

material was obtained. This crystalline material obtained from rabbits has proved to be non-carcinogenic for 9 mice that have been under observation 6 months after injection. Nine litter-mate controls injected with the same amount of dibenzanthracene have developed tumors. This observation suggests that in certain animals an immunity to carcinogenesis by chemicals depends upon the ability to convert the carcinogen from a neutral to a phenolic compound.

Summary. From the extracts of excreta of rabbits, rats, and mice injected with 1,2,5,6-dibenzanthracene, substances of a phenolic nature were isolated which are considered to be conversion products of dibenzanthracene. The substance isolated from injected rabbits was non-carcinogenic and gave absorption bands different from those of the substance obtained from injected rats and mice. This fact suggests that different species metabolize dibenzanthracene differently. The absorption bands of unchanged dibenzanthracene were present in the fraction containing neutral compounds of feces of injected rats, mice, and *rarely* of rabbits.

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A "Sulfapyridine-Fast" Strain of Pneumococcus Type I.

COLIN M. MACLEOD AND GIUSEPPE DADDI. (Introduced by O. T. Avery.)

From the Hospital of the Rockefeller Institute for Medical Research, New York.

Sulfapyridine exerts *in vitro* a bacteriostatic effect on the pneumococcus under aerobic conditions. It was of interest to determine whether a strain of this organism could be adapted to growth in increasing concentrations of the drug and so become "sulfapyridine-fast." The acquisition of "sulfapyridine-fastness" by a strain of pneumococcus has been reported recently by Maclean, Rogers, and Fleming.¹

A mouse-virulent strain of pneumococcus Type I (SV-I) was used in the present experiments. The stock solutions of sulfapyridine were made by dissolving the drug in N/10 HCl, diluting with distilled water and neutralizing with N/10 NaOH. The dilutions of sulfapyridine in 2% serum-broth were stored in the ice-box.

tive isolated from rabbits' urine. The shape of the curve and the positions of the maxima and minima are identical with those of the absorption curve of the phenolic derivative isolated by us from rabbits.

¹ Maclean, Rogers, and Fleming. *Lancet*, 1939, **1**, 562.

The strain of pneumococcus was transferred serially in serum-broth containing sulfapyridine, beginning with a concentration of 1:160,000 and increasing gradually to a concentration of 1:16,000. By this process the pneumococcus became adapted to growth in relatively high concentrations of sulfapyridine.

Throughout the period of adaptation no alteration in the morphology of the organism was apparent; the colonies on blood agar were smooth, and no change in its specific immunological characteristics was demonstrated.

After 33 transfers in serum-broth containing sulfapyridine, the strain which had become tolerant to high concentrations of the drug *in vitro*, was tested in experimental infections of mice to determine whether "sulfapyridine-fastness" could be demonstrated *in vivo* as well.

In Table I are shown the results of an experiment in which mice were infected intraabdominally with the "drug-fast" strain and treated with sulfapyridine, as compared with the results observed when the parent strain of pneumococcus was used under similar conditions.

TABLE I.
Results of Treatment with Sulfapyridine of Mice Infected with Parent Strain and "Sulfapyridine-fast" Strain of Pneumococcus Type I.*

| Strain of pneumococcus Type I | Infecting dose cc of culture | Treatment with sulfapyridine | Result | | |
|--|---------------------------------|---------------------------------|--------|---|----|
| SV-I Parent strain | 10-2 | 3 doses, 30 mg, 2 days | S | S | D† |
| | | | S | S | D |
| | | | S | S | D |
| | 10-2 | 4 " 30 " 3 " | S | S | S |
| | | | S | S | S |
| | | | S | S | S |
| | 10-7 | 0 | D | | |
| | 10-8 | 0 | D | | |
| SV-I/P/43 "Sulfapyridine-fast" strain | 10-2 | 3 " 30 " 2 " | D | D | D |
| | | | D | D | D |
| | | | D | D | D |
| | 10-2 | 4 " 30 " 3 " | D | D | D |
| | | | D | D | D |
| | | | D | D | S |
| | 10-7 | 0 | D | | |
| | 10-8 | 0 | D | | |
| | | | D | | |
| | | | S | | |

*All mice were injected intraabdominally. The drug was administered by stomach-tube in 30 mg doses. The first dose was given immediately following infection, the second five hours later. Subsequent doses of 30 mg each were given at daily intervals.

†D indicates death; S indicates survival.

Six out of 9 mice infected with the parent strain (SV-I) survived when treated with sulfapyridine for 2 days, a total of 90 mg being given. However, all of the mice died which were infected with the "sulfapyridine-fast" strain, (SV-I/P/43) and treated with sulfapyridine for 2 days. In other groups of mice sulfapyridine was given over a period of 3 days, the total amount of drug administered being 120 mg. All of the treated mice which were infected with the parent strain survived, whereas all but one of the mice died after infection with the "sulfapyridine-fast" strain and similar treatment with sulfapyridine.

The "sulfapyridine-fast" strain retains the typical lanceolate form and is gram-positive. There is no evidence of dissociation to the rough phase and its virulence for mice is unimpaired. Likewise it retains its specific immunological characteristics. It shows the typical "quellung" phenomenon in Type I antipneumococcal rabbit serum and is agglutinated specifically by Type I antiserum. Mice infected with the "drug-fast" strain are protected by Type I antiserum, and mice immunized with the parent strain are resistant to infection with the drug-fast strain.

The acquisition of "sulfapyridine-fastness" by pneumococcus Type I under these circumstances appears to be relatively permanent. After 30 serial transfers in broth not containing the drug, sulfapyridine-fastness was retained. Similarly fastness was still present after 10 passages in untreated mice.

Summary. A strain of pneumococcus Type I has been made "sulfapyridine-fast" by repeated transfers in broth containing increasing concentrations of sulfapyridine. "Sulfapyridine-fastness" is demonstrable both *in vitro* and *in vivo*. The alteration is not associated with changes in morphology, virulence, or specific immunological characteristics.