Effect of Oxytetracycline and Tetracycline on Glucose Tolerance and Serum Lipids. (32161)

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We reported(1) impaired metabolism of carbohydrate and lipid in rats, rabbits and Rhesus monkey after treatment with pyrrolidinomethyl tetracycline. The purpose of the present investigation was to study the effect of administration of 2 other similar antibiotics, oxytetracycline and tetracycline, on glucose tolerance and on different fractions of serum lipids of rabbits and Rhesus monkeys.

Materials and methods. Male albino rabbits of average weight of 2 kg were used. After collecting fasting blood samples from the marginal ear vein for estimation of glucose(2) and serum lipids(3), an oral glucose tolerance test was performed(4). Each animals was subsequently given intramuscularly 20 mg of either oxytetracycline or tetracycline per day in two divided doses for 10 days. On the eleventh day after collecting the fasting blood sample for estimation of glucose and serum lipids, the glucose tolerance test was repeated.

Rhesus monkeys of average weight of 4 kg were used. After collecting fasting blood samples from the femoral vein an intravenous glucose tolerance test was performed(1). From the following day 40 mg of either oxytetracycline or tetracycline was injected daily in 2 divided doses for 10 days. Fasting blood sample was collected on the eleventh day and glucose tolerance test was repeated. Glucose was estimated in the different samples(2) and serum was used for estimation of different fractions of lipids(3). The dose of the drugs used simulated that usually used in a human adult.

Results. After treatment with oxytetracycline the following changes were noted. *Rabbits:* The fasting blood sugar level increased. Rise in the blood sugar level after glucose load was slower up to one hour, increased subsequently above normal and had not come to the basal level 3 hours after glucose feeding (Table I). In the serum total cholesterol, phospholipids, triglycerides, free fatty acids, β-lipoprotein cholesterol and β-lipoprotein percentage increased while α-lipoprotein percentage decreased (Table II). *Monkeys:* Blood sugar levels at ½ and 1 hour after glucose load were higher, without any change in the fasting blood samples and samples collected 1½ and 2 hours after glucose (Table I). Triglycerides, free fatty acids, β-lipoprotein cholesterol and β-lipoprotein percentage of serum increased without any significant change in the total cholesterol and phospholipids of serum (Table II).

After treatment with tetracycline the following changes were observed. *Rabbits:* Blood sugar levels at 1½ and 3 hours after glucose load were higher, without any change in the fasting blood samples, and samples collected 45 minutes and 135 minutes after glucose (Table I). In the serum total cholesterol, phospholipids, triglycerides, free fatty acids, β-lipoprotein cholesterol and β-lipoprotein percentage increased (Table II). *Monkeys:* Blood sugar levels 1½ and 2 hours after glucose load were higher, without any change in the fasting blood samples and samples collected ½ and 1 hour after glucose (Table I). In the serum phospholipids, triglycerides and β-lipoprotein percentage increased while α-lipoprotein percentage decreased.

Discussion. Prolonged use of both oxytetracycline and tetracycline in rabbits and monkeys induced defective utilization of glucose. They also produced profound changes in the serum lipids. The alteration of carbohydrate metabolism after the use of antibiotics has been attributed to the suppression of the anaerobic phase(5). Chlortetracycline inhibited phosphorylation associated with oxidation of Krebs cycle substrates under certain conditions(6). The uncoupling of oxidation from phosphorylation might be due to the formation of Mg-tetracycline complex which is the uncoupling agent or due to the reaction of tetracycline with the Mg^{++} bound with the enzyme without actually removing it

(7). Succinic dehydrogenase is inhibited by oxytetracycline(8) and chlortetracycline(9). It may be possible that the diminished utilization of glucose after treatment with the different tetracyclines observed by us is due to above mentioned associated defects.

The changes in the pattern of serum lipids observed in the present investigation are due to the factors discussed previously(1). The changes had been comparable to those observed by us after arministration of pyrrolidinomethyl tetracycline(1). As tetracyclines

TABLE I. Glucose Tolerance Test in Animals Before and After Treatment with Oxytetracycline or Tetracycline.

		Fasting blood sugar (mg/100 ml)	Rise in blood sugar (mg/100 ml) from fasting level Min after administration of glucose 30	45	60	90	120	135	180
			After intramuscular injection of oxytetracycline, 10 mg/kg/day, for 10 days						
Rabbits (7)	B+	111 ± 5		75 ± 12		96 ± 12		67 ±13	3 ± 2
(glucose, 2 g/kg,	A+	136 ± 3		86 ± 10		96 ± 10		81 ± 8	38 ± 5
fed)	*t*	4.57*		1.87		—		2.91*	6.94*
Monkeys (7)	B+	103 ± 31	144 ± 11		54 ± 10	2 ± 2	—10 ± 3		
(glucose, 1 g/kg,	A+	96 ± 7	168 ± 6		70 ± 4	7 ± 8	— 2 ± 1		
intravenously)	*t*	.22	2.0*		2.12*	.57	1.9		
			After intramuscular injection of tetracycline, 10 mg/kg/day, for 10 days						
Rabbits (6)	B+	131 ± 5		67 ± 12		134 ± 10		56 ± 8	—8 ± 2
	A+	127 ± 5		91 ± 9		179 ± 10		50 ± 9	38 ± 4
	t	.49		1.56		3.18*		.50	10.27*
Monkeys (5)	B+	109 ± 9	183 ± 9		92 ± 13	16 ± 7	—3 ± 5		
	A+	119 ± 11	201 ± 10		86 ± 16	50 ± 19	29 ±13		
	t	.69	1.39		.29	2.69*	2.35*		

Values = Mean ± S.E. Figures in parentheses indicate No. of animals.
* Significant at 5% level. B+, before treatment; A+, after treatment.

TABLE II. Different Fractions of Serum Lipids in Rabbits and Rhesus Monkeys Before and After Treatment with Oxytetracycline or Tetracycline.

Serum lipids		Before treatment with antibiotic	After intramuscular inj of antibiotic 10 mg/kg/day for 10 days	*t*	Before treatment with antibiotic	After intramuscular inj of antibiotic 10 mg/kg/day for 10 days	*t*
		Oxytetracycline					
		Rabbits (7)			Monkeys (7)		
Cholesterol (mg/100 ml)		33 ± 1	37 ± 1	2.0 *	131 ± 8	119 ± 7	1.09
Phospholipids (")		66 ± 1	90 ± 5	3.49*	186 ±10	206 ±12	1.33
Triglycerides (")		58 ± 4	103 ± 9	4.79*	81 ± 5	129 ± 6	6.16*
Free fatty acids (μEq/l)		416 ±97	3319 ±123	19.36*	336 ±31	533 ±28	4.71*
β-lipoprotein cholesterol (mg/100 ml)		22 ± 1	32 ± 2	4.47*	54 ± 4	68 ± 4	2.43*
Lipoproteins (%)	α	29 ± 2	24 ± 1	2.2 *	34 ± 1	26 ± 1	7.43*
	β	71 ± 2	76 ± 1	2.0 *	66 ± 1	74 ± 1	5.94*
		Tetracycline					
		Rabbits (6)			Monkeys (7)		
Cholesterol (mg/100 ml)		32 ± 1	57 ± 4	5.63*	130 ± 8	117 ± 4	1.36
Phospholipids (")		64 ± 5	93 ± 4	4.33*	192 ± 6	217 ± 8	2.61*
Triglycerides (")		69 ± 1	115 ± 11	4.05*	99 ± 1	118 ± 5	4.66*
Free fatty acids (μEq/l)		429 ±72	2582 ±250	9.04*	211 ±44	240 ±61	.38*
β-lipoprotein cholesterol (mg/100 ml)		20 ± 1	41 ± 5	4.29*	47 ± 2	53 ± 8	.72*
Lipoproteins (%)	α	26 ± 1	19 ± 3	5.19*	37 ± 2	28 ± 3	2.99*
	β	74 ± 2	81 ± 1	4.33*	63 ± 2	72 ± 1	4.24*

Values = Mean ± S.E. Figures in parentheses indicate No. of animals. * Significant at 5% level.

produced profound changes in the metabolic pattern of the body, these antibiotics should not be used indiscriminately.

Summary. Oxytetracycline or tetracycline, 10 mg/kg, was administered for 10 consecutive days to rabbits and rhesus monkeys. Glucose tolerance test was performed and different fractions of serum lipids were estimated in these animals before and after treatment with the antibiotics to find if their prolonged use interfered with carbohydrate and lipid metabolism. Both antibiotics diminished glucose tolerance. The pattern of serum lipids was changed. There were increases in the serum triglycerides, phospholipids, β-lipoprotein cholesterol and free fatty acids in most of the animals after treatment with the antibiotics. Tetracyclines should be used with caution due to the metabolic disturbances they might produce.

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A Rapid Screening Method for Detection of T Antigens in Sera of Tumor-Bearing Hamsters.* (32162)

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Cells present in hamster tumors induced by papovavirus SV-40 contain new cellular antigens (tumor or T antigens). These T antigens were first discovered by *in vivo* immunity tests(1). Similar antigens have been found in hamster tumors induced by human adenoviruses(2). Hamsters bearing tumors induced by either SV-40 or by oncogenic human adenoviruses develop circulating antibody capable of reacting with their respective T antigens *in vitro*. The presence of T antigens in cells transformed *in vitro* and in cells infected with the virus during the early stages of viral replication has been demonstrated by the techniques of complement fixation (CF) and immunofluorescence by using sera from tumor-bearing hamsters(2-9). Good correlation between immunofluorescence and CF antigen titers has been reported(10).

Use of particles of lecithin and cholesterol as inert carriers of viral antigens in agglutination tests with specific antisera has been recently documented. We have modified the basic methods of Klein et al(11) to demonstrate antibody response to the T antigens of papovavirus SV-40 and human adenovirus type 31 by an agglutination technique. The reactions are type specific. Results obtained in screening sera from tumor-bearing hamsters for the presence of T antibodies by utilizing the agglutination technique compare favorably with those obtained by the CF technique.

Materials and methods. A. Tumor antigens. The SV-40 T antigens utilized were from

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