aminophylline by mouth daily. In one instance the patient could not be controlled with Norisodrine plus additional medication, but she did not respond to epinephrine either.[2] Of the 8 patients requiring medication in addition to Norisodrine, 1 patient did not respond to Norisodrine at all, 4 patients gave a good response, and 3 responded satisfactorily. The results in these patients requiring additional medication might have been anticipated, since they did not respond to Norisodrine alone. In those instances where no additional therapy was required the response to Norisodrine was satisfactory in all instances. In normal subjects the inhalation of a single dose of Norisodrine dust did not appear to influence the pulse rate or the blood pressure. No discomforting symptoms were reported by this group. Four asthmatic patients reported symptoms of dizziness and/or palpitation after the inhalation of the Norisodrine dust. These reactions were not alarming and disappeared in all instances within 10 min. The blood pressure changes in these 4 patients showed a drop in systolic pressure ranging from 3 to 20 mm of mercury. In this group of 4 patients the pulse rate showed an increase ranging from 4 to 12 beats/min. There were no reactions in the remaining 20 patients. One patient, treated while in status asthmaticus, required a considerable amount of Norisodrine to maintain comfort. Since she tolerated the drug exceptionally well, she was permitted to inhale the Norisodrine dust freely. This patient consumed as much as 100 mg of the drug daily without any untoward reactions whatsoever. None of the patients, including the latter, has so far shown any tendency of fastness toward this drug. This group of patients has been using Norisodrine dust for 10 months.

On the basis of the clinical results obtained with the inhalation of Norisodrine dust, either alone or in addition to other medication, it would appear that this drug has a definite place in the symptomatic treatment of asthmatic diseases. It should be useful in many instances of bronchospasms of a nonasthmatic origin. It can apparently be inhaled in dust form with a wide margin of safety.

References

1. CHARLIER, R. *Rev. belge Sci. Med.*, 1946, **17**, 42–56.
2. CHARLIER, R. *Rev. belge Sci. Med.*, 1946, **17**, 108.
3. DAUTREBANDE, L. *Arch. int. Pharm. Therap.*, 1945, **71**, 109–128.
4. KONZETT, H. *Klin. Wschr.*, 1940, **19**, 1303–1306.
5. KRASNO, L., KARP, M., and RHOADS, P. *Science*, 1947, **106**, 249–250.
6. KRASNO, L., KARP, M., and RHOADS, P. *Ann. int. Med.*, March, 1948.
7. KRASNO, L., KARP, M., and RHOADS, P. *J.A.M.A.*, 1948, **5**, 344–348.
8. QUITSCHAL, W. *Dtsch. med. Wschr.*, 1942, **68**, 942–944.
9. SEGAL, M., and BARSKY, J. *Bull. New Engl. med. Center*, 1947, **9**, 62.
10. SEGAL, M., and BARSKY, J. *J. Ann. Allergy*, 1947, **5**, 317.
11. STOLZENBERGER-SEIDEL, M. *Klin. Wschr.*, 1940, **19**, 1306–1310.

[2] This patient appeared to be resistant to all forms of therapy. Her attacks would persist for 3–5 days and then stop spontaneously.

Inhibition of Anaphylactic Shock by Acetylsalicylic Acid

BERRY CAMPBELL

Department of Anatomy, University of Minnesota Medical School

Data have recently accumulated which indicate an effect on antigen-antibody reactions of members of the salicylate group. Coburn and Kapp (*2*) reported that salicylates modify the precipitation of normal rabbit serum protein by tungsten and partly inhibit the precipitation of horse serum euglobulin by rabbit antiserum. The salicylate effect on immune precipitation was noted to be reversible and appeared to be due to inactivation of antibody. Derick, Hitchcock, and Swift (*3*), in an inquiry into the beneficial effects of salicylates on rheumatic fever, concluded that by use of the drug circulating antibodies are kept at a low level, presumably through an effect on the antibody-forming mechanisms, as shown earlier by Swift (*8*). Homburger (*4*) reported the impairment in the formation of anti-Rh agglutinins in rabbits and guinea pigs given sodium salicylate prior to and during the exposure to the antigen. Jager (*5*) has shown that massive salicylate therapy aborts the local and systemic reactions of human subjects to vaccine. In the treated individual the antibody response was found to be usually impaired as compared with the control. On the other hand, Rantz, Boisvert, and Spink (*6*), in a study on the effects of salicylates, sulfa compounds, and penicillin on antibody response to streptococcal (sore throat) infection, found no significant alteration of antibody response in those individuals treated, rather conservatively, with sodium salicylate. In a more recent paper, Sullivan, Parker, and Hibbert (*7*) report protection of rabbits against arteritis, apparently through interference with antigen-antibody reaction.

The experiments reported below were designed to clarify the protection offered by these drugs to anaphylactic shock and were related to a study of their effects on neurotropic virus disease.

Young adult (ca. 2-kg) rabbits were sensitized to egg albumin by injection of egg white on alternate days in the following doses: 1 cc, i.v.; 0.5 cc, i.v.; 1 cc, i.m. Acetylsalicylic acid was used as the drug and was administered orally as 5-grain (0.324-gm) tablets. The animals were restrained in a stock-like box and the tablets inserted, with long forceps, well back in the mouth. A squirt of water from a syringe followed the tablet and speeded its dissolution. Care was taken to replace any drug which was spit out.

Twenty-one rabbits were sensitized on March 24, 1947. At 2:00 P.M. on April 9, 11 were given 5 grains of acetylsalicylic acid orally. This was repeated at 10:00 P.M. the same day and at 10:00 A.M. on April 10. One hour later, these animals, together with the remaining 10 for controls, were injected intravenously with 0.6 cc of egg white. Nine of the 11 experimentals (Table 1) showed no shock, the remaining 2 showing moderate and

mild shock, respectively. All of the 10 controls showed shock, 2 died, 1 was severely shocked, and the rest showed moderate or mild shock.

Three weeks later some of the survivors of both the experimental and the control group were again challenged without the drug with 0.6 cc of egg white, i.v. All showed shock.

TABLE 1

EFFECTS OF ADMINISTRATION OF 15 GRAINS (.968 GM) OF ACETYLSALICYLIC ACID, IN DIVIDED DOSES, ON ANAPHYLACTIC SHOCK

No.	Dosage	Shock	21 days later
931	15 grains in 3 doses	0	..
935	"	0	3
937	"	0	4
939	"	0	1
941	"	0	..
943	"	0	..
945	"	0	..
947	"	0	..
949	"	0	..
953	"	2	..
955	"	1	..
933	None	3	4
934	"	2	4
936	"	1	1
938	"	1	..
940	"	4	..
942	"	2	..
944	"	2	..
946	"	1	..
948	"	2	..
954	"	4	..

To test the effect of acetylsalicylic acid on histamine shock, 11 rabbits weighing 2–2.5 kg were given 5 grains of acetylsalicylic acid, orally, at 3:30 P.M. on March 11, 1947. This dosage was repeated at 9:00 A.M. on March 12 and again at 2:30 P.M. the same day. One hour later, each rabbit was injected intravenously with 2.75 mg of histamine phosphate. Seven of the 11 died (#4 shock), 2 showed severe (#3) shock, and 2 showed moderate (#2) shock.

The animals which were premedicated with acetylsalicylic acid showed striking protection against anaphylactic shock. It may be presumed, on the basis of the literature reviewed above, that this was due to a decrease in the antibodies at the time of the challenging dose. There is nothing to indicate any protective effect against histamine shock, for though unaccompanied by simultaneous controls, the morbidity in the above series was similar to that reported in a previous communication (*1*). It is interesting to note that the effects of the drug were temporary and that the treated animals showed considerable hypersensitivity 3 weeks later.

The contrast between the results with this drug and those reported earlier (*7*) for Benadryl is complete. Benadryl gave good protection, in similar experiments, against histamine shock but was without effect on anaphylactic shock. The present drug, acetylsalicylic acid, however, effectively protects against anaphylactic shock but not against histamine. It is, with the other salicylates, apparently a true antianaphylactic drug in that it interferes with the antigen-antibody reactions to prevent or decrease the untoward results of the challenging dose of antigen.

References

1. CAMPBELL, BERRY, BARONOFSKY, IVAN D., and GOOD, ROBERT A. *Proc. Soc. exp. Biol. Med.*, 1947, **64**, 281.
2. COBURN, A. F., and KAPP, E. M. *J. exp. Med.*, 1943, **77**, 173.
3. DERICK, C. L., HITCHCOCK, C. H., and SWIFT, H. F. *J. clin. Invest.*, 1928, **5**, 427.
4. HOMBURGER, F. *Proc. Soc. exp. Biol. Med.*, 1946, **61**, 101.
5. JAGER, B. V. *Proc. Amer. Fed. clin. Res.*, 1947, 93.
6. RANTZ, L. A., BOISVERT, P. J., and SPINK, W. W. *Science*, 1946, **103**, 352.
7. SULLIVAN, C. J., PARKER, T. W., and HIBBERT, R. W. *Proc. Soc. exp. Biol. Med.*, 1948, **67**, 508.
8. SWIFT, H. F. *J. exp. Med.*, 1922, **36**, 735.

Effects of 2,4-Dichlorophenoxyacetic Acid on Chicks[1]

MELVIN K. BJORN and HENRY T. NORTHEN

Department of Botany, University of Wyoming

With the increasing use of 2,4-D as a herbicide it is important to inquire into the possible toxic effects of the chemical on animals. Several investigators have studied the effects of 2,4-D on mammals. The lethal dose for mice, when injected subcutaneously or intravenously, has been determined by Bucher (*1*) to be 280 mg/kg of body weight. Mitchell and Marth (*2*) reported that they fed 200 mg of 2,4-D daily to small experimental animals with no ill effects.

TABLE 1

EFFECT OF ALKANOLAMINE OF 2,4-D ON WHITE ROCK CHICKS

Dosage (mg of acid/kg of body weight)	Increase in weight at end of four weeks (%)
0.00 (control)	456
.28	444
2.80	469
28.00	427
280.00	373

In the present experiment White Rock chicks were used. The alkanolamine of 2,4-D was administered orally through a pipette. In the first experiment, data for which are given in Table 1, one part of the alkanolamine was diluted with 19 parts of water. The dosages recorded are in terms of the acid equivalent. Five chicks (each weighing approximately 50 gm at the beginning) were used in each group. The chicks were weighed and then were given the appropriate dose (Table 1) three times a week on alternate days for a period of four weeks, making a total of 12 doses. As the chicks gained in weight, the

[1] Contribution No. 210 from the Department of Botany and the Rocky Mountain Herbarium, University of Wyoming.