attack them. If this is so, the failure of the 'D-polypeptide' studied by Gill *et al.* to stimulate antibody formation may be the result of its presence at a concentration corresponding to antigen excess. I conclude that there is probably no inherent reason why antibodies could not be formed to 'D-polypeptides', and by changing the experimental conditions slightly it should be observable.

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## Suppression of Immune Response by 'Vincristine' and 'Vinblastine'

Chemical suppression of immunological responsiveness has been achieved in recent years by several classes of compounds. In particular, the alkalating agents[1], the antipurines[2] and the folic acid antagonists[3] have been effective chemicals. However, since none of these drugs has offered complete suppression under conditions of clinical trial, the discovery of new classes of chemicals which inhibit immune reactions remains an important objective. The double indole-indoline alkaloids[4] 'Vincristine' (vincristine sulphate) and 'Vinblastine' (vincaleukoblastine sulphate) were isolated from the common periwinkle plant *Vinca rosea* by two groups of investigators working independently[5,6]. Since these compounds have been effective growth inhibitors of a variety of lymphoid neoplasms[7–9], it appeared worth while to investigate their effects on immune responses. This communication reports inhibition of antibody formation and delayed hypersensitivity to bovine serum albumin in rats following administration of the two drugs.

Inbred male rats of the Fischer strain weighing 125–150 g were immunized by the injection of crystalline serum albumin (0·5 mg in 0·1 ml. of complete Freund's adjuvant) in one hind-foot pad. The animals were treated by the daily intraperitoneal injection of 'Vinblastine' or 'Vincristine' for 21 days beginning on the day of immunization. On the 7th, 14th, 21st and 28th days after immunization the animals were bled from the tail for antibody measurement by the tanned sheep cell hæmagglutination technique[10], and were tested for delayed hypersensitivity by the injection of 30 μg of bovine serum albumin in 0·1 ml. of saline into the shaved flank[11].

Table 1 indicates that 'Vincristine' at the 0·100 and 0·200 dose-levels, and 'Vinblastine' at the 0·200 dose-level, completely inhibit both antibody formation and delayed hypersensitivity to bovine serum albumin. Lower levels of drug caused partial suppression of immune response to this protein antigen. 'Vincristine' is well tolerated even at the higher dose-levels, experimental animals gaining weight during the period of administration (though the gain in weight is somewhat less than untreated controls). On the other hand, 'Vinblastine' at the higher dose-level is more toxic and fatalities are observed if the animals are not weighed daily and occasional doses of the drug omitted when undue loss in weight is observed. It will be noted that a close parallel exists between depression of antibody formation and delayed hypersensitivity for a particular animal.

The finding of a new class of compounds which inhibit immune responses at relatively non-toxic levels is of interest. Whether 'Vinblastine' or 'Vincristine' will prove valuable as experimental or clinical tools cannot be predicted at the present time. Their ability to inhibit the growth of a variety of human lymphoid neoplasms is a hopeful omen. Preliminary investigations indicate that in the rat it is possible to suppress both the development of hypersensitivity to tuberculin and the established hypersensitivity to tuberculin and bovine serum albumin, and also to influence the homograft reaction. However, these effects have been possible only at considerably greater toxicity than that needed for the suppression of responsiveness to bovine serum albumin reported in the present communication. Experiments on these other aspects of the immune inhibitory effects of 'Vincristine' and 'Vinblastine' are in progress in this laboratory.

Table 1. Effect of 'Vincristine' and 'Vinblastine' on Antibody Formation and Delayed Hypersensitivity to Bovine Serum Albumin

| Rat No. | Drug (dosage*) | Antibody formation† | | | | Delayed hypersensitivity‡ | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Day 7 | Day 14 | Day 21 | Day 28 | Day 7 | Day 14 | Day 21 | Day 28 |
| 1 | None | 7 | 8 | 9 | 11 | 0 | 8 | 9 | 12 |
| 2 | None | 0 | 7 | 9 | 10 | 2 | 4 | 10 | 10 |
| 3 | None | 0 | 7 | 7 | 9 | 3 | 4 | 10 | 14 |
| 4 | 'Vincristine' (0·025) | 0 | 5 | 7 | 11 | 0 | 6 | 7 | 10 |
| 5 | 'Vincristine' (0·025) | 0 | 5 | 6 | 9 | 0 | 2 | 9 | 11 |
| 6 | 'Vincristine' (0·025) | 0 | 4 | 8 | 9 | 0 | 4 | 5 | 14 |
| 7 | 'Vincristine' (0·050) | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 2 |
| 8 | 'Vincristine' (0·050) | 0 | 0 | 6 | 8 | 0 | 0 | 6 | 11 |
| 9 | 'Vincristine' (0·050) | 0 | 6 | 5 | 8 | 0 | 3 | 0 | 12 |
| 10 | 'Vincristine' (0·100) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 11 | 'Vincristine' (0·100) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 12 | 'Vincristine' (0·100) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 13 | 'Vincristine' (0·200) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 14 | 'Vincristine' (0·200) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 'Vincristine' (0·200) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 16 | 'Vinblastine' (0·100) | 0 | 5 | 7 | 8 | 0 | 3 | 6 | 13 |
| 17 | 'Vinblastine' (0·100) | 0 | 7 | 6 | 9 | 2 | 3 | 5 | 12 |
| 18 | 'Vinblastine' (0·100) | 2 | 3 | 5 | 8 | 2 | 3 | 6 | 12 |
| 19 | 'Vinblastine' (0·200) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20 | 'Vinblastine' (0·200) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

* Drugs were administered daily by intraperitoneal route for 21 days beginning on the day of immunization, except for 'Vincristine' (0·200), which was given on the first three days and then on alternate days. Dosage is expressed as mg/kg/day.
† Antibody formation was measured on days 7, 14, 21 and 28 after immunization and is expressed as the highest tube with hæmagglutination of bovine serum albumin–tanned sheep cells.
‡ Delayed hypersensitivity was measured on days 7, 14, 21 and 28 and is expressed as average diameter of induration of the 24-h skin reaction.

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## RADIOBIOLOGY

### Photo-reactivation after Division II

It was reported earlier that in a strain of *Tetrahymena pyriformis* grown in this laboratory the lethal effect of ultra-violet light could be photo-reactivated even after the irradiated individuals had divided once or twice[1]. There are several ways in which this phenomenon might be used to elucidate the lethal action of ultra-violet light.