cythemia is produced. No significant difference in this respect could be demonstrated between cobalt when administered as the glutamate or the nitrate.

Summary. Cobalt (0.5 mg.), as cobalt glutamate and as cobalt nitrate, produces a polycythemia in young rats, when fed as a supplement to a whole milk (klim)-iron-copper diet. The animals receiving cobalt glutamate showed the same growth as the control groups, while that of the cobalt nitrate group was retarded.

7301 C

The Haptene-Protein Complex in Canine Anaphylaxis.

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Recent studies of specific allergic and immune reactions against artificial protein-crystalloid conjugates have suggested that the superficial crystalloids of a protein molecule are the essential units of specific antigenicity. If so, the whole theory of specific immunity must be rewritten in terms of sub-colloidal antigenic "determinants".

Most of these studies, however, are inconclusive. This is due in part to the high haptene-protein ratios almost invariably used. In many cases the conjugates were "carriers" of no less than 150 to 200 haptene "determinants".[1] Moreover, from the point of view of clinical medicine, both rabbit antiserum and guinea pig anaphylaxis distort the quantitative perspective. We have, therefore, repeated some of the classical tests, using haptene-protein complexes of relatively low ratios, with dogs as the experimental animals.

The proteins used in this work were horse serum (HS), cow serum (CS), dog serum (DS), egg white (EW) and crystallized excelsin (Ex). Conjugation was made with benzoyl (Bz) and benzene-sulfonyl (Su) radicals, the quantitative relationships being such as to give final products with an average of from 25 to 40 haptene groups per protein molecule. This represents an approximate 20% haptene saturation.

Dogs were sensitized by a single intracardial injection of 40 mg.

[1] Kurtz, A. C., Sox, H. C., and Manwaring, W. H., PROC. SOC. EXP. BIOL. AND MED., 1932, **30**, 138.

protein per kg. of body weight. This is the optimum sensitizing dose with HS. Anaphylactic tests were made 3 weeks later, the routine shock dose being 80 mg. protein by kg. of body weight injected intravenously. This is about 10 times the minimum shock dose with HS.

Fully 95% of all dogs become demonstrably hypersensitive after a single intracardial injection with HS and fully 75% with CS. In contrast with this, the percentage of successful sensitizations with BzHS, BzCS, SuHS, and SuCS was little more than 30%. Of the 37 dogs injected with these conjugates but 12 became demonstrably hypersensitive. BzEW, BzDS, and BzEx are apparently without sensitizing power for dogs.

Discarding 25 dogs which failed to become demonstrably hypersensitive following routine injection with haptene-conjugates, haptene and "carrier" cross-reactions were tested with 6 dogs. But 2 (33 1/3%) of these dogs gave definite (+ or ++) cross-reactions,

TABLE I.

Haptene and "Carrier" Cross-Reactions in Canine Anaphylaxis.

Severity of the anaphylactic reaction was judged from kymograph records: +, ++, +++ representing non-fatal shocks; ++++ recording lethal anaphylaxis.

Sensitizing antigen	Anaphylactic test		Retest with original antigen
	Antigen	Severity	
BzCS	BzDS	+	+++
BzHS	BzES	0	+++
BzHS	BzCS	±	0
BzHS	SuHS	++	0
BzHS	SuHS	0	++±
BzHS	SuHS	0	++

TABLE II.

"Carrier" Cross-Reactions with Native Proteins.

Sensitizing antigen	Anaphylactic test		Retest with original antigen
	Antigen	Severity	
HS	BzHS	+	0
HS	BzHS	+++	+++
HS	BzHS	0	++
HS	BzHS	0	++
HS	SuHS	0	+++
HS	SuHS	0	+++
HS	SuHS	+++	0
CS	BzCS	0	+
CS	BzCS	+	0
CS	BzCS	0	+++
CS	BzCS	+	++++

either with the haptene or "carrier" groups, in spite of the use of the decimultiple test dose. (Table I.)

Eleven "carrier" tests were made on dogs demonstrably hypersensitive to undenatured HS or CS (Table II). In but 5 (45%) of these dogs were "carrier" cross-reactions demonstrated with the decimultiple dose. But three (25%) of these "carrier" reactions demonstrably desensitized the dog to the homologous undenatured native protein.

The above data give a quite different quantitative perspective from that suggested by previous studies of haptene-saturated antigens and highly immunized or sensitized herbivorous animals.

7302 P

Differential Ovarian Responses After Injections of Follicle-Stimulating and Pregnancy Urine in Very Young Female Rats.*

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It has been reported by Collip *et al.* that P.U. extract injections begun on the 6th day of life cause a thecal hypertrophy after 10 injections. In 5 litters of rats (each composed of 4 treated and 1 control) we have injected, daily, an amount of extract of follicle-stimulating urine which will induce a marked response in hypophysectomized male and female rats. Injections continued from the 6th to the 11th day of life up to the 16th or 17th day did not induce any ovarian change so far as we have been able to determine. Neither ovaries nor uteri were increased in weight and the vaginae did not open. In a series autopsied on the 21st day of life there was an increased ovarian weight and a marked stimulation of the follicles, but no thecal hypertrophy. These results show a marked difference between the action of F.-S.U. and P.U. extracts. They also show that the gamete and granulosa must undergo some maturation change before they are capable of responding to the follicle-stimulating hormone.

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