

Atropine appears to be definitely limited in its ability to inhibit normal propulsion as shown by the fact that a subcutaneous dose of 2 mg/kg is apparently as effective as 16 times that dose. The results suggest that higher doses of atropine introduce a factor which opposes peripheral inhibition of propulsion. An exaggeration of this phenomenon could be expected in the case of new synthetic agents whose actions may be less specific than those of atropine and other agents included in this report.

The insulin antipropulsion test has several advantages over the charcoal meal test for comparing activity of new antipropulsive agents. Besides economy and convenience afforded by the fact that smaller doses of drugs are required, one is much less likely to encounter unwanted side effects which may prevent a true evaluation of the antipropulsive potency. Because papaverine-like agents, in otherwise asymptomatic doses, are capable of producing pronounced inhibition of the pro-

pulsive effect of insulin, one is much less likely to overlook an important agent of this type. Finally, a comparison of the effect of the compound in both tests may be very informative.

Summary. A new intestinal antipropulsive test in intact insulin-treated rat is described. The insulin test provides certain advantages over the commonly-used charcoal meal test for screening of synthetic antispasmodic or antipropulsive agents. The use of both tests permits determination of the effect of the agent on both normal and hyperactive states of intestinal muscle and provides information relative to the mechanism of action of the agent. The specificity and some limitations of the test are discussed.

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Glomerular Filtration Rate and Renal Plasma Flow in Cholera and Acute Gastroenteritis. (23046)

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Cholera is characterized by acute purging and vomiting leading to marked dehydration of body and acute depletion of plasma volume. The renal plasma flow is likely to be interfered with and either transitory or permanent damage to kidney might be possible. Death is mostly due to development of anuria which indicates failure of function of the kidney. Hence assessment of kidney functions is of importance to predict prognosis, to learn progress of the disease and to suggest treatment. Anuria is invariably present but not so in conditions of acute gastroenteritis, though clinical features resemble each other closely. Whether the hemodynamic factors in the formation of urine are altered in the above 2 conditions, either due to effect of specific toxins or to depletion of plasma vol-

ume, remains to be elucidated. In the present investigation glomerular filtration rate and renal plasma flow were determined in patients suffering from cholera and acute gastroenteritis. The same studies were also carried out in normal persons for comparison.

Methods. Selection of cases. All patients suffering from cholera and gastroenteritis admitted into the Nilratan Sircar Medical College Hospitals, with clinical features of acute purging, vomiting and showing signs of dehydration were selected. As soon as patients were admitted, their dehydration was corrected by transfusion of hypertonic saline followed by normal saline with sodium bicarbonate or hypertonic glucose (25%) with calcium gluconate and ascorbic acid. Patients whose stool on culture did not show *vibrio*

cholerae were taken to be cases suffering from acute gastroenteritis. When dehydration was controlled, there was improvement in clinical condition and normal urination was established 2 to 13 days from onset of the disease, glomerular filtration rate and renal plasma flow were determined by inulin and para-amino hippuric acid clearance tests respectively. Patients admitted into the surgical ward with fracture of long bones, hernia, hydrocele, gun shot injury of limbs, etc., when recovered and fit to be discharged were selected as normal subjects for determination of inulin and para-amino hippuric acid (PAHA) clearance tests. These patients came from the same strata of society as those suffering from cholera and acute gastroenteritis. *Inulin and PAHA clearance tests.* For measurement of glomerular filtration rate, inulin and for measurement of renal plasma flow PAHA, were used as test substances. Subjects drank 40 oz water, one hour before the test, in the morning after breakfast. A sterile rubber catheter was passed and retained to drain the urinary bladder continuously. The bladder was evacuated continuously and a portion of urine kept to be used as blank. 5 cc blood was withdrawn from the antecubital vein and through the same needle 30 cc freshly prepared 10% inulin in normal saline mixed with 4 cc 20% PAHA dissolved in normal sodium hydroxide were introduced, and the time when the injection was completed was noted. The needle was then fitted to a transfusion set and 250 cc of .9% sodium chloride containing 35 cc of 10% inulin and 10 cc of 20% PAHA, were introduced at 4 cc/minute. At intervals of 30, 50 and 90 minutes after injection, 5 cc blood samples were withdrawn from the antecubital vein of the other arm. Urine samples which accumulated during each experimental period were also separately collected and every time the bladder was washed with 20 cc saline followed by injection of air. The washings were mixed with urine and total volume of urine collected during each experimental period noted. After collection of final sample of blood and urine, the catheter and injection needle were removed. Blood samples were collected in vials

TABLE I. Inulin and PAHA Clearance Values in Normal Subjects and in Patients Suffering from Cholera.

Subjects	Inulin clearance (glomerular filtration rate), cc/min.	PAHA clearance (renal plasma flow), cc/min.
Cholera (14)	60 $\pm$ 12*	272 $\pm$ 46
Normal (19)	114 $\pm$ 8	517 $\pm$ 46
Diff. of means	54	245
Stand. error of diff.	14.07	62.44
<i>t</i>	3.8	3.9

* Mean $\pm$ stand. error.

Figures in parentheses indicate No. of subjects.

TABLE II. Inulin and PAHA Clearance Values in 6 Patients Suffering from Acute Gastroenteritis.

Inulin clearance, cc/min.	PAHA clearance, cc/min.
41 $\pm$ 16	193 $\pm$ 64

containing a mixture of ammonium and potassium oxalate crystals. Some subjects had shivering during the transfusion. Inulin was estimated by the method of Roe(1) and PAHA by the method of Bratton and Marshall(2). From total amount of inulin and PAHA excreted in the urine samples, collected between 30 and 50 minutes and between 50 and 70 minutes after injection of these solutions, amounts of these substances excreted in urine/minute were calculated. From plasma concentration of inulin and PAHA, volume of blood plasma cleared of these substances in urine in one minute was calculated. The results are given in Tables I and II.

Results. Inulin clearance (glomerular filtration rate) was 114 cc/minute in normal subjects, 60 cc in cholera patients and 41 cc in patients suffering from acute gastroenteritis. PAHA clearance (renal plasma flow) was 517 cc/minute in normal subjects, 272 in cholera patients and 193 cc in patients suffering from acute gastroenteritis.

Discussion. In patients suffering from cholera and acute gastroenteritis both the values for glomerular filtration rate and renal plasma flow were diminished and the differences were statistically significant. From postmortem studies on kidney of patients who died of shock, Bywaters and Dible(3) reported pallor of cortex and congestion of

medulla. They could not account for such changes in the kidney. Trueta *et al.*(4) ascribed this interference of blood flow to persistent arterial spasm demonstrated experimentally to accompany shock. Tomb(5) was of the opinion that anuria and renal damage in shock were due to anoxia of the kidney. De and Sen Gupta(6) demonstrated evidence of cortico-medullary diversion of blood flow in the kidneys, in shock associated with various surgical and obstetrical conditions and in cholera. All patients suffering from cholera, who were investigated, survived and became normal. This excluded any possibility of permanent parenchymatous lesion in kidneys. Therefore in conditions like cholera where acute purging and vomiting results in circulatory deficiency, the cortico-medullary diversion of blood flow might take place. The diminished circulatory blood volume in acute stage of cholera might produce anoxia resulting in renal cortical vasospasm and diversion of blood flow through the medulla. The low figures obtained in clearance values are the result of diminished blood flow. This state of circulation persists for a number of days, even after correction of circulatory deficiency. If renal anoxia is of short duration, so as not to cause permanent damage to the kidney, normal circulation is gradually established with the onset of diuresis. It has, however, been shown that no change in oxygen content of whole blood of cholera patients takes place(7).

The clearance values obtained in patients suffering from acute gastroenteritis were similar to those of cholera cases. These observa-

tions are likely to exclude the possibility of any specific toxin acting on the kidney.

Summary. Glomerular filtration rate and renal plasma flow were determined by inulin and para-amino hippuric acid clearance tests in 19 normal subjects, in 14 cholera patients and in 6 patients suffering from acute gastroenteritis. In patients suffering from cholera and acute gastroenteritis, glomerular filtration rate and renal plasma flow were greatly diminished to the same degree, when these patients had apparently normal urination after transfusion of saline. The diminished clearance values might be due to renal anoxia causing temporary diminution in blood flow through the cortex of the kidney and not due to any specific toxins of the disease.

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