therapy of experimental murine typhus infections in Swiss mice (*4*) and guinea pigs (*2*).

Since p-aminobenzoic acid (PABA) had previously been shown by Snyder, *et al.* (*5*) to be effective in the therapy of mice infected with the etiological agent of endemic typhus, an effort to determine the relative efficacy of MTC and PABA in

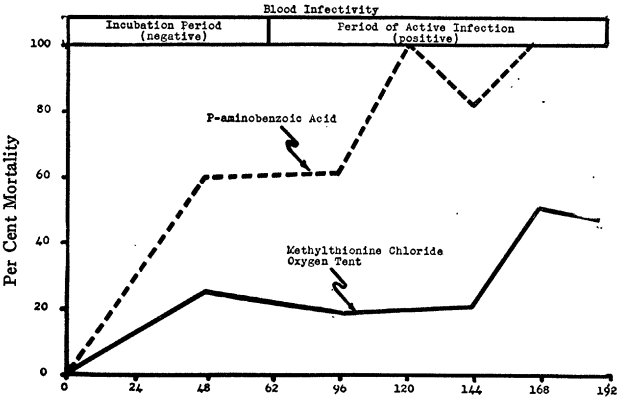


FIG. 2. Relative efficacy of MTC and PABA in *tsutsugamushi* (Karp) infected mice. Therapy interval indicates the elapsed time between inoculation of the mice and institution of therapy.

experimental *R. tsutsugamushi* infections was made. The concentrations of the two drugs in the ground fox chow were made equivalent—0.4 per cent. Institution of therapy was delayed for various time intervals up to and including 192 hours postinoculation. The results of this experiment (Fig. 2) show that while PABA was no longer effective when institution of therapy was delayed for more than 120 hours, MTC plus oxygen was still partially effective even when treatment was delayed up to 192 hours. Furthermore, the per cent mortality

TABLE 1

EFFECT OF MTC, MTC PLUS OXYGEN, AND PABA ON THE AMOUNT OF PERITONEAL FLUID FOUND ON AUTOPSY

| Agent | No. of mice | Percentage of mice showing graded amounts of peritoneal fluid* | | | | |
|---|---|---|---|---|---|---|
| | | Neg. | + | ++ | +++ | ++++ |
| MTC (normal atmosphere).... | 56 | 39.2 | 44.7 | 13.6 | 0.0 | 2.3 |
| MTC (oxygen)..... | 26 | 44.0 | 32.1 | 19.5 | 4.5 | 0.0 |
| PABA..... | 43 | 4.1 | 30.5 | 32.7 | 19.2 | 13.1 |
| Control (untreated)..... | 44 | 9.1 | 15.9 | 45.4 | 15.9 | 13.6 |

* Peritoneal fluid graded as neg. = none; + = 0–0.2 cc.; ++ = 0.2–0.5 cc.; +++ = 0.5–1.0 cc.; ++++ = greater than 1 cc.

in all instances was significantly lower in the group treated with MTC.

When the concentration of PABA was increased to 1 per cent, its effectiveness as a therapeutic agent in the experimental infection increased but still was not of the order of magnitude of MTC.

Peritoneal fluid, one of the predominant gross pathological signs found at necropsy of untreated mice, was significantly reduced in quantity in the MTC-treated mice that died. In this respect, PABA-treated mice and the untreated control mice closely paralleled each other (Table 1).

In view of the well-established functions of MTC as an oxygen carrier and as a catalyst of numerous enzymatic reactions, studies on the mechanism of the action of this drug in the subject infection may reveal principles underlying the effective chemotherapy of virus and rickettsial diseases. Such studies are under way at this Institute.

These results clearly establish the beneficial effect of methylthionine chloride as a therapeutic agent in the treatment of *R. tsutsugamushi* infections in Swiss mice and the synergism of the drug with oxygen in such infections.

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# Insecticidal Action of 1-Trichloro-2,2-Bis-(p-Bromophenyl) Ethane (Colorado 9)[1]


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The compound made by condensing one molecule of chlorohydrate with two molecules of bromobenzene is 1-trichloro-2,2 bis(p-bromophenyl) ethane (*4*), which has been designated as Colorado 9. This has had a definite killing effect on certain insects and, like its relative, DDT, is stable and does not have an unpleasant odor.

Colorado 9 kills flies at the low spray level of 0.1 ml. of 5 per cent petroleum solution per cubic meter of air space. The flies lose their motor ability after 10 minutes and die within an hour. Early in 1945 it was determined by laboratory tests that Colorado 9 was lethal for the potato and tomato psyllid, *Paratrioza cockerelli* Sulc. During the growing season the material was used in potato plot tests by dissolving it in xylene at the rate of 1 pound to 1 quart of xylene and emulsifying by adding 1 part Triton 100 X to 50 parts of the above mixture. The spray solution carried 1 pound of Colorado 9 to 100 gallons of water. Five applications were made during the season, the usual schedule followed for psyllid control. At no time were any indications of plant injury from the spray applications detected. The variety of potato was the Irish Cobbler.

The yield of potatoes of marketable size ($1\frac{7}{8}$ inches in diameter or larger) has been found to be the most reliable measure of successful psyllid control. The treated plots yielded at the rate of 313.2 bushels/acre; untreated plots, at the rate of 22.8 bushels.

Colorado 9 was again used in plot tests in 1946 and at mid-

[1] Published with the approval of the director as paper No. 223, Scientific Journal Series, Colorado Agricultural Experiment Station.

This compound was synthesized in November 1944 by Merle G. Payne and E. L. Bailes. The latter, at that time a member of the chemistry section of the Colorado Experiment Station, has since resigned.

season gave indications, as determined by weekly sweepings by means of the insect net, of promising control of psyllids, tuber flea beetles, and leaf hoppers.

In studying a new approach to the control of the European elm scale, *Gossyparia spuria* (Modeer), it was found that Colorado 9 was definitely lethal to this insect.

The insecticide DDT, when used on leguminous plants at high concentrations, has a definite depressing effect on the bacterial nodules (*1*). In agricultural crop rotation where legumes are grown for increasing the soil nitrogen, this was a distinct disadvantage for DDT. Colorado 9 has the advantage of having no depressing effect at high concentrations on bacterial nodules of legumes when used as an insecticide (*2, 3*). Extensive field investigation indicates that there was no injurious effect when insecticidal preparations using this compound were sprayed on plants.

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## Lesions of the Pancreatic Islets Produced in Cats by Administration of Glucose


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Previous studies (*1*) have suggested that an elevated level of blood glucose may, under certain circumstances, result in lesions of the islands of Langerhans. Thus, in animals with subtotal pancreatectomy or in those treated with anterior pituitary extract, a period of hyperglycemia precedes hydropic degeneration of the beta cells. Furthermore, measures which lower the blood glucose (e.g. diet, insulin, or phlorizin) will prevent or reverse such changes during the early stages. The literature concerning the effect of the administration of glucose upon the pancreatic islets reveals either failure to secure prolonged hyperglycemia in dogs or the occurrence of only minor changes in granulation of the beta cells of other species.

It has been found possible to elevate the level of blood glucose in cats by means of repeated intraperitoneal injections of glucose. Twenty per cent glucose in physiological saline was given at approximately 8-hour intervals, the amount injected being gradually increased from 50 to as much as 140 ml./dose (150–420 ml. daily). The amount of food eaten and the urine glucose excreted were determined daily. Extra vitamins, particularly thiamine, were administered in large amounts. Blood glucose determinations were made at frequent intervals, usually just before the intraperitoneal injection of the glucose-saline solution. Normal cats and four cats from which approximately half to two-thirds of the pancreas had been removed were employed. These were observed for several weeks before starting the glucose injections and were known to have normal blood glucose concentrations.

After a few days of injections some of the cats exhibited a syndrome of marked weakness of the hind legs, ataxia, anorexia, occasional convulsions, and death—an effect noted by others in dogs and cats. However, some of the cats did not develop this syndrome, or recovered from it so that injections could be continued for weeks.

TABLE 1

| No. of cats* | Total period of glucose injections | | Days of hyperglycemia‡ | Hydropic degeneration of beta cells |
|---|---|---|---|---|
| | Days | Avg. blood sugar† (mg./100 ml.) | | |
| 4 | 14–27 | 209–326 | 9–19 | Marked |
| 4 | 6–16 | 133–296 | 0– 5 | None |

* Each group consisted of two normal and two partially depancreatized cats.

† Average of all blood glucose determinations made just before injections of glucose.

‡ Morning hyperglycemia indicates a blood glucose concentration of greater than 149 mg. per cent prior to the 8:00 A. M. injection of glucose.

To date, sections of the pancreas of 8 animals have been examined, and the histological changes in the islands of Langerhans have been related to the degree and duration of hyperglycemia (Table 1). The morning preinjection blood glucose value has been selected as a criterion because more observations were made at this time and, in the great majority of instances, it was the lowest preinjection value in the 24 hours. This was due to the fact that this sample of blood was usually obtained at a somewhat longer interval after the previous injection of glucose.

In addition to these animals, a normal cat was maintained hyperglycemic for a period of 39 days by means of glucose injections. When these were stopped, the cat remained severely diabetic. It was sacrificed while in diabetic acidosis 22 days after the last injection. Prior to death it had excreted approximately 100 per cent of the available glucose of the meat diet and had developed acetonuria. Terminal blood samples showed greatly increased concentrations of glucose and fatty acids, and the serum $CO_2$ was 11 vols. per cent.


*Summary.* Hydropic degeneration of the islands of Langerhans and permanent severe diabetes mellitus have followed the prolonged injection of intraperitoneal glucose-saline solution in normal as well as in partially depancreatized cats. Positive results were associated with prolonged hyperglycemia. These findings add further evidence in support of the hypothesis that a sustained elevation of blood glucose may, under certain conditions, lead to the production of damage to the islands of Langerhans in this species. Besides hyperglycemia, other disturbances which might be responsible wholly or in part for the island lesions are under study.


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