TABLE I.*

Cat No.	1	2	3	4	5	6	7	8	9†
Before	125(67)	145(42)	117(65)	132	130	120(40)	120	111(50)	215(50)
	105(58)	148(33)		120			125	123(18)	120(18)
After	72(10)	70(14)	60(10)			67(14)		67(12)	67(12)
	69(14)	71(23)	64(14)			70(23)		71(14)	68(14)

*Time in minutes for barium introduced in stomach to reach the caecum. Figures in parenthesis indicate No. of days before or after operation.
†Cat 9 on first control reading was extremely excited.

TABLE II.

	No. of cats	No. observations	Mean of observations Minutes	Standard deviation	Standard deviation of mean	P_t
Before	9	15	130	26.0	6.7	
After operation	6	12	68	3.4	.98	<.01

is considered that the grades of excitement and consequent actual or abortive sympathetic inhibition were approximately the same in the animals before and after operation. The removal of the sympathetic innervation of the adrenals tends to prevent increased epinephrine output from excitement and resultant hormonal intestinal inhibition.

Conclusion. Sympathetic denervation of the small intestine and adrenals of the cat reduces the average time for barium sulphate suspension to reach the caecum from the stomach to about 52%. The difference observed appears statistically significant.

8803 P

Influence of Magnesium Oxide on Antipyretic Action and Toxicity of Acetylsalicylic Acid in Rabbits.

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Issekutz,[1, 2] and Barbour and his coworkers[3-6] have shown that

1 Issekutz, B., *Therap. Monatschr.*, 1915, **39**, 379.

2 Issekutz, B., *Arch. f. ges. Physiol.*, 1913, **151**, 456.

3 Winter, J. E., and Barbour, H. G., Proc. Soc. Exp. Biol. and Med., 1928, **25**, 587.

4 Barbour, H. G., and Winter, J. E., *J. Pharm. Exp. Therap.*, 1929, **35**, 425.

5 Barbour, H. G., and Winter, J. E., Proc. Soc. Exp. Biol. and Med., 1928, **25**, 582.

6 Winter, J. E., Richey, C. H., and Barbour, H. G., *J. Pharm. Exp. Therap.*, 1930, **38**, 3.

the simultaneous administration of magnesium compounds together with certain depressant drugs, produces a depressant action which is considerably greater than that which results from the administration of either one of these substances. Meltzer and his coworkers[7, 8] have shown that this is primarily a central, rather than peripheral action, and have demonstrated that the narcotic action of ether may be enhanced by the simultaneous administration of magnesium sulphate.

It is the purpose of this investigation to examine critically some of these statements because of their importance both from the utilitarian therapeutic point of view and from the theoretical point of view in elucidating the phenomenon of potentiation or synergism.

In dealing with such a problem, a mensurable, objective reaction which will serve as a criterion of the depressant activity is of primary importance. Also, the experimental work should cover a sufficiently large group of animals to allow for a statistical analysis of the results. This was carried out in the present investigation by measuring the antipyretic action of a given dose of acetylsalicylic acid, magnesium oxide, and of combinations of the two.

The experimental work was divided into a series of 23 experiments, using 3 groups of animals with 4 or 5 animals in each group, the total number of animals being 266. The experimental animals were all normal, healthy adult rabbits of both sexes, in which pyrexia was induced by the intravenous injection of 0.1 cc./kg. body weight of a Typhoid Toxin.* The body temperature was taken at 3 different intervals over a period of 2 hours prior to any experimental interference in order to establish a normal level for each animal. Immediately after the intravenous injection of the typhoid toxin, a stomach tube was passed and a suspension of the antipyretic drug in water was administered; in the case of the control animals the same quantity of water was passed into the stomach as was used for the suspension of the drug in the experimental animals. The body temperatures were taken at regular intervals for a period of 4 to 6 hours after this experimental interference. During this period, when observations were being made, the animals were immobilized by placing them in small, open boxes in such a manner

[7] Meltzer, S., and Auer, J., *Am. J. Physiol.*, 1905, **15.**

[8] Meltzer, S. J., *Med. Rec.*, 1905, Dec. 16.

* Typhoid Toxin: 1 cc. represents:

B. typhosus	1000	million
B. paratyphosus A	750	"
B. paratyphosus B	750	"

as to minimize the effect of extraneous temperature changes which took place around them. Body temperatures were taken with a large bulb, chemical thermometer reading to 0.1°C., the bulb being left in the rectum until the column of mercury reached a maximum; this usually required about 2 minutes.

Figures 1 and 2 show the antipyretic action of the following agents compared against the pyrexia of the control animals:

a) acetylsalicylic acid (50 mg./kg.)—(each point represents the average of 46 animals).
b) magnesium oxide (50 mg./kg.)—(each point represents the average of 46 animals).
c) acetylsalicylic acid (100 mg./kg.)—(each point represents the average of 57 animals).
d) acetylsalicylic acid (50 mg./kg.) plus magnesium oxide (50 mg./kg.) —(each point represents the average of 59 animals).
e) control—(each point represents the average of 58 animals).

A statistical analysis of these results is given in Table I.

It becomes obvious from an examination of these results that the oral administration of 50 mg./kg. of acetylsalicylic acid or magnesium oxide has practically no antipyretic action, but that the antipyretic action of the combination of these 2 is as great as the antipyretic effect produced by a dose of 100 mg./kg. of acetylsalicylic acid.

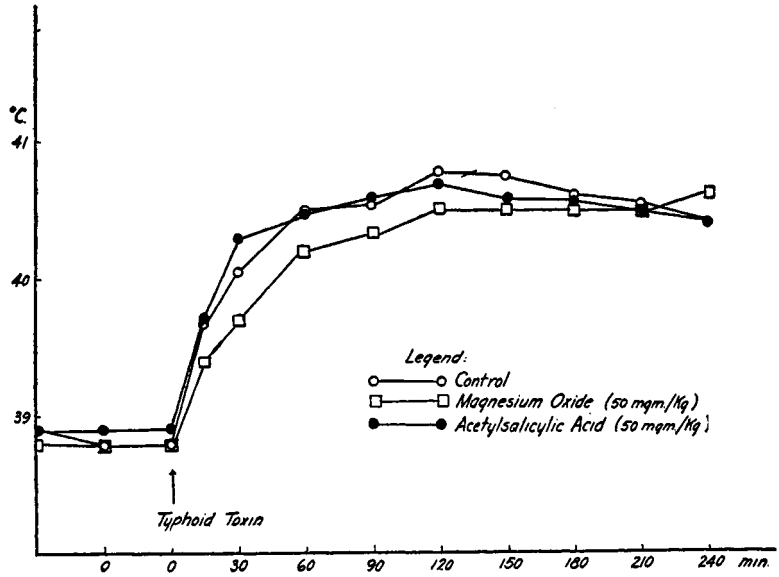

Fig. 1.

TABLE I.
Comparative Antipyretic Effect of Acetylsalicylic Acid, Magnesium Oxide, and of a Mixture of the Two.

Time in min.	Group A		Group B		Group C		Group D		Group E	
	Mean Temp.	Standard error of mean	Mean Temp.	Standard error of mean	Mean Temp.	Standard error of mean	Mean Temp.	Standard error of mean	Mean Temp.	Standard error of mean
0	38.9	.072	39.0	.059	39.0	.064	38.9	.091	38.8	.036
0	38.8	.078	39.0	.057	39.0	.060	38.9	.093	38.8	.036
0	38.8	.079	39.1	.060	38.9	.064	38.9	.112	38.8	.046
15	39.7	.064	39.2	.070	39.2	.059	39.7	.105	39.4	.054
30	40.1	.100	39.5	.067	39.4	.066	40.3	.134	39.7	.068
60	40.5	.105	39.8	.076	39.9	.055	40.5	.122	40.2	.084
90	40.5	.112	40.0	.075	40.1	.077	40.6	.134	40.3	.080
120	40.8	.108	39.7	.084	40.2	.070	40.7	.130	40.5	.076
150	40.8	.118	40.1	.088	40.2	.081	40.6	.144	40.5	.076
180	40.6	.126	40.1	.086	40.3	.084	40.6	.133	40.5	.100
210	40.6	.123	40.1	.087	40.3	.089	40.5	.088	40.5	.107
240	40.5	.110	40.2	.084	40.2	.089	40.4	.120	40.6	.086

Group A—Control series. (Each reading represents the average of 58 animals).
Group B—Acetylsalicylic Acid (50 mg./kg.) plus Magnesium Oxide (50 mg./kg.). (Each reading represents the average of 59 animals.)
Group C—Acetylsalicylic Acid (100 mg./kg.). (Each reading represents the average of 57 animals).
Group D—Acetylsalicylic Acid (50 mg./kg.). (Each reading represents the average of 46 animals).
Group E—Magnesium Oxide (50 mg./kg.). (Each reading represents the average of 46 animals).

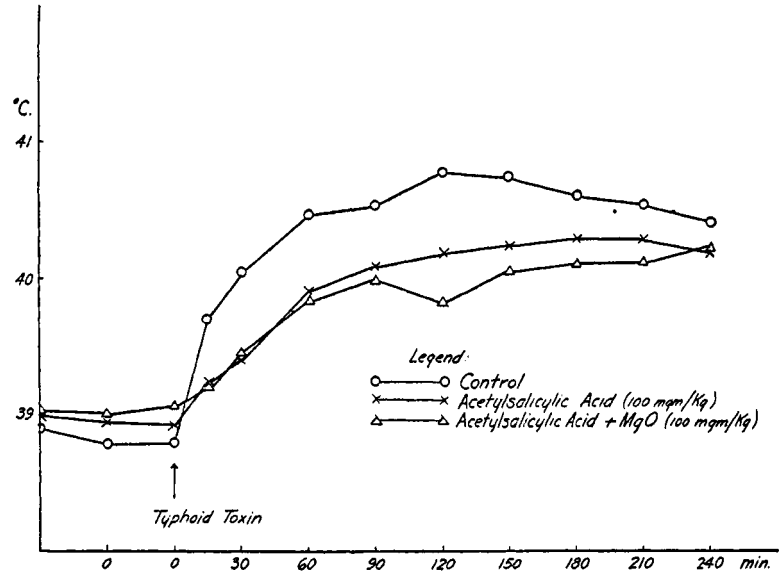

Fig. 2.

The oral toxicity of acetylsalicylic acid and of a mixture of equal parts by weight of acetylsalicylic acid and magnesium oxide is given in Table II. An examination of these results shows that the toxicity of acetylsalicylic acid is not influenced by the magnesium oxide.

TABLE II.
Toxicity (Oral) of Acetylsalicylic Acid and of Acetylsalicylic Acid Plus Magnesium Oxide.

	Acetylsalicylic Acid			Acetylsalicylic Acid (50%) + MgO (50%)		
Dose, mg./kg.	Total No. of animals	Died	Recovered	Total No. of animals	Died	Recovered
200	5	0	5	5	0	5
400	5	0	5	5	0	5
750	5	1	4	5	0	5
1000	10	5	5	10	1	9
1200	5	2	3	5	2	3
1500	10	8	2	5	2	3
1700	—	—	—	5	1	4
2000	10	10	0	5	1	4
2500	—	—	—	10	3	7
3000	—	—	—	10	8	2
	—			—		
Total	50			65		

Conclusions. 1. Quantities of acetylsalicylic acid and magnesium oxide, which have no antipyretic action when administered separately, have a marked antipyretic action when administered together.

2. The toxicity of acetylsalicylic acid is not influenced by the simultaneous administration of magnesium oxide. 3. The toxicity of a mixture of 50% magnesium oxide and 50% of acetylsalicylic acid is half as great as the toxicity of the amount of acetylsalicylic acid which is required to produce the same therapeutic effect.

8804 C

Incidence of Hemolytic Streptococci and Pneumococci in the Pharyngeal Flora of Normal Rhesus Monkeys.

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The normal bacteriologic flora of the pharynx of chimpanzees has been described by Dochez, Shibley and Mills[1] in connection with their experiments on the transmission of the common cold. The bacteria occurring in the throats of apes were similar, for the most part, to those found in human throats, although the percentile incidence varied for some organisms. Apparently, no such complete study of the pharyngeal flora of lower primates has been reported. The few reports of throat-cultures in the monkey are primarily concerned with the presence of *C. diphtheriæ* in the nasopharynx. Dold and Weigmann,[2] and Ramon and Erber[3] found diphtheria-like organisms in some monkeys, but Jungeblut[4] in 50 normal rhesus monkeys found no *C. diphtheriæ*. Dold and Weigmann reported the presence of staphylococci and streptococci but did not specify the reaction of these organisms in blood-media.

During studies of experimentally induced hemolytic streptococcal infection of rhesus monkeys, a survey of the incidence of hemolytic streptococci in the normal throats of 49 animals* was undertaken. The cultures were taken during the 2nd week of January, 1936, and within 9 days of receiving the animals in the laboratory from the dealer. A swab was rubbed firmly over the faucial surface, streaked

1 Dochez, A. R., Shibley, G. S., and Mills, K. C., *J. Exp. Med.*, 1936, **52**, 701.

2 Dold, H., and Weigmann, F., *Zeitsch. f. Hyg.*, 1934, **116**, 154.

3 Ramon, G., and Erber, B., *Revue D'Immunologie*, 1935, Sept., 415.

4 Jungeblut, C. W., *J. Imm.*, 1934, **27**, 17.

* These monkeys were made available through the courtesy of Dr. Jungeblut.