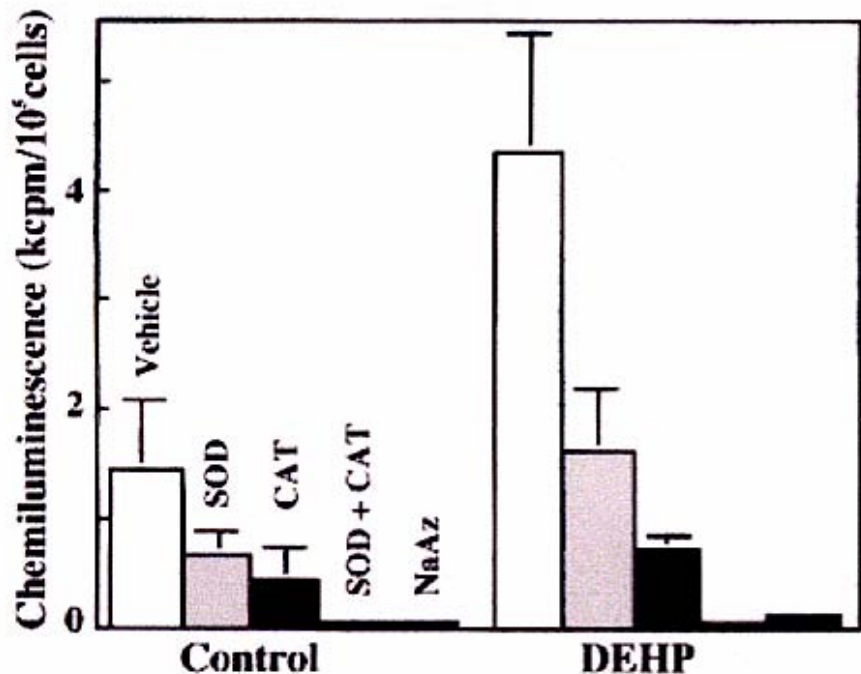
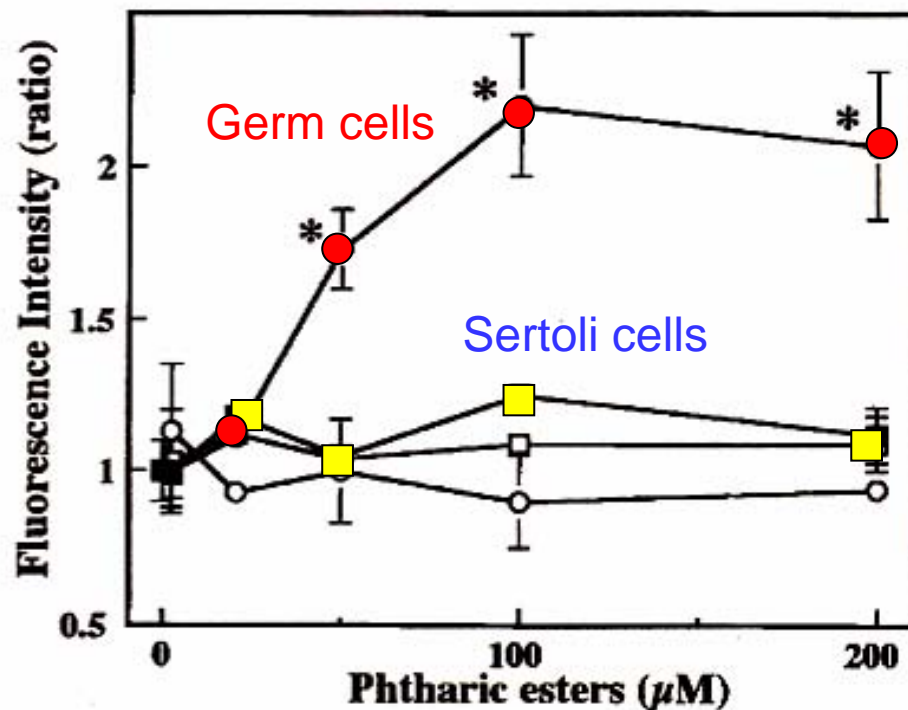


# Superoxide radical and H<sub>2</sub>O<sub>2</sub> in the germ cells are responsible for the increase of ROS



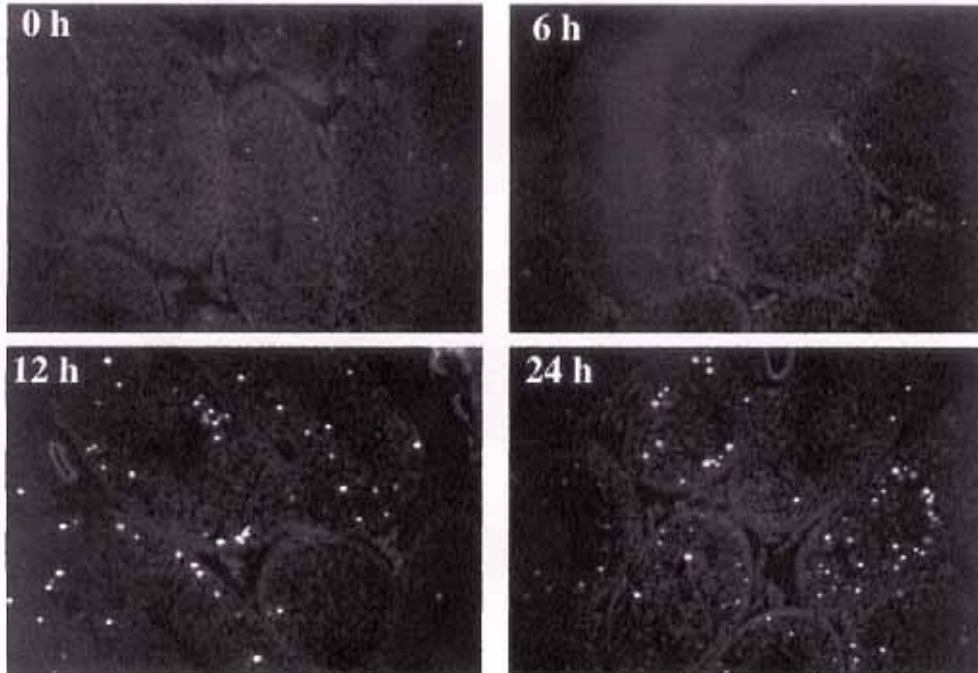
SOD: Cu/Zn-super oxide dismutase  
 CAT: Catalase



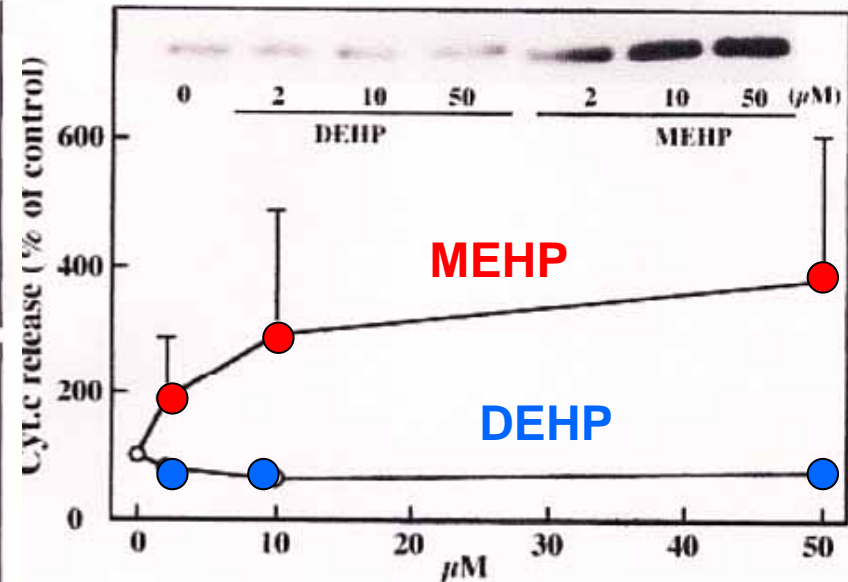
- Germ cells (MEHP treatment)
- Germ cells (DEHP treatment)
- Sertoli cells (MEHP treatment)
- Sertoli cells (DEHP treatment)

# Generation of ROS induces the apoptosis of germ cells

Tunnel staining of testis



Release of cytochrome C



- Tunnel staining shows apoptosis of **germ cells** but not Sertoli cells.
- Generation of ROS in germ cells leads to apoptosis of these cells within 12 hrs.
- **Release of cytochrome C, an apoptosis marker**, from mitochondria is enhanced in apoptotic germ cells.

# Summary 1

1. Oral administration of DEHP, when converted to MEHP, causes an increase of ROS production in testis.
2. ROS are mainly superoxide radicals and H<sub>2</sub>O<sub>2</sub>.
3. ROS production mainly occurs in germ cells not in Sertoli cells.
4. Oxidative stress causes apoptosis of germ cells.

# **Search for the materials protecting DEHP-induced atrophy of the testis**

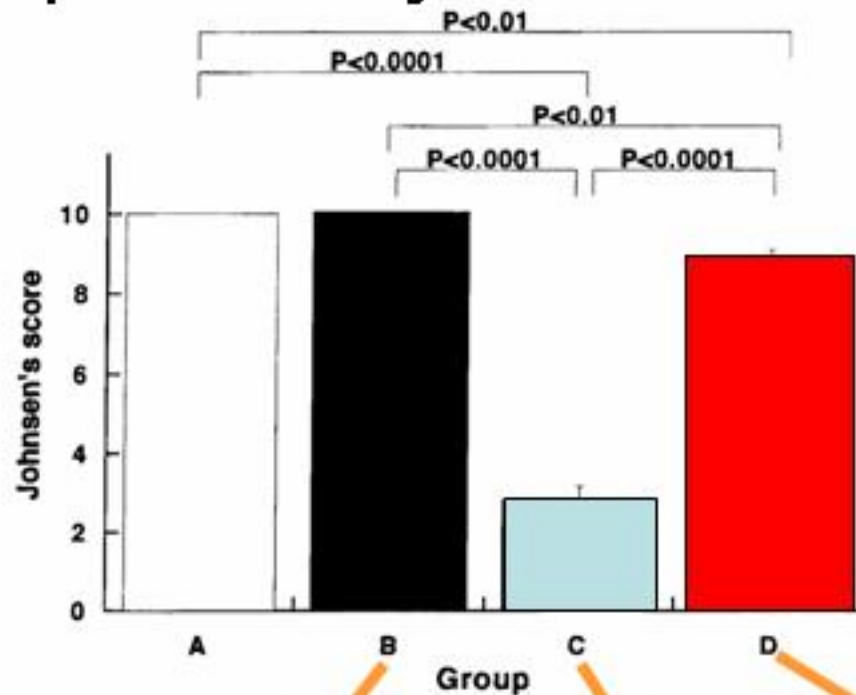
- 1) Safety (=natural resources)**
  - 2) Inexpensiveness**
  - 3) Easy and wide applicability**
- Food additives**



- 1) Vitamins C & E**
- 2) Various monosaccharides**
- 3) Others**

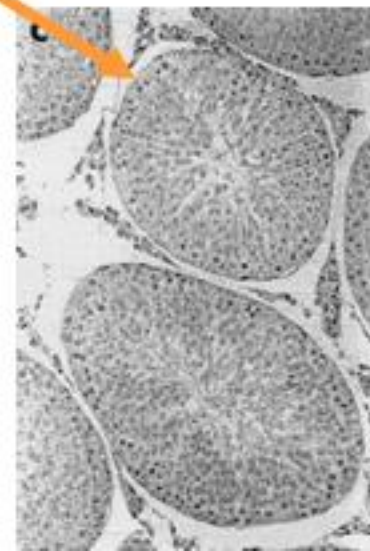
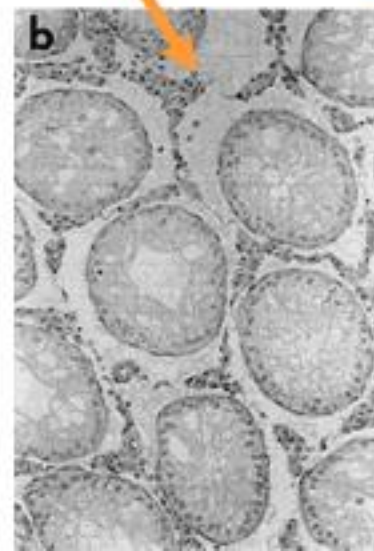
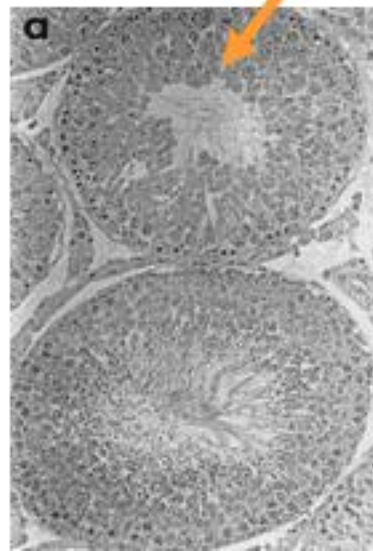
# DEHP-induced Spermatogenic disturbance is significantly prevented by treatment with antioxidant vitamins C and E

Int J Androl. 2000 Apr;23(2):85-94.



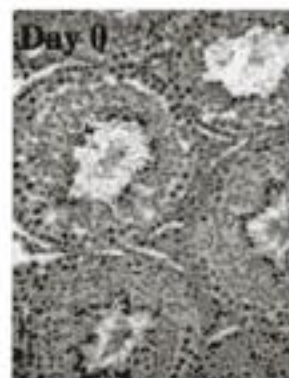
A: DEHP-free diet  
B: DEHP-free diet with vitamin-supplemented water (Vit C: Vit E=2:1)  
C: DEHP-containing diet  
D: DEHP-containing diet + vitamin-supplemented water (Vit C: Vit E=2:1)

Vitamin C: 500mg/kg/day  
Vitamin E: 250mg/kg/day

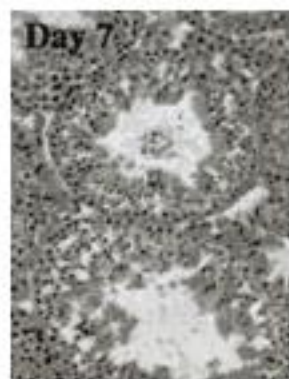


# Antioxidant vitamins supplementation accelerates regeneration of the seminiferous epithelium

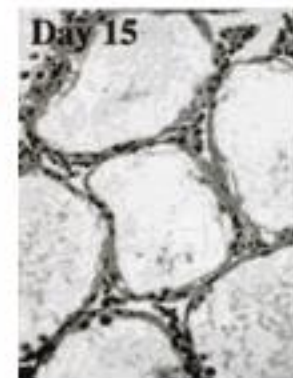
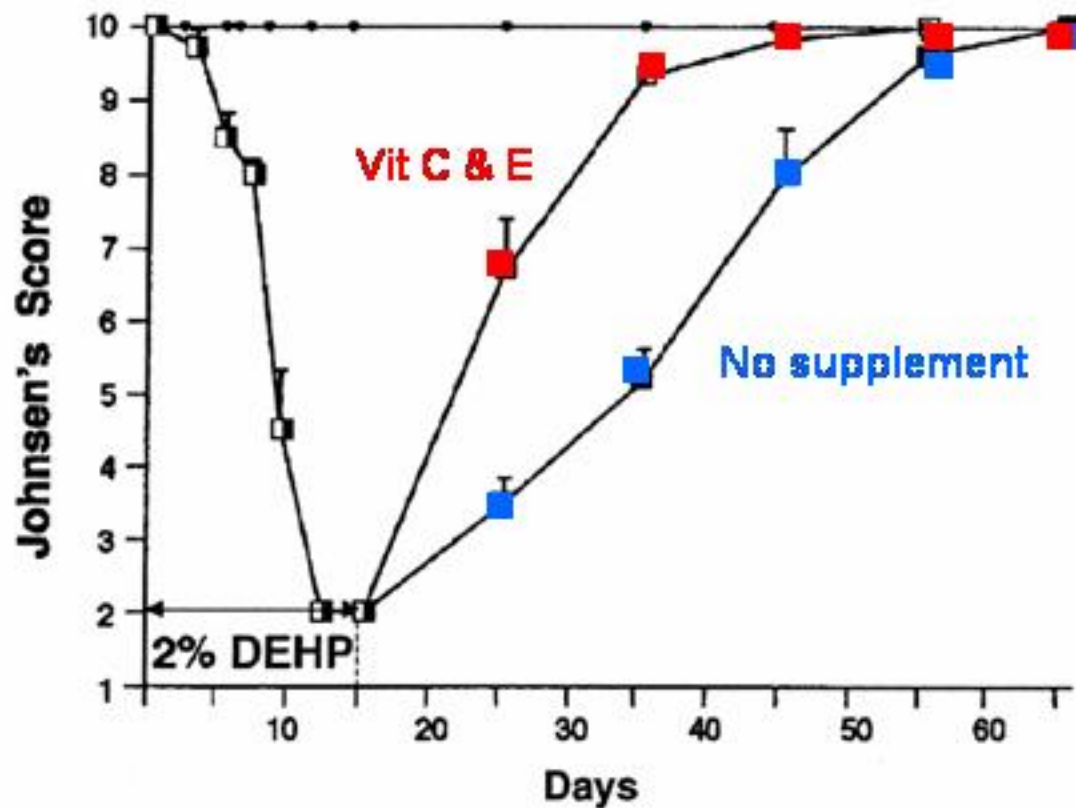
Int J Androl. 2004 Oct;27(5):274-81.



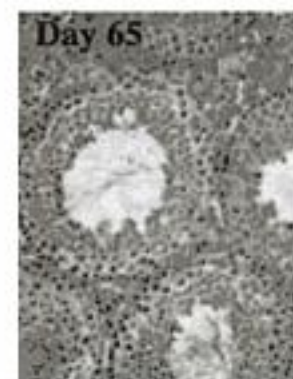
Day 0



Day 7



Day 15



Day 65