metic stimulant, urecholine. 2. In an effort to explain these phenomena, 3 possible modes of action of the antihistaminics present themselves: (1) a specific (antihistaminic) effect, (2) an atropine effect, (3) a local anesthetic effect. The evidence presently available does not as yet permit of any preference among these several hypotheses.

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Efficiency of Intestinal Absorption of Vitamin B_{12} Measured by Hepatic Uptake of $Co^{60}B_{12}$.* (23208)

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In an earlier work(1) we studied the intestinal absorption of vit. B_{12} by means of measurement of hepatic uptake of $Co^{60}B_{12}$ (2). Booth and Mollin had compared this method with measurement of fecal excretion of $Co^{60}B_{12}$ and showed that hepatic uptake of radioactive B_{12} a week after oral administration is proportional to amount of B_{12} absorbed in the intestine(3). We have also expressed the efficiency of intestinal absorption of vit. B_{12} in terms of parenteral equivalents (1), by repeating measurement of hepatic uptake in the same individual after oral and parenteral administration of similar doses of $Co^{60}B_{12}$. Pollycove and Apt(4) demonstrated that the determination of efficiency of intestinal absorption of B_{12} by this method gives results similar to those obtained by measurement of fecal excretion of $Co^{60}B_{12}$. The present investigation was undertaken to add more information on the efficiency of intestinal absorption of vit. B_{12} under various pathological conditions, by this technic.

Method. Hepatic uptake of $Co^{60}B_{12}$ was measured by a previously described method (2) on 31 patients with a variety of diseases, and a total of 112 individual tests were made. The determinations were done 6-7 days following a) oral administration of tracer dose of 0.5 μg $Co^{60}B_{12}$ containing 0.35 resp. 0.50 μc Co^{60}†, b) same dose of $Co^{60}B_{12}$ together with potent intrinsic factor preparation‡, c) same dose of $Co^{60}B_{12}$ intramuscularly. Each of these 3 tests was done on the same patient at intervals of 10-14 days. This is the time interval at which a plateau of hepatic counts appears(2-6). This leveling off of radioactivity over the liver makes it possible to use final radioactivity counts in one test as a base line for the next. As many as 4-6 individual tests were done on 12 patients. Efficiency of intestinal absorption of B_{12} was calculated in terms of parenteral equivalents according to the formula:

$$\text{Parenteral equivalent of intestinal absorption (in \%)} = \frac{\text{Hepatic uptake on oral admin.}}{\text{Hepatic uptake on parenteral admin.}} \times 100.$$

The cases included 7 patients with pernicious anemia, 4 with sprue, 3 with macrocytic

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‡ Supplied through the courtesy of Dr. K. W. Thompson of Organon, Inc., Orange, N. J. The preparation used (#5333) did not contain any appreciable amount of B_{12} on microbiological assay and was used at dose of 62 mg, equivalent to dose contained in 2 USP units of oral anti-anemia preparation.

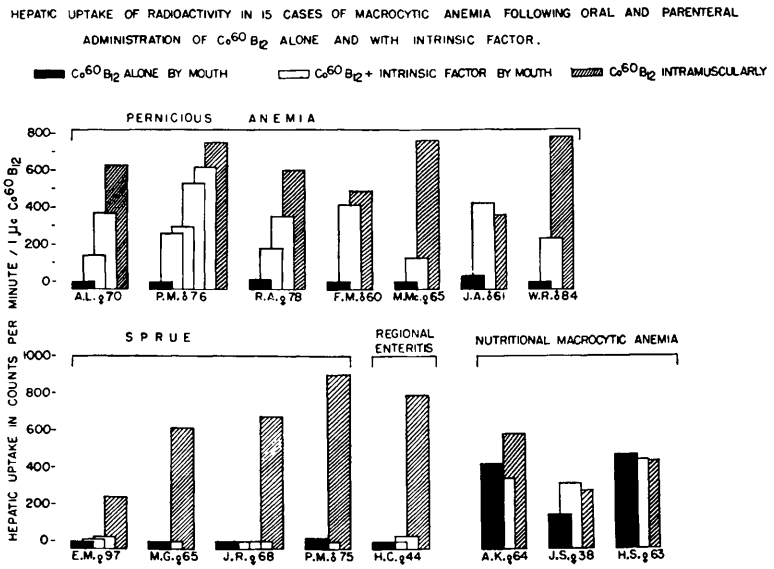

FIG. 1. Hepatic uptake of radioactivity in 15 cases of macrocytic anemia following oral and parenteral administration of $Co^{60}B_{12}$ alone and with intrinsic factor.

non-pernicious anemia, 3 patients following total, and 3 following subtotal gastrectomy, 3 with hepatitis, 2 patients with histamine-fast anacidity, 2 with cirrhosis of the liver, 1 with regional enteritis, and 3 normal controls. The hepatic uptake in 3 cases of total and 1 case of subtotal gastrectomy was counted at a higher voltage with somewhat different equipment. This accounts for relatively higher counts than that obtained in the remaining cases.

Results. These are shown in Fig. 1 and 2. The efficiency of intestinal absorption of $Co^{60}B_{12}$ in various patients, as calculated in parenteral equivalents of absorption, ranged from 0 to 113%. No absorption was noted in 5 out of 7 cases of pernicious anemia, in 3 out of 4 cases of sprue, in the 3 cases of total gastrectomy, and in one case of regional enteritis. It was only 3% and 10% each in the 2 remaining cases of pernicious anemia in remission, and 2% in the remaining case of sprue. No hepatic uptake was noted in a case of hepatic cirrhosis with hepatic insufficiency, studied a few days before death, whereas it had been normal 2 weeks before. In the other cirrhosis case, in one case of hepatitis, and in one case of histamine-fast anacidity without other symptoms, the efficiency of intestinal absorption was 24-38%, *i.e.* below the lower limits of normal, which is about 40% at a dose of 0.5 μg B_{12} orally administered(6). Efficiency of B_{12} absorption was within normal range (40-109%) in the 3 cases of subtotal gastrectomy, in the 3 cases of macrocytic non-pernicious nutritional and hemolytic anemia, in 2 of the 3 cases of hepatitis, in one of the 2 cases of histamine-fast anacidity, and in the 3 control cases.

Addition of intrinsic factor preparation markedly raised efficiency of intestinal absorption of B_{12} in all 7 instances of pernicious anemia (from 0-14% to 16-113%), and also raised it in the 3 cases of subtotal gastrectomy, in one of the 3 cases of histamine-fast anacidity, in one of 3 cases of cirrhosis, and in one case of the macrocytic non-pernicious anemia (Fig. 1 and 2). The intrinsic factor had no effect upon B_{12} absorption in the 3 cases of sprue, and the effect was only very slight in the case of the one other sprue patient. Only in one case of hepatitis and in one control, did we note a marked inhibitory effect by the intrinsic factor preparation used upon efficiency of intestinal B_{12} absorption. In these 2 cases B_{12} absorption decreased from 63-80% and 47% respectively to 9% in both instances.

Comment. It is not known whether the same percentage of B_{12} is deposited in the

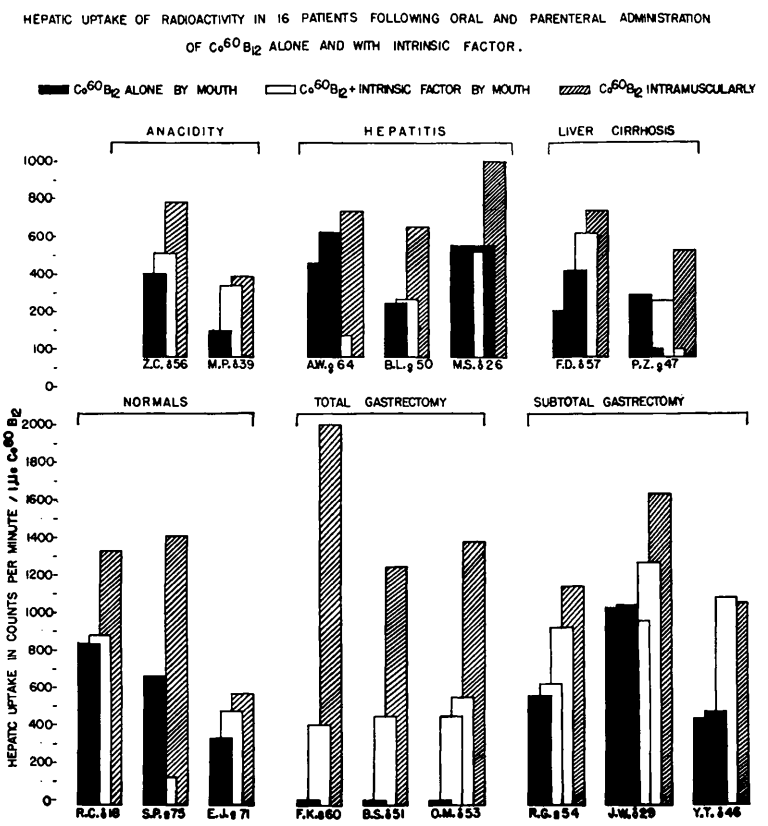

FIG. 2. Hepatic uptake of radioactivity in 16 patients following oral and parenteral administration of $Co^{60}B_{12}$ alone and with intrinsic factor.

liver when given intramuscularly, as when absorbed upon oral administration. The method used in this study, therefore, does not quantitate the intestinal absorption of vit. B_{12}, but provides a way to express the efficiency of absorption of B_{12} in terms of parenteral equivalents of intestinal absorption. It supplies comparable values which agree very well(4) with the figures derived from the method of measuring fecal excretion of Co^{60} B_{12}. This agreement is due to the fact that a) the hepatic deposition of B_{12} at the end of the first week is proportional to the amount of B_{12} absorbed in the intestine(3) and to the dose injected intramuscularly(7-8); b) if the i.m. administered dose of vit. B_{12} is small, as was the case in these studies, B_{12} is completely absorbed within a few hours at the site of injection(7-8) and will be excreted in the urine only in traces(9); c) the pattern of hepatic deposition of vit. B_{12} after oral (2-5) and parenteral administration(7-8) is similar and shows a slow rise, which comes to a peak at the end of the first week. It levels off thereafter. Proportionately, more B_{12} is deposited, however, in the kidneys after parenteral injection(15) than is the case after oral intake(10). Following oral administration, therefore, the distribution of B_{12} in the body favors the liver more than when B_{12} is injected, which would cause higher values of parenteral equivalents of intestinal absorption. This, in turn, would indicate somewhat higher efficiency of intestinal absorption than is really the case.

Our actual data on the abolished intestinal absorption of vit. B_{12} in pernicious anemia, sprue, and after total gastrectomy, correction of this defect by intrinsic factor preparation, and the lack of effect of intrinsic factor upon B_{12} absorption in sprue, are in line with our previous observations obtained by measurement of hepatic uptake of $Co^{60}B_{12}$ after its oral administration only(2,11-13). Efficiency

of intestinal absorption of B_{12}, calculated in terms of parenteral equivalents, is more suitable for comparison than figures of hepatic uptake of B_{12} obtained in various individuals. The shape, size and position of the liver and the crystal of the scintillation counter influence the hepatic count. Calculation of efficiency of intestinal absorption of B_{12} in terms of parenteral equivalents disposes of these technically interfering elements. For clinical purposes, however, such as differentiation of macrocytic anemias, or detection of asymptomatic forms of pernicious anemia or sprue, calculation of parenteral equivalents of intestinal absorption has no advantages. Here the simplified, 48-hour technic of measuring hepatic uptake of radioactivity following oral administration of $Co^{60}B_{12}$, alone or with intrinsic factor, is entirely adequate and satisfactory(14).

Summary and conclusions. Hepatic uptake of radioactivity following oral administration of a tracer dose of $Co^{60}B_{12}$ alone and with intrinsic factor preparation was compared with that after intramuscular injection of the same dose of $Co^{60}B_{12}$ on 31 individuals with various diseases. Efficiency of intestinal absorption and effect of intrinsic factor preparation was quantitated in this way and was expressed in terms of parenteral equivalents of intestinal absorption.

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Effect of *H. pertussis* on Sensitivity of Mice to Serotonin. (23209)

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It is well known that injection of *Hemophilus pertussis* cells to mice of certain strains produces a marked increase in histamine sensitivity(1,2,3) as well as an increase in ability of mice to become anaphylactically sensitive (4,5). Since histamine plays an important role in anaphylaxis of guinea pigs and other animals as well as man(6), it was tempting to conclude that pertussis increased susceptibility of mice to anaphylaxis mainly by increasing their susceptibility to histamine(7). This, however, does not explain why some strains do not become sensitive to histamine after pertussis injection(3,11) while becoming highly susceptible to anaphylaxis(11). Moreover, the state of histamine hypersensitivity in susceptible strains disappears much sooner than that of anaphylactic sensitivity.