Effect of Antimetabolites on Antigen *Vi* Synthesis and Variability in *S. typhi*

S. typhi grown at 18° C. fails to produce antigen *Vi* and is immune to *Vi* phages[1]. We submitted such a culture of *S. typhi* to the influence of various factors, transferred it into 37° C., and studied in suitable media the synthesis of antigen *Vi*, growth of the bacteria and synthesis of cell protein (Mazia)[2]. We determined antigen *Vi* in hot saline extracts by passive hæmagglutination[3-5].

Bacteria inhibited by chloromycetin retained their ability to produce antigen *Vi* (curve 1), though they failed to synthesize protein or to grow. There are data indicating that the enzyme responsible for synthesis of antigen *Vi* exists in the cells at a temperature of 18° C. over a number of generations in spite of absence of actual synthesis of the antigen.

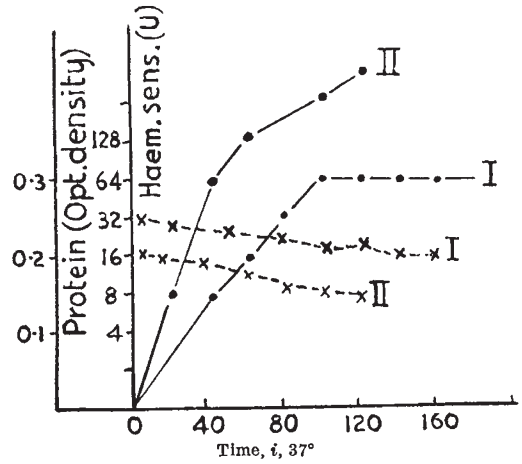

Fig. 1. —.—, *Vi* antigen; – – . – –, cell protein

Examination of growth-inhibiting factors demonstrated that all those inhibiting respiration or reducing cell metabolism and suppressing the Krebs cycle inhibit at the same time antigen *Vi* synthesis at 37° C. This effect is exerted by cyanides, malonic acid, vacuum, absence of oxygen (evacuation or flushing with inert gases) and, finally, by high concentrations of dinitrophenol. Chloromycetin and lethal doses of ultra-violet radiation, on the other hand, fail to inhibit antigen *Vi* synthesis (Table 1). The effect on antigen *Vi* synthesis of malonic acid was examined in particular. Bacteria originally sensitive to 0·005 *M* malonic acid are easily adapted to 0·025 *M* malonic acid by consecutive passages in increasing concentrations. Already in 0·01 *M* concentrations of the acid (in the second passage) the bacteria fail to synthesize antigen *Vi*.

Table 1. INFLUENCE OF VARIOUS FACTORS ON ANTIGEN *Vi* SYNTHESIS

Factor	Antigen *Vi*
Acriflavin 0·5 per cent	Absent
Acriflavin 0·1 per cent	Absent
Dinitrophenol 0·005 *M*	Present
Dinitrophenol 0·01 *M*	Present
Dinitrophenol 0·025 *M*	Absent
Malonic acid 0·005 *M*	Present
Malonic acid 0·010 *M*	Present
Malonic acid 0·025 *M*	Absent
Potassium cyanide 0·005 *M*	Absent
Vacuum	Absent
Carbon dioxide	Absent
Ultra-violet irradiation	Present
Chloromycetin	Present
Control	Present

In higher concentrations they grow as a sediment on the bottom of the vessel. Centrifuged and transferred into fresh media, the micro-organisms are lysed almost completely within 0–30 min. (from optical density 0·3 to 0·02). Plating of a thick suspension grown in 0·25 *M* malonic acid produces only a few dozen colonies from 1 ml. The factors responsible for lysis of the bacteria grown in a malonate medium are not yet known. The possible presence in the cells of a prophage seems unlikely to be the cause, in view of the rapid rate of lysis. The few surviving micro-organisms yield a large percentage (20–40 per cent) of colonies producing no antigen *Vi* and immune to *Vi* phages, but still susceptible to typhus *O* phages.

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Late Effects of Gamma Radiation on Mice protected with Cysteamine or Cystamine

THE short-term value of cysteamine (β-mercaptoethylamine) and its disulphide (cystamine) as protective agents against whole-body irradiation is now well established[1]. Little is known, however, about the ultimate fate of the survivors from the radiation syndrome. This communication is concerned with the induction of lymphosarcoma and lymphatic leukæmia by cobalt-60 in *C* 57 *BL*/6 mice protected with one of these substances.

A total of 553 mice of both sexes, aged 38 ± 3 days, was randomly assigned to four treatment groups receiving different total doses in two exposures five days apart. Before each exposure, mice of the protected group received an intraperitoneal injection of cysteamine (3 mgm./10 gm.) or a gastric instillation of cystamine (4 mgm./10 gm.). Irradiated mice of the control group similarly received saline. In two other control groups, mice received cysteamine or cystamine but were not irradiated. The 50-day protection afforded by these compounds under the experimental conditions was significant[2].

Evaluation of the long-term protection, however, has brought up other problems. Survivors in all groups have been observed for a period of 300 days after the first exposure. Incidence of tumours in all groups has been tabulated (Table 1). In the group receiving 703 r. total dose, seven mice died prematurely from a late post-irradiation infectious and necrotic process. Numerous disseminated and confluent caseous lesions were found in lungs, liver and kidney. Therefore results on tumours from this group are not statistically significant. In the group receiving 301 r. total dose, the percentage of tumours approached the level expected in the controls. According to Kaplan[3], the threshold for tumour induction by single exposure to X-radiation is about 283 r. At both other dose-levels, however, incidence