, H. J., *J. Immunol.*, 1941, **42**, 109.