tance to the drug *in vitro*, but were nevertheless reduced in number. Strains of *Ps. aeruginosa* and *B. proteus* which are sensitive *in vitro* to aureomycin can be eliminated from urine infected with these organisms. In all patients who were cured treatment was continued for 2 or 3 days after the urine was first found to be sterile, because in one patient not listed, on whom the drug was discontinued as soon as the urine became sterile, recurrence took place within 2 days.

Summary. 1. Aureomycin is highly effective against many strains of gram-negative bacilli *in vitro*, including many which were found to be resistant to sulfonamides, penicillin, and streptomycin. The sensitivity of various strains of a given species, however, varies greatly.

2. Clinical trial in 10 patients with urinary infections which were refractory to previous treatment with other antibiotics, resulted in a clinical cure of all ten patients. Bacteriologically eight patients were cured, and 2 were markedly improved.

16963

Effects of a Quaternary Amine* Capable of Blocking Functions of the Autonomic Nervous System.

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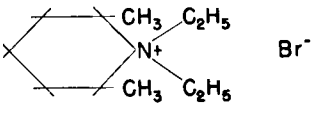
Much interest has been directed in recent years to functions of the autonomic nervous system, and to effects of drugs which interfere with activation of adrenergic or cholinergic end organs or with cholinergic synaptic transmission in autonomic ganglia. Acheson and Moe[1] and Lyons[2] have reported effects of the tetraethylammonium ion (TEABr) in the experimental animal and in man, and have shown that it blocks cholinergic transmission at autonomic ganglia and does not prevent activation of adrenergic end organs.

2, 6 dimethyl diethyl piperidinium bromide (SC 1950), a quaternary amine (Fig. 1), has been synthesized and studied by I. C. Winter and associates.[3] They found that this drug was 7 times as potent as TEABr in blocking transmission through the superior cervical ganglion of the cat and 5 times as potent as TEABr in producing block of transmission through the ganglion of the pelvic nerve which supplies the urinary bladder of the dog. It had little spasmolytic action on excised intestine, but in anesthetized and unanesthetized dogs following a preliminary contraction it generally reduced intestinal tone and contractility. Intravenous injection in anesthetized dogs produced a decrease of blood pressure. They also noted that large doses (20-25 mg/kg) in unanesthetized animals produced a flaccid paralysis and respiratory death resembling that caused by curare.

Experiments were undertaken to investigate effects of this drug upon the circula-



2,6 dimethyl diethyl piperidinium bromide

FIG. 1.

* Drug number SC 1950 furnished by the Research Laboratories of G. D. Searle and Co. Aided by a grant from G. D. Searle and Co.

† U. S. Public Health Service Research Fellow in Surgery.

1 Acheson, G. H., and Moe, G. K., *J. Pharm. and Exp. Therap.*, 1946, **87**, 220.

2 Lyons, R. H., Moe, G. K., Neligh, R. B., Hoobler, S. W., Campbell, K. N., Berry, R. L., and Rennick, B. R., *Am. J. Med. Sc.*, 1947, **213**, 315.

3 Personal communication from Dr. I. C. Winter of the Research Laboratories of G. D. Searle and Company.

tory system and gastrointestinal tract of dogs and of man.

I. Action of SC 1950 in the dog. A. Effect on the circulatory system. Pulse rate, blood pressure, vasomotor reflexes, and response to epinephrine and neostigmine were determined in seven dogs weighing 9-16 kg. Each was anesthetized using intravenous chloralose, 0.1 g/kg. A tracheal cannula was inserted, the carotid arteries were isolated, and the vagi were divided. A left lumbar sympathectomy was performed transperitoneally. The right femoral artery was cannulated proximally and distally. The left was ligated proximally and cannulated distally. This permitted recording of 3 blood pressures using a mercury manometer connected to the proximal cannula for systemic blood pressure and 2 others connected to the distal segments for back pressure from the 2 femoral arteries. Respirations were measured by a pneumograph connected to a recording tambour.

After preparation of each animal standard tests of the circulation were employed. Carotid sinus reflexes were elicited by occlusion of both common carotid arteries using bulldog clamps applied for one minute. Peripheral vagal stimulation was accomplished using for 15 seconds a tetanizing current from a Harvard inductorium set at 7 or 8 cm. For central vagal stimulation a tetanizing current was also used for 15 seconds but the setting of the inductorium was reduced to 6 or 7 cm. Anoxia was produced by administering 7% oxygen and 93% helium for a period of 3 to 5 minutes without permitting rebreathing. Epinephrine was injected as a 1:10,000 solution through a venous cannula. Neostigmine methylsulfate, 0.5 to 1.0 mg, was also given intravenously. After preparation of the dog and performance of standard tests SC 1950 was injected intravenously in doses of 0.5 to 20 mg/kg. Tests were then repeated, contrasting results after drug with those before. Usually the drug was again administered several times using larger amounts and repeating tests before and after each injection. Three of the 7 dogs received small amounts (0.02 to 1.0 mg/kg) in repeated doses. Four received 5 to 20 mg/kg at each injection, an amount apparently necessary for constant therapeutic effects.

(1) *Effect on blood pressure and pulse.* Initial mean systolic blood pressure of anesthetized animals varied from 80 to 120 mm Hg. With 3 exceptions initial and subsequent doses of SC 1950 in amounts varying from 0.05 mg/kg to 20 mg/kg reduced pressure. The 3 exceptions occurred when blood pressure had been reduced by previous injections. Transient increases of pressure then occurred ranging from 6 to 34 mm Hg and lasting less than 2½ minutes. Other than for these three exceptions SC 1950 promptly reduced pressure. With doses ranging from 0.05 to 1.0 mg/kg reductions of blood pressure were moderate and transient, lasting 2 to 5 minutes. As dose was increased depression of blood pressure became more pronounced and duration of the period of depression lengthened. Following doses of 5 to 20 mg/kg blood pressure was reduced to ½ or 1/3 the level before injection and depression persisted for 25 to 50 minutes. A representative effect is shown in Fig. 2. After long periods of anesthesia and after several doses of SC 1950, blood pressure gradually declined and did not return to its initial level between injections.

Effect on cardiac rate also varied with amount of drug injected. Small doses (0.02 to 1.0 mg/kg) produced no change. Larger doses (5 to 20 mg/kg) caused slowing of heart rate which persisted as long as did depression of blood pressure. Before larger doses of SC 1950 pulse rates varied from 104 to 208, averaging 159. Following 5 to 20 mg/kg, pulse rates fell to from 56 to 132, averaging 93.

(2) *Effect of SC 1950 on vascular reflexes.* In the 4 animals receiving larger amounts of SC 1950 the rise of blood pressure normally occurring in response to occlusion of the carotid arteries was uniformly prevented. This response was completely abolished in each of 10 test periods following injections of 5 mg/kg or more. (Fig. 2) Stimulation of the proximal end of the divided right vagus normally produced marked increase of blood pressure and cessation of respiration (Fig. 2).

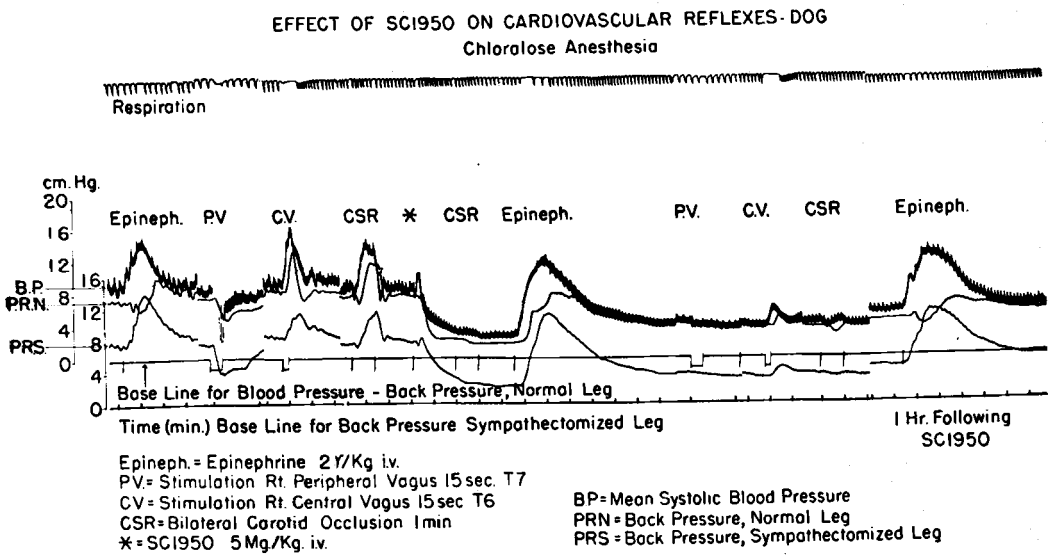


FIG. 2.

Systemic blood pressure and back pressures in normal and sympathectomized extremities (see text) are shown in response to epinephrine, peripheral and central vagal stimulation, and bilateral carotid occlusion, before and after 5.0 mg/kg SC 1950.

After 5 mg or more of SC 1950 the increase of blood pressure was blocked during all tests on 3 dogs. In the fourth dog this response was reduced but not abolished following 5 mg/kg and again following 10 mg/kg 2 hours later. Normally stimulation of the distal end of the divided right vagus effected cardiac slowing or arrest and fall of blood pressure. In 3 animals after SC 1950, 5 to 20 mg/kg, this response was completely blocked, heart rate continuing unchanged during vagal stimulation. In a fourth 5 mg/kg reduced but did not prevent cardiac slowing. Ten mg/kg 90 minutes later, however, prevented slowing. Anoxia produced an elevation of blood pressure of 20 mm Hg before the drug in only one of these 4 animals. After the drug this response did not occur. It is of interest that following removal of the gas an overshoot of blood pressure occurred once before and once after the drug. In the 3 dogs remaining small amounts of SC 1950 (0.02 to 1.0 mg/kg) did not block reflexes.

Blood pressure measured in the distal ends of the divided femoral arteries, representing "back pressure" or, indirectly, peripheral resistance, was lower in the sympathectomized extremity and responded slowly or passively in this limb during reflexes before the drug. Following SC 1950 peripheral or back pressure in the normal extremity decreased to equal that in the sympathectomized limb, and responses to cardiovascular reflexes were equally slow and passive.

(3) *Effect on response of blood pressure to intravenous epinephrine.* Epinephrine, 2 to 4 γ/kg, injected intravenously normally produced blood pressure increases ranging from 30 to 56 mm Hg following which the pressure returned to preinjection levels in two minutes or less. Following administration of SC 1950, 5 to 10 mg/kg, and during the associated reduction of systemic blood pressure, pressor responses to equal doses of epinephrine increased, reaching 46 to 168 mm Hg, a response 2 to 4 times as great as that before SC 1950 (Fig. 2). The duration of the pressor response also increased, ranging from 3.5 to 7.0 minutes following SC 1950 as compared with 2 minutes or less prior to the drug. Even after systemic blood pressure had returned to normal levels a half hour or more after injections of SC 1950, increased and prolonged responses to epinephrine occurred. Before SC 1950 back pressure of the normal leg decreased immediately following intravenous epinephrine and then increased. Initial decreases did not occur in the sympa-

thectomized leg. After the drug such initial decreases no longer occurred in the normal leg. The maximum increase of back pressure or "peripheral resistance" occurring after epinephrine was not as great in the normal extremity as in the sympathectomized extremity either before or after SC 1950.

(4) *Reversal of SC 1950 by neostigmine.* In 4 instances 0.5 to 1.0 mg neostigmine methylsulfate was administered intravenously after doses of 5 to 20 mg/kg SC 1950 had produced the above described reduction of blood pressure and block of reflexes. In each instance blood pressure rose promptly to levels near those before SC 1950, and the vascular reflexes again became active after neostigmine.

(5) *Effect on response to increased intracranial pressure.* Increase of intracranial pressure was effected by injection of saline into the skull through a trocar in 4 dogs anesthetized with chloralose. Intracranial pressure was kept greater than mean systolic blood pressure until death occurred. In normal animals[4] the terminal or agonal increase of blood pressure usually exceeds 200 mm Hg. This hypertensive response was not reduced in 3 dogs given 5 to 15 mg/kg of SC 1950, an amount adequate to block the pressor response to occlusion of the carotid arteries. The response to increased intracranial pressure was partially blocked in the fourth, receiving 15 mg/kg. The increases of blood pressure during increase of intracranial pressure after SC 1950 were respectively 58 to 218, 100 to 280, 54 to 204, and in the fourth dog 40 to 98 mm Hg.

(6) *Effect on pulse and blood pressure of unanesthetized dogs.* SC 1950, 2 to 15 mg/kg, was given intravenously to trained dogs whose blood pressure had been measured frequently by puncture of a femoral artery using a needle connected to a mercury manometer. Some of these dogs had been made hypertensive 3 months to one year previously by excision of the carotid sinuses and division of the cardio-aortic depressor nerves.[5] Others were normal animals without hypertension. Mean systolic blood pressure in the normal dogs ranged from 112 to 140 mm Hg (average 126) before the drug. In 12 tests on these normal dogs 2 to 15 mg/kg SC 1950 was injected intravenously. There were moderate increases of blood pressure in 11, blood pressures after the drug ranging between 130 and 162, the average being 147 mm Hg. Two of these dogs developed an initial rise of less than 20 mm Hg followed by a fall of pressure to below normal. One dog only had an immediate depressor response, blood pressure falling from 126 to 104 mm Hg. The moderate rise of blood pressure occurring after the drug lasted an average time of 36 minutes. All normal unanesthetized dogs developed increases of pulse rate following SC 1950, pulse rates before drug being 72 to 116 per minute, average 88, and after drug being 112 to 168, average 142 per minute.

In 11 tests on dogs made hypertensive by excision of the carotid sinuses and division of the depressor nerves, blood pressure before SC 1950 ranged from 198 to 264, average 223 mm Hg. Intravenous injection of 2 to 10 mg/kg SC 1950 consistently caused a decrease of blood pressure to levels ranging from 76 to 154, average 127. This reduction of blood pressure lasted 30 to 230 minutes, averaging 115 minutes. Pulse rates of these dogs ranged from 104 to 248, average 180 before the drug. Afterward the rate ranged from 84 to 144, average 114.

B. *Effect on the Gastrointestinal Tract.* Fluoroscopic and roentgenographic studies of the gastrointestinal tracts of 11 normal dogs were undertaken following administration of 30 g of barium sulfate in a 100 cc aqueous suspension by stomach tube. Fluoroscopy was performed immediately after administration of the barium observing gastric activity and timing the interval between administration of barium and initial emptying of the stomach. Roentgenograms were obtained 30 and 60 minutes following ingestion of barium and at hourly intervals thereafter until 6 hours had elapsed. Before the drug gastric peristalsis was active in all animals. Emptying of barium into the duodenum began in from

[4] Grimson, K. S., Wilson, H., and Phemister, D. B., *Ann. Surg.*, 1937, **106**, 801.

[5] Grimson, K. S., *Arch. Surg.*, 1941, **43**, 284.

less than one minute to slightly less than 8 minutes. Average time of initial emptying was 4.1 minutes in 11 animals. Time required for complete emptying of barium from the stomach varied markedly in a few normal animals but in most the emptying times were similar. Average amount of emptying at ½ hour was 30%, at 1 hour 46%, and at two hours 84%. Gastric emptying was complete at 3 hours in 8 of 10 dogs and at 4 hours in 9 of 10. Of 9 dogs in which observations could be made with accuracy, the first of the barium had traveled through the ileum and reached the colon at 2 hours in 3 dogs, and at 3 hours in 6 dogs.

On another day these control animals were given SC 1950 intravenously and barium sulfate by stomach tube as before 10 minutes following drug. Doses of 0.4 to 1.0 mg/kg were used in 5 animals. These small doses caused an acceleration of initial gastric emptying in 4, all beginning to empty in less than 2 minutes, and no change in the fifth. In the first 4 dogs subsequent emptying of the stomach was also accelerated, averaging 68% in ½ hour, 88% in 1 hour and 95% in 2 hours. The fifth dog had a normal emptying rate. The first barium reached the colon in 2 hours in 3, and 3 hours in 2.

Larger doses, 5 and 10 mg/kg, were then administered to 6 dogs. In each of these animals there was a definite delay of time of initial emptying and of total emptying. In 4 cases transit time through the small intestine was also prolonged. The time of initial emptying varied from 10 minutes to more than an hour, average 29 minutes. At ½ hour 4 animals showed no emptying, one 1% emptying, and one 20% emptying. By 1 hour average emptying was 17%, one animal still having complete gastric retention and 2 others having passed only traces of barium into the small intestine. At 2 hours emptying averaged 60%, at 3 hours 71%, and at 4 hours 82%. In the 4 dogs receiving 10 mg/kg SC 1950, barium traversed the ileum and reached the colon only after 4 to 6 hours. In the 2 receiving 5 mg/kg, barium appeared in the colon at 2 and 3 hours.

Fluoroscopy following the smaller doses (0.4 to 1.0 mg/kg) of SC 1950 revealed little change in gastric motility from the control animals. Following larger doses peristalsis was markedly decreased in 5, but appeared normal in one although initial and total emptying was delayed.

II. *Action of SC 1950 in Man.* Doses of SC 1950 varying from 0.5 to 2.0 mg/kg or 31 to 150 mg per patient were administered intravenously and of 2.0 mg/kg or 100 to 192 mg per patient intramuscularly to 53 patients without evident ill effects and without subsequent abnormality evident in blood counts or urinalysis. Immediately after intravenous injection patients had reddening of the skin and experienced a feeling of warmth. Most had a sense of general relaxation and some became slightly drowsy. Within a few minutes dryness of mucous membranes, dilatation of pupils, and loss of accommodation were noted. Occasionally ptosis of the upper eyelids and engorgement of conjunctival blood vessels appeared. Most of these changes persisted 30 to 60 minutes after intravenous injection. Following intramuscular administration these effects of the drug were noted in approximately 15 minutes and persisted 2 to 3 hours. One patient had pain from a duodenal ulcer at the time the drug was given and experienced relief for 1½ hours following 1.0 mg/kg intravenously. Another had right upper quadrant pain persisting 3 months following cholecystectomy and experienced relief for 110 minutes following 1.5 mg/kg. A burning pain of the foot in another, evidently associated with diabetic neuropathy, was repeatedly relieved for several hours following injections of 1.5 mg/kg. Several patients experiencing nausea before SC 1950 were relieved immediately after its injection. Oral administration of 2 to 15 mg/kg (100 to 900 mg total dose) produced only slight and inconsistent effects.

A. *Effect on Cardiovascular System of Man.* With the exception of one patient who had slight pressor responses with repeated doses of SC 1950, 0.5 to 1.5 mg/kg, lowering of blood pressure was consistently produced by the drug. The decrease following intravenous injection in normotensive patients

in the supine position was from an average of 125/77 before the drug to an average of 94/62 afterward. In hypertensive patients in the supine position the reduction was from an average of 190/130 before the drug to 114/80 afterward. The greatest fall of blood pressure occurred within two minutes following intravenous injection, following which pressures gradually rose to their former levels in from 10 to 120 minutes, usually about ½ hour. With standing, decrease of blood pressure (postural hypotension) was more pronounced. This postural hypotension occurred immediately after the drug and could be demonstrated a half hour or longer following return of supine blood pressure readings to levels equal to those before the drug.

Pressor responses normally occurring with immersion of the hand in ice water for 60 seconds and with breath holding were tested before and after SC 1950 in 12 patients. In each of the 12 pressor responses were obtained with both stimuli before the drug. After 1.0 to 1.5 mg/kg pressor responses to cold were prevented or reversed in 9 cases, reduced in 2, and still active in one. Pressor responses to breath holding were blocked or reversed in 8 patients, and reduced in 4.

The temperature gradients of lower extremities were tested at a constant room temperature of 25° C before and after 1.0 to 2.0 mg/kg SC 1950 in 12 patients. Skin temperatures were obtained with a Cambridge thermocouple. Before the drug toes were several degrees colder than the umbilicus. Afterward in 9 patients the gradient was completely abolished, warmth of toes and feet equaling that at the umbilicus. In one patient with arteriosclerotic occlusive vascular disease gradient was reduced but not abolished. Another with marked arteriosclerotic arterial insufficiency had no change of gradient. The final patient had no change of gradient. She weighed only 44 kg and had only 66 mg total dose of SC 1950.

As a rule cadiac rate was not markedly affected by SC 1950. Most patients had a slight tachycardia during the hypotensive action of the drug. A few patients with tachycardia before SC 1950 had moderate cardiac slowing following the drug.

B. *Effect on Human Gastrointestinal Activity.* Balloon studies of activity of the stomach and small intestine were performed in 20 patients. Gastric motility was studied using a full-sized condom fastened over the tip of a No. 14F Levine tube. Balloon tension or pressure at 300 cc was first recorded on the kymograph. The balloon was then deflated and passed with the tube into the stomach, placing the tip approximately 5 inches past the cardia under fluoroscopic guidance. The Levine tube was connected to a bromoform manometer and the balloon then reinflated to 300 cc by 50 cc increments of air. Rate of respirations was recorded by a pneumograph attached to the chest of the patient and connected to a tambour. In 2 patients studies of activity of the small intestine were made with a small balloon passed into the intestine on a Miller Abbot tube and inflated to 20 cc. In 3 more detailed studies were carried out employing the 4 lumen tube method described by Chapman[6] with the proximal balloon in the stomach or upper duodenum and 3 other balloons 8 inches apart distributed in the duodenum and jejunum.

Intravenous administration of 1.0 to 1.5 mg/kg SC 1950 consistently caused an immediate decrease of resting intragastric pressure or "tone" and cessation of forceful fluctuation of pressure or "peristalsis" of the stomach and the small intestine. The "tone" of the stomach began returning 25 to 40 minutes following SC 1950 and after 60 to 80 minutes tone was often slightly greater than before the drug. Gastric peristaltic activity was entirely absent for 30 minutes or more in all cases, and an average time of 58 minutes elapsed before any return of contractility was noted. Complete recovery of gastric activity was never regained in less than one hour, and usually 1½ hours were required before contractions became relatively normal.

Observations of activity of the small intestine closely paralleled those described for the stomach, reduction of tone and cessation of contractions occurring after the drug. When the 4 lumen tube was used it was noted that increased tone and contractions reap-

[6] Chapman, W. P., Stanbury, J. B., and Jones, C. M., *J. Clin. Invest.*, 1948, **27**, 34.

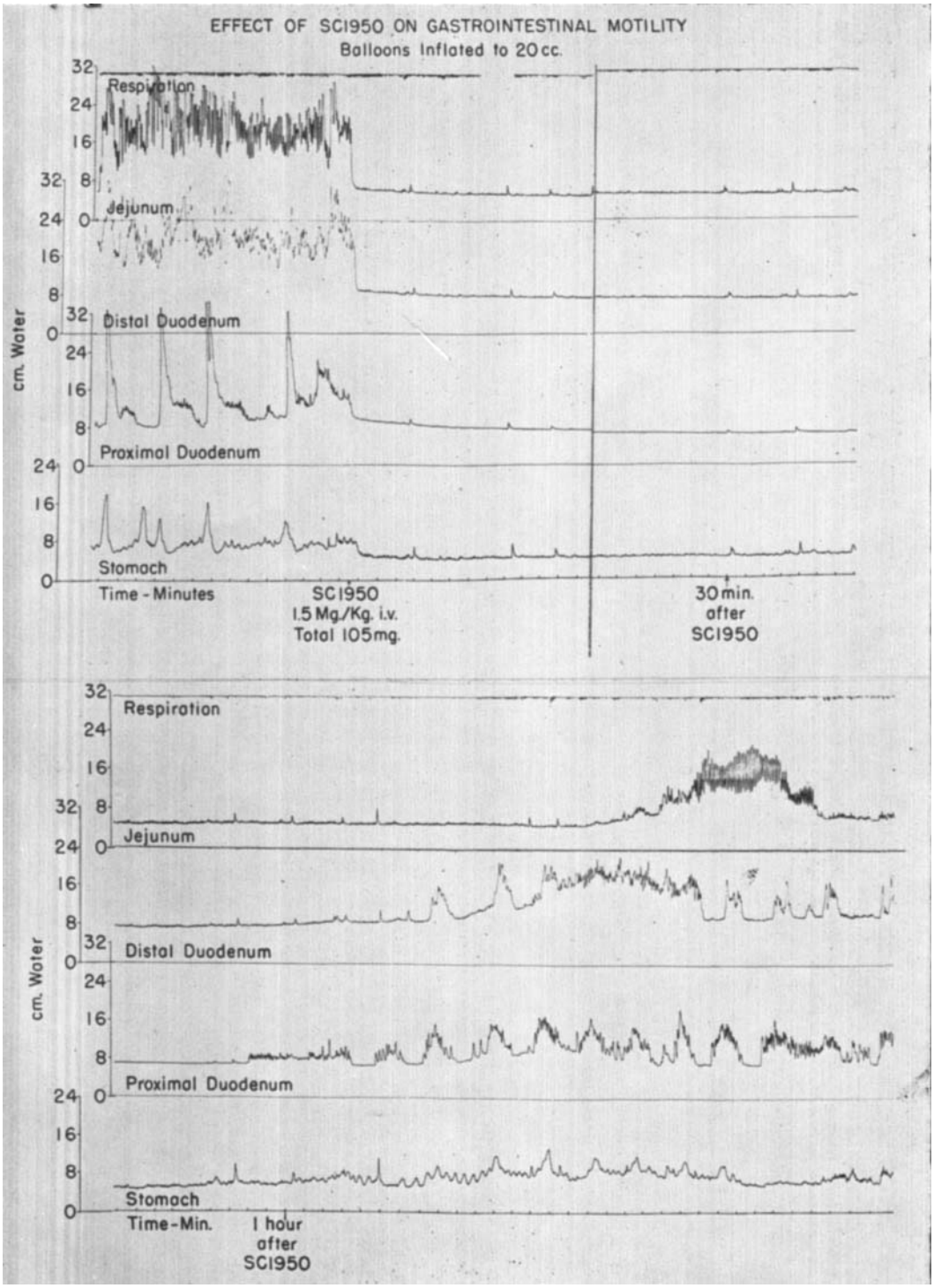


FIG. 3.

Activity of the stomach and upper small intestine as measured by 4 balloons 8 inches apart. SC1950 reduces tone and stops contractions for a period of one hour. Recovery occurs first in the more proximal segments.

TABLE I.
Effect of Urecholine and Prostigmine on Human Gastric Activity Following SC 1950 I.V. Dose 1.5 mg/kg. Gastrometric Studies. (300 cc Balloon.)

Gastric activity following SC 1950	Interval before second drug (min.)	Second drug	Total dose, No. mg	Route	Recovery time (min.)	
					Following second drug	Following SC 1950
0	12	Urecholine	2.5	I.M	20	32
0	12	"	2.5	"	19	31
0	13	"	4.0	"	15	28
0	5	"	5.0	"	6	11
0	7	Prostigmine	1.0	"	41	48
0	11	"	0.5	"	23	34
0	12	"	0.5	I.V.	8	20
0	10	"	0.5	"	11	21

peared first in the balloon located most proximally and then successively in the more distal balloons. Usually 6 to 8 minutes elapsed before activity appeared in successive segments 8 inches apart (Fig. 3). Four to 10 minutes after resumption of peristaltic activity the small intestine occasionally became excessively active for a period of 8 to 10 minutes. The duration of the period of reduced tone and absence of contractions following doses of 1.5 mg/kg SC 1950 was with one exception an hour or more and averaged 72 minutes. The exception occurred in a patient weighing only 40 kg, receiving a total dose of 80 mg. Total cessation of activity in this patient lasted 40 minutes. In the small intestine normal contractions appeared within a few minutes of resumption of activity.

Four subjects were given 1.5 mg/kg SC 1950 intravenously and 12 minutes later were given Urecholine 2.5 to 5 mg intramuscularly. In each patient SC 1950 produced lowering of tone and complete cessation of activity as measured by gastric balloons (Table I). After Urecholine all developed a slight increase of tone within 10 minutes and all had resumption of peristaltic activity within 20 minutes following Urecholine, or 11, 28, 31, and 32 minutes after SC 1950. As described above the average time of return of peristalsis following SC 1950 alone was 58 minutes, only one patient of 8 showing return of gastric activity 30 minutes following administration. Four other gastric motility studies were done giving neostigmine 0.5 mg 7 to 12 minutes after tone had been decreased and contractions abolished by 1.5 mg/kg of SC 1950 given intravenously. In 2 of these studies 0.5 mg neostigmine was given intravenously and in 2 intramuscularly. Motility returned 8 and 11 minutes following intravenous neostigmine or 20 and 21 minutes following SC 1950 (Table I). In one of 2 patients receiving 0.5 mg neostigmine intramuscularly, motility returned 23 minutes following neostigmine and 34 minutes following SC 1950. The other subject received two intramuscular injections of 0.5 mg neostigmine, the first 7, the last 22 minutes following 1.5 mg/kg SC 1950 intravenously. No recurrence of contractions was noted until 41 minutes following the first neostigmine or 48 minutes following the SC 1950.

Six patients with apparently normal gastrointestinal tracts had fluoroscopic and roentgenologic studies performed after ingestion of barium. Five of these had control studies in which 120 g barium sulfate suspended in 200 cc water was given orally. Fluoroscopy was done immediately and gastric activity and rate of emptying were noted. Roentgenograms were obtained at hourly intervals for 6 hours following ingestion. No abnormalities were noted. Gastric peristalsis was evident in all immediately after ingestion of barium and emptying into the duodenum occurred promptly. At one hour gastric emptying was at least 50% complete in all, average being 70% (Fig. 4A). The most distal barium was in the ileum at one hour in all. Two hours after ingestion 98%-100% of barium had passed through the stomach, and the most distal barium had advanced to the midileum, terminal ileum,

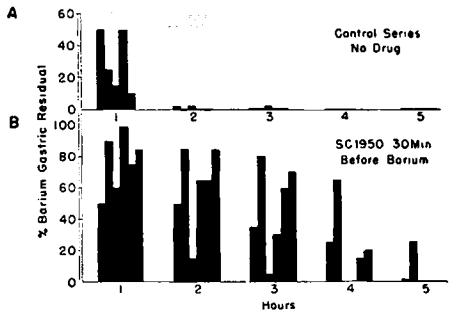


FIG. 4.

Roentgenographic study of the human gastrointestinal tract. Gastric emptying before and after 2 mg/kg SC 1950 IM.

or cecum. Barium had reached the cecum at 1, 2, 3, 3, and 4 hours respectively.

On another day SC 1950 was given to these same patients in amounts of 2 mg/kg intramuscularly, 30 minutes before ingestion of barium. Following SC 1950 and immediately after giving barium no peristaltic activity was noted by fluoroscopy in any patient. Only one demonstrated slight emptying immediately after barium. At one hour only one patient had as much as 50% emptying, and average emptying was 25%. At 2 hours there was a 40% average emptying with variations from 15% to 85% (Fig. 4B) Also at 2 hours the most distal barium was in the duodenum or jejunum in 5 patients and in the upper ileum in one. At 4 hours 2 of 6 had 100% gastric emptying and at 6 hours 4 of 6 had 100% emptying. By 4 hours barium had reached the cecum in all control patients but in only one of 6 patients after SC 1950.

C. *Effect on Gastric Secretions.* Preliminary studies have been performed on 4 patients testing effect of SC 1950 on volume and acidity of gastric secretions. Continuous gastric aspiration was employed, and samples were taken every 15 minutes. These patients all had duodenal ulcers and secreted large volumes of highly acid gastric juice. Following SC 1950 (1.5 mg/kg) intravenously, volume and acidity of gastric secretions was markedly diminished for an hour or more. Free acid was present in all specimens prior to SC 1950. Afterward there was no free acid in 2 or more specimens from 3 patients. In the fourth the total acid secreted was reduced from an average of 0.51 m eq during each 15 minute period to an average of 0.09 m eq during each 15 minute period. Although free acid never disappeared, this reduction of acidity following SC 1950 persisted 1¼ hours.

Conclusion. A new quaternary amine, 2,6, dimethyl, diethyl piperidinium bromide, described as a ganglionic blocking agent,[4] has an inhibitory or blocking action upon functions mediated by the sympathetic and parasympathetic divisions of the autonomic nervous system. In dog and in man it reduces blood pressure and prevents several vasomotor reflexes, but does not prevent the vasopressor action of epinephrine. It causes a reduction of tone of the stomach and small intestine and abolishes their motor activity, reduces gastric acidity, and causes pupillary dilatation, loss of accommodation, and dryness of mucous membranes. Urecholine causes a reversal of effect on gastric motility. Neostigmine apparently causes a reversal of all effects of the drug.

16964

Specificity of Differential Sheep Cell Agglutination Test in Rheumatoid Arthritis.*

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Rose and his associates[1] recently described a sheep cell agglutination test which may prove to be helpful as an aid in the differential diagnosis between rheumatoid arthritis and other diseases with arthritic manifestations. These authors found that a 16-fold difference