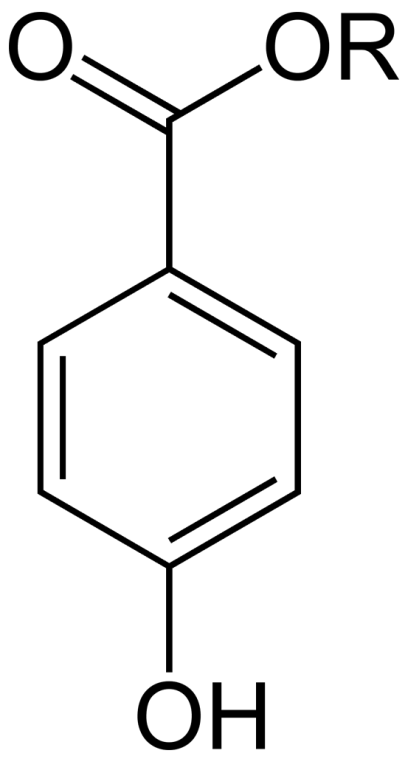
Small molecules like parabens

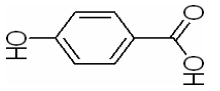
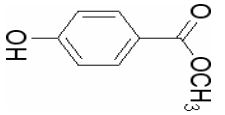
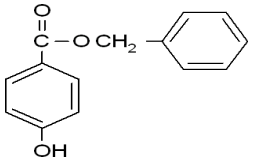
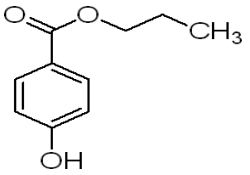
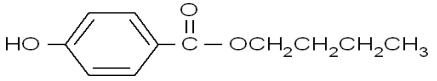
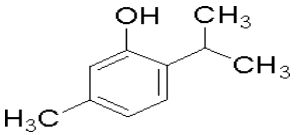
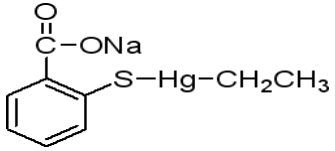
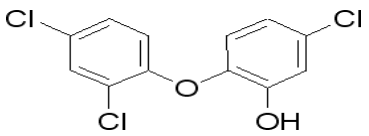
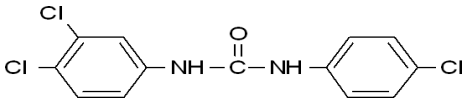
A New Type EDS?

What are “parabens”

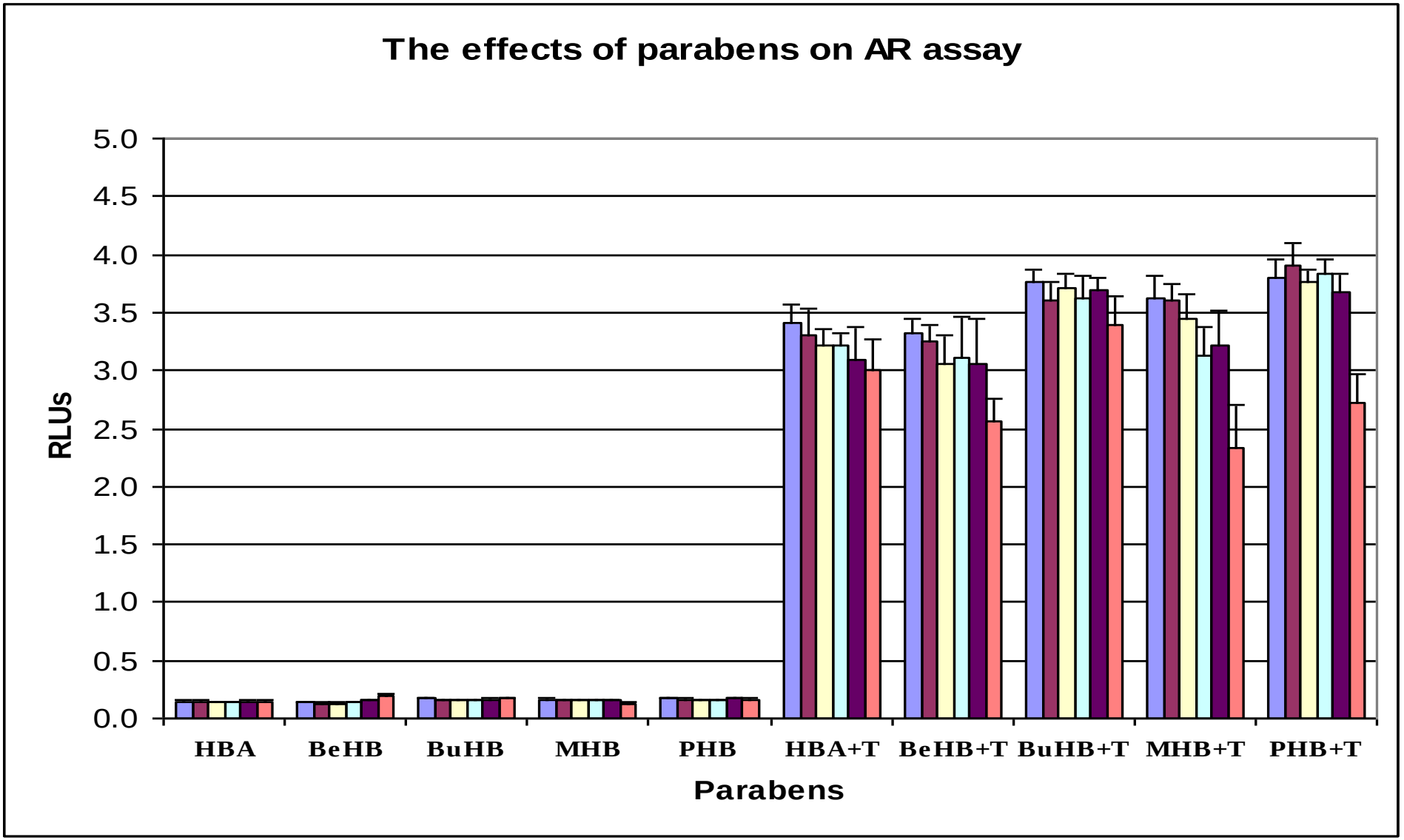


…small molecules used by cosmetic/personal care manufacturers as preservatives….

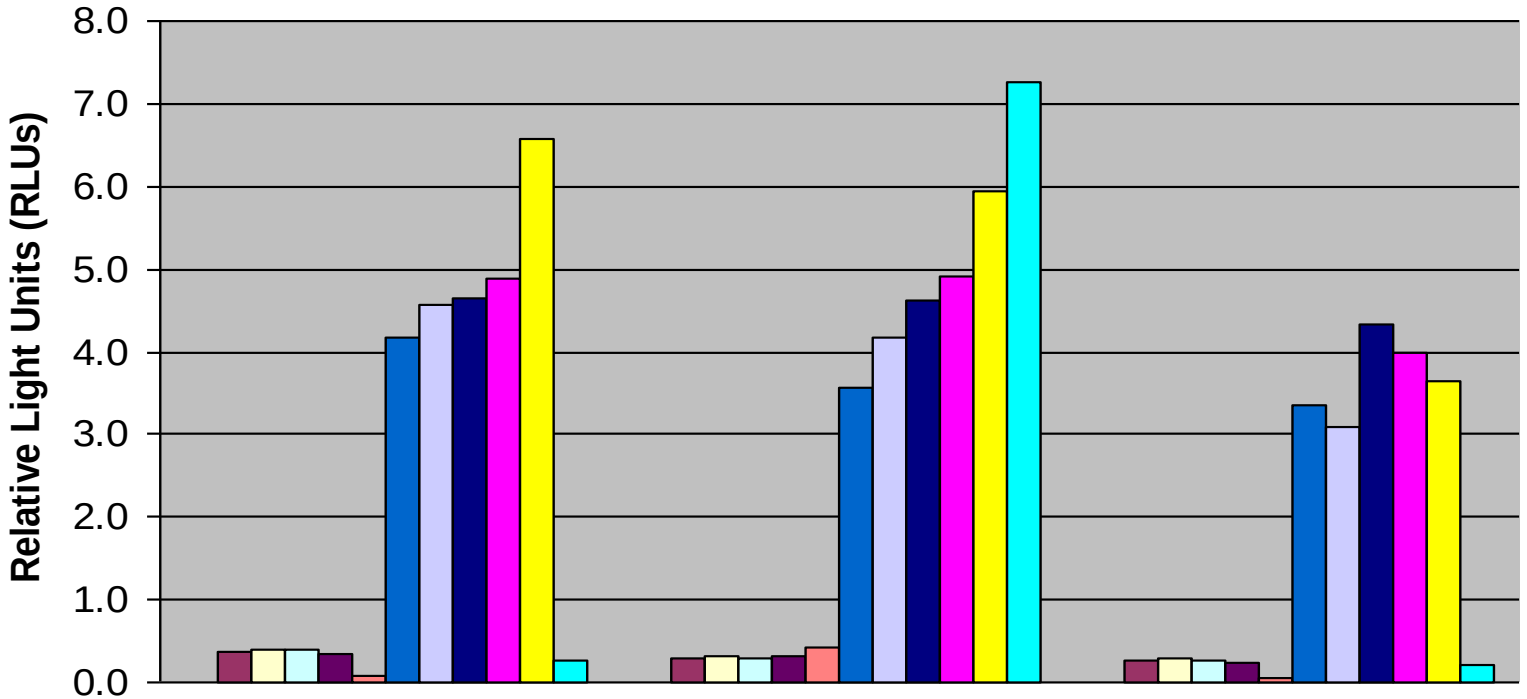
Table 1. The structures of tested antimicrobial and preservative compounds

ρ-hydroxybenzoic acid	
Methyl 4-hydroxybenzoate	
Benzyl 4-hydroxybenzoate	
Propyl 4-hydroxybenzoate	
Butyl 4-hydroxybenzoate	
Thymol	
Thimerosal	
Triclosan	
Triclocarbanilide	

Most parabens are weak antagonists



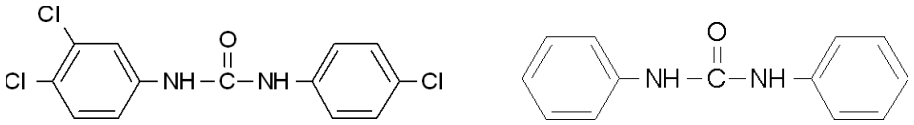
One group acts as “augmentors”



T (0.125 nM) - - - - - + + + + ++ - - - - - + + + + + + - - - - - + + + + ++

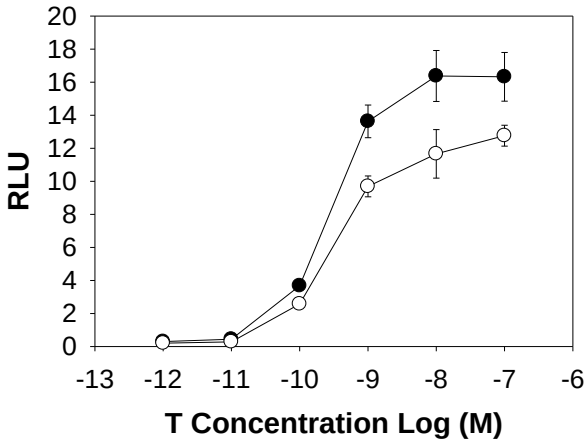
Compounds **Triclocarban** **Carbanilide** **CM-10.6-03**

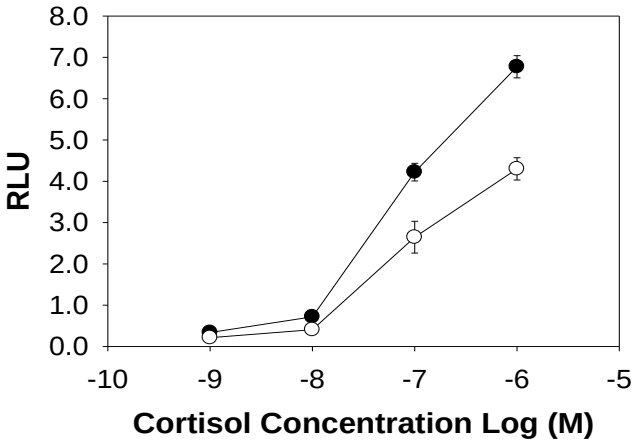
# of Chorine **3** **0** **4**

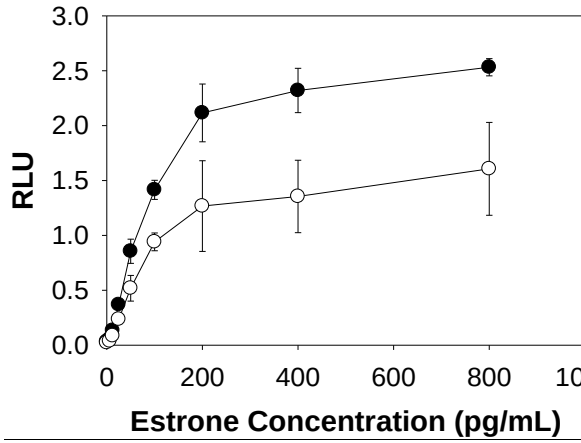


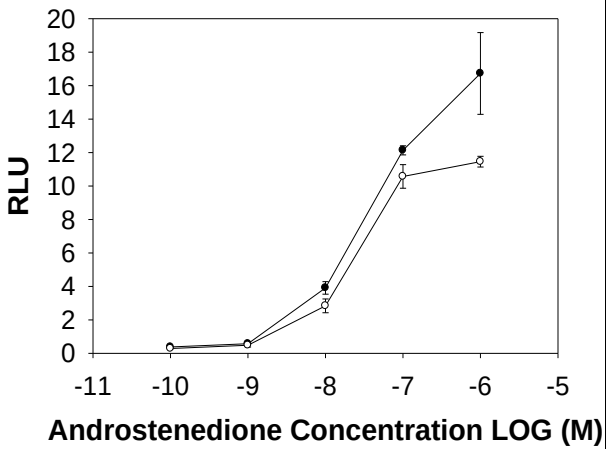
Concentrations from Low to high (0, 0.001, 0.01, 0.1, 1, 10 uM)

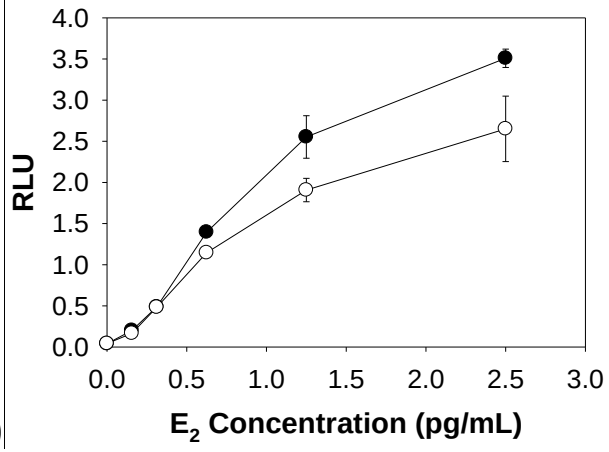
Signal Transduction Amplification of Native Ligands by TCC in Cell-based Bioassays

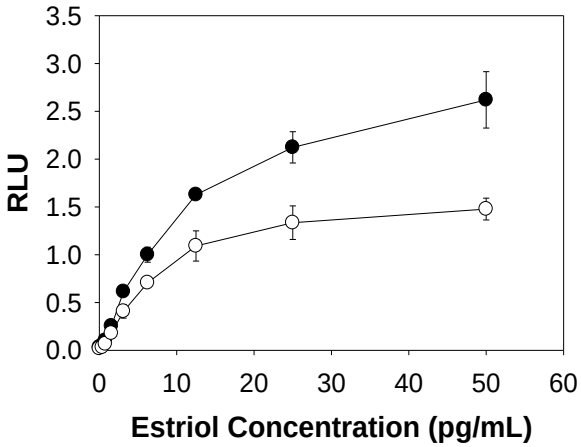












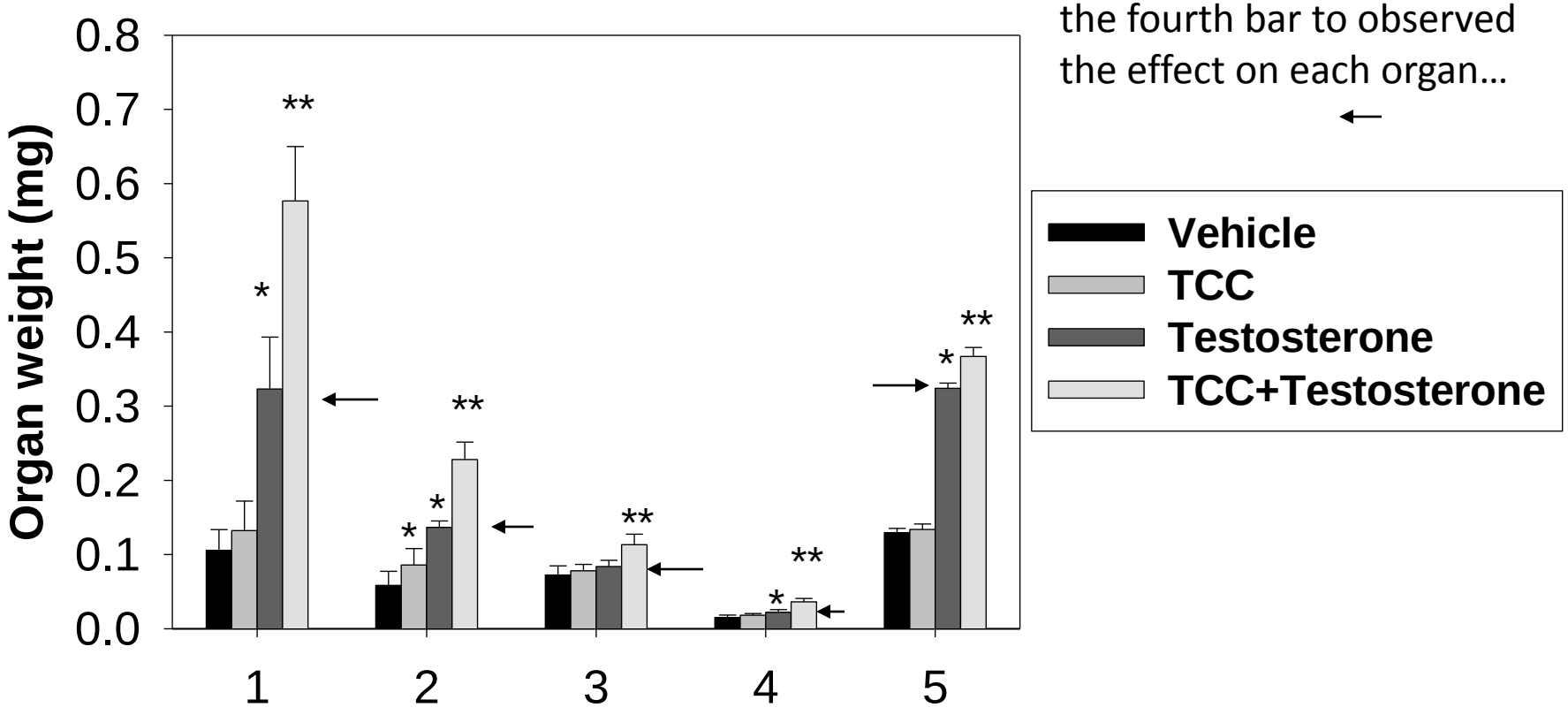
Variable	Weight (g)			Weight as percent of terminal body weight		

Table 1 Effect of TCC on weights of animals and individual organs; each value represents mean±SD of 12 rats per group

	Control	TCC	P-value	Control	TCC	P-value
Pre-treatment body Weight	226.7±20.9	223.2±14.9	0.64			
Post-treatment body Weight	293.7±11.7	308.8±18.8	0.028			
Liver	11.7±1.1	13.3±1.2	0.002	3.99±0.34	4.31±0.38	0.004
Kidney	2.74±0.27	2.94±0.26	0.08	0.93±0.07	0.95±0.10	0.54
Adrenal	0.080±0.016	0.081±0.012	0.82	0.027±0.005	0.026±0.004	0.73
Testes	2.82±0.19	2.82±0.20	0.99	0.96±0.07	0.92±0.08	0.16
Seminal vesicle	0.625±0.11	0.894±0.153	<0.0001	0.21±0.04	0.29±0.04	<0.0001
Ventral prostate	0.342±0.082	0.468±0.085	0.001	0.12±0.03	0.15±0.02	0.002
LABC	0.226±0.048	0.532±0.186	<0.0001	0.077±0.016	0.174±0.063	<0.0001
Glans penis	0.103±0.014	0.138±0.016	<0.0001	0.035±0.005	0.045±0.004	<0.0001

Effect of TCC treatment on sex accessory organ weight in castrate rats

Compare the third bar to the fourth bar to observed the effect on each organ…



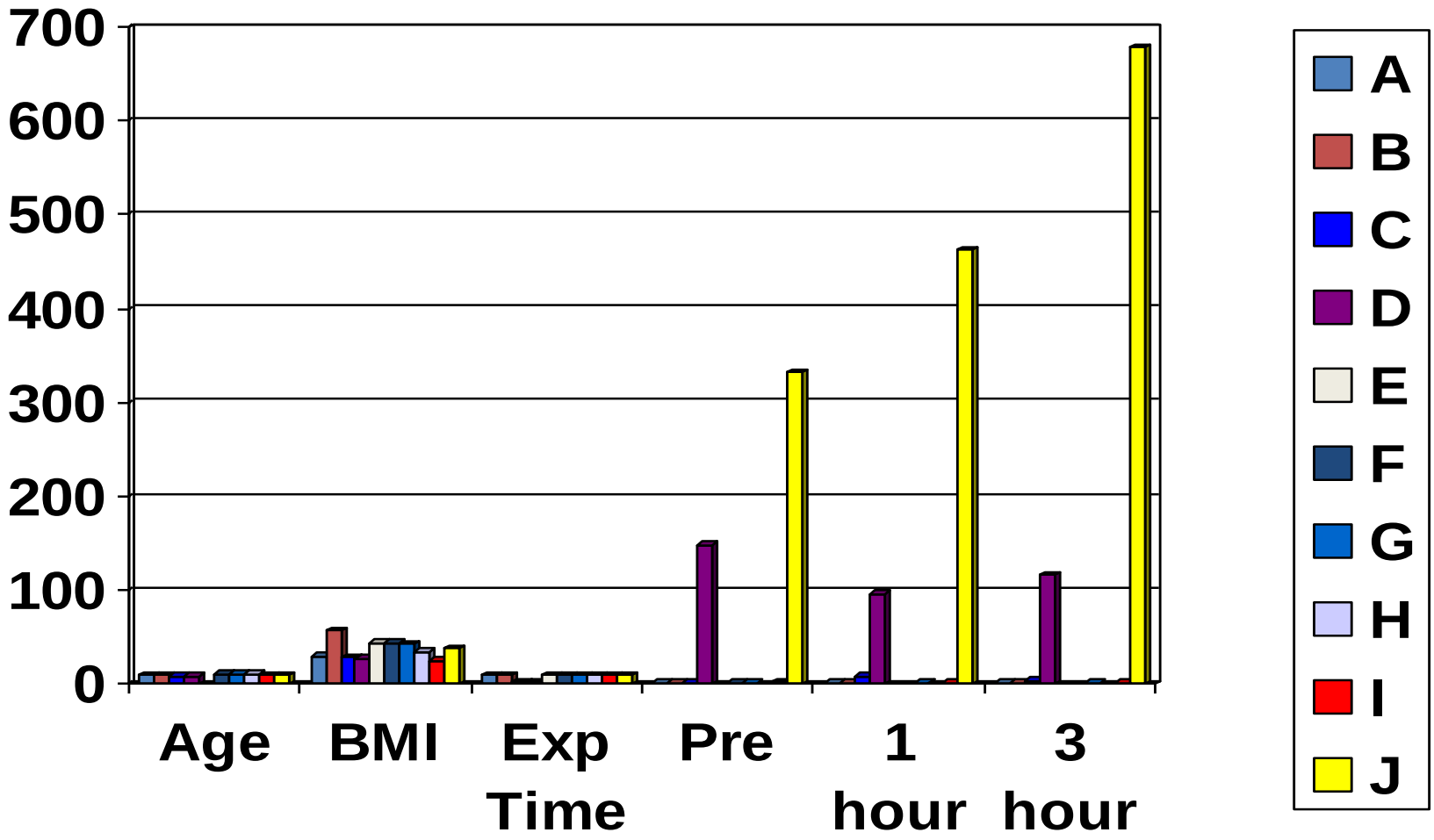
1. Seminal Vesicles 2. Ventral Prostate
3. Glans Penis 4. Cowper's Gland
5. Levator Anibulbocavenosus Mucles

Circulating TCC levels in Pediatric Subjects

	TCC (ng/mL)		
Subject	**Pre**	**Post-1h**	**Post-3h**
1	0.22	0.81	1.04
2	0.31	1.17	2.56
3	0.30	0.94	1.41
4	0.56	1.63	1.98
5	0.23	0.87	*39.32
6	0.65	2.39	*71.32
7	0.50	1.69	3.88
8	0.27	0.75	1.27
9	0.30	0.83	1.59
10	0.25	0.79	1.97
Mean±SD	0.36±0.15	1.19±0.55	12.63±23.7

Subjects were instructed to “lather up” and wait 10 minutes. Unfortunately, they all didn’t do that because it was too cold.

IL-10


700
600
500
400
300
200
100
0
Age
BMI
Exp Time
Pre
1 hour
3 hour
A
B
C
D
E
F
G
H
I
J

Maternal-fetal gradients in rats fed 0.5% TCC for ten days (GD 9-19)

TX	TCC (ng/mL)		
Rat ID	Amniotic Fluid	Fetal Serum/Fluid	Maternal Serum
2	1.83	17.96	3.86
3	2.83	22.43	3.97
5	4.07	18.90	7.44
6	9.49	15.99	10.74
8	8.67	27.69	37.13
10	13.27	33.05	24.87

C	TCC (ng/mL)		
Rat ID	Amniotic Fluid	Fetal Serum/Fluid	Maternal Serum
1	0.44	0.49	1.20
4	0.42	1.35	0.56
7	0.42	0.96	1.16
9	0.28	1.49	1.73