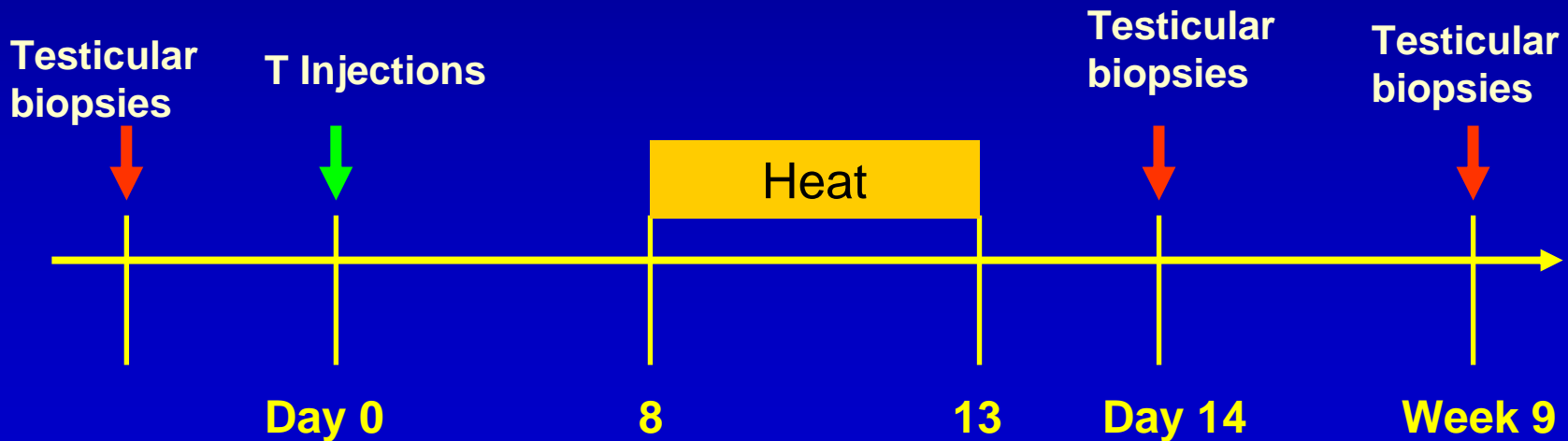


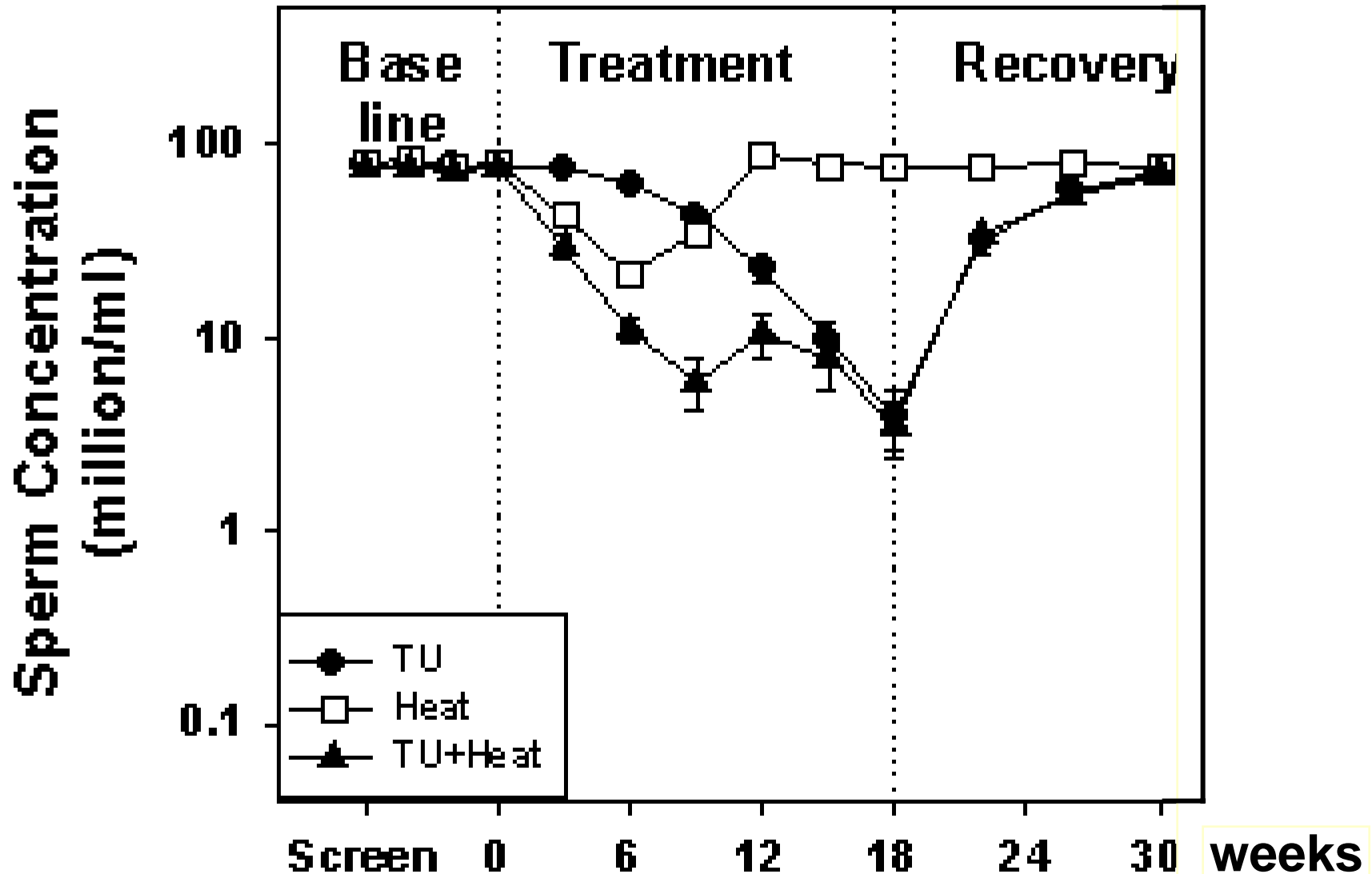
# Heat Exposure to scrotum induces germ cell

## death in men

- Testosterone injections was administered at day 1 and heat treatment was from day 8 to 13
- Open testicular biopsy was performed on four volunteers before treatment, and four participants from each group at 2 and 9 weeks after TU 1000 mg at day 0 alone or TU + Heat treatment



# Transient testicular hyperthermia in men decreased sperm concentration which is increased by concomitant treatment with Testosterone Undecanoate injection

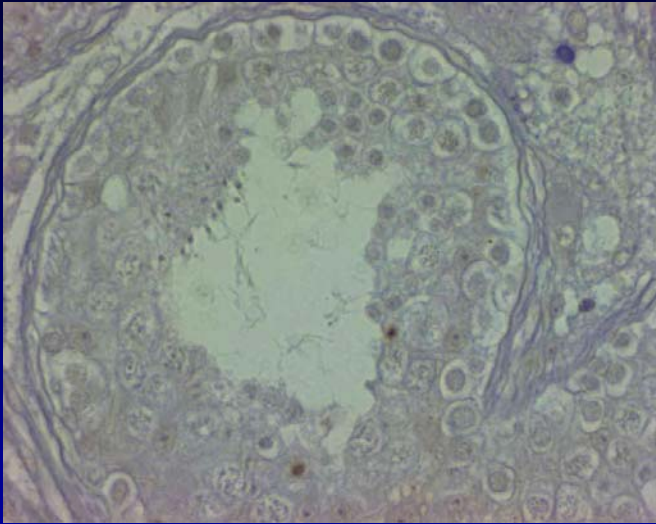


# Transient Testicular Hyperthermia in Men

- Sperm motility and morphology changes followed that of sperm concentration
- We did not examine DNA damage in the ejaculated sperm

# Heat induced germ cell apoptosis in men

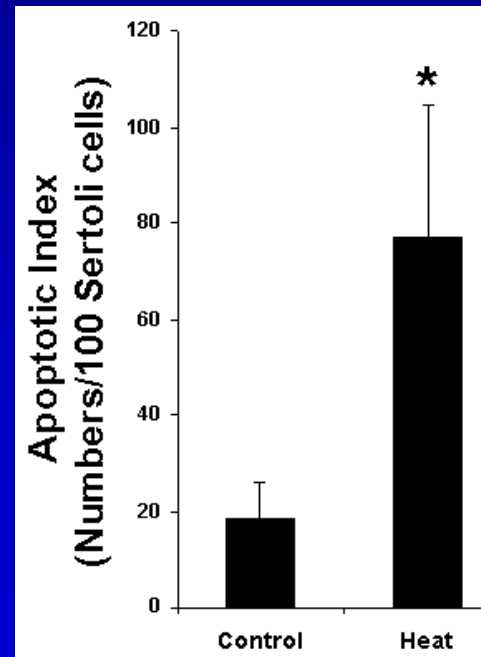
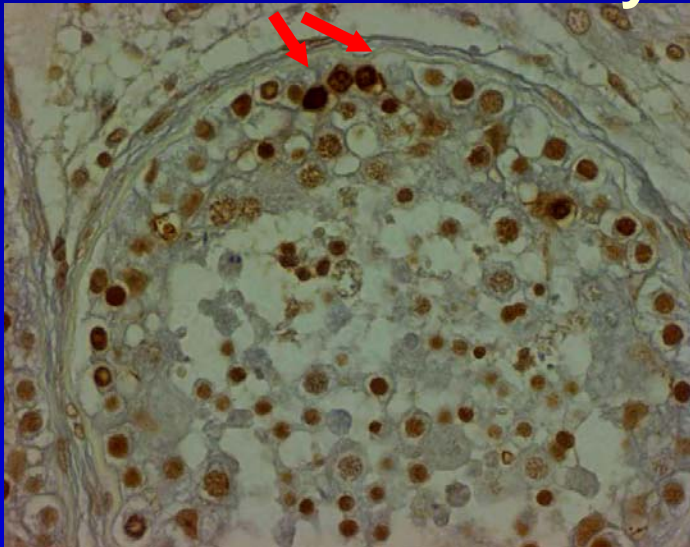
## Control

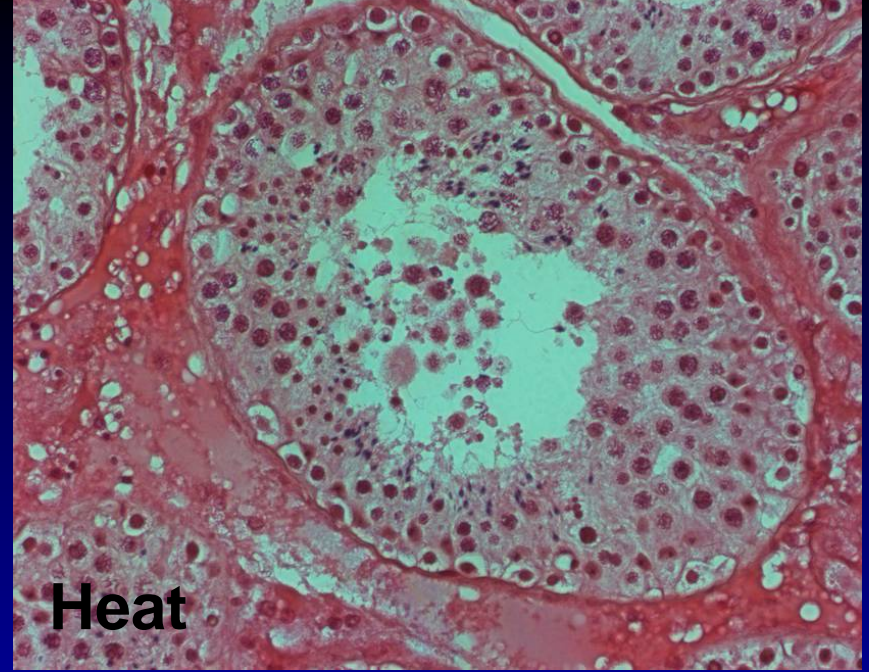
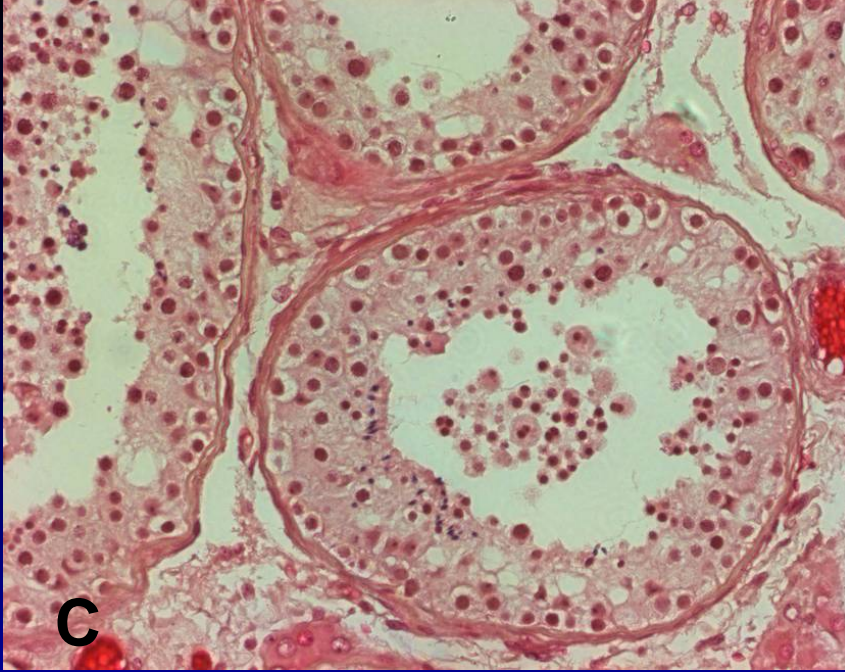


Germ cell apoptosis was significantly increased after scrotal heat exposure at 43 C for 6 days in male volunteers

Wang et al, 2007

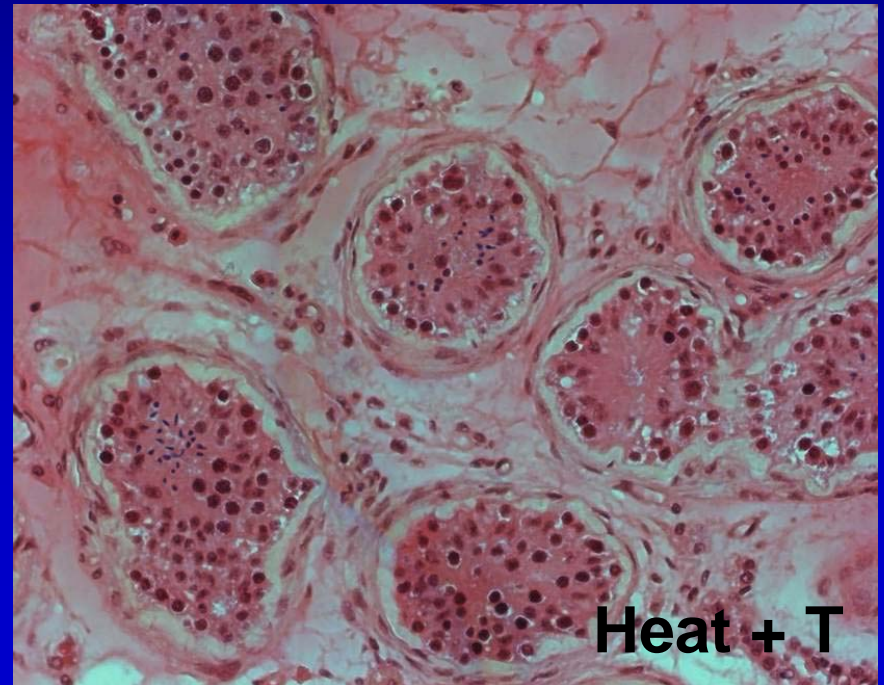
## After heat for 6 days





Testicular histology showed no difference between control and heat only groups at 9 weeks. Loss of Spermatocytes and spermatids and decrease tubule diameter after 9 weeks of TU +heat treatment in healthy men.

Wang et al, 2007



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# Effect of Heat on Testis Physiology & Function

## ■ Goal Questions

### ■ Health endpoints (priority order)

- Sperm number per ejaculate, sperm concentration
- ? DNA damage in sperm
- ? Sperm function

### ■ Time periods for acute and chronic exposure

- Days for 43° C
- Months for lower temperature increases (1 to 2 °C)

### ■ Well established time-temperature thresholds

- Acute effect demonstrated at 43° C, threshold of temperature for acute damage not known
- Chronic effect demonstrated at ??? + 1 to 2 °C, threshold not known

# Effect of Heat on Testis Physiology & Function

- Support / contrast with the REPORT
  - Need non-invasive temperature measurements of testicular temperature
  - Surrogate markers of fertility or chromatin damage – total sperm number per ejaculate, assessment of DNA damage . Sperm function???

# Effect of Heat on Testis Physiology & Function

- Targeted and cost effective research to better time-temperature threshold
  - Define thresholds for germ cell damage after acute heat exposure in men (feasible), design studies based on animal data
  - Studies to define the thresholds for lower temperature requires long term exposure in men (possible: new methods to achieve constant desired temperature, follow semen parameters, adherence to method, reversibility issues)
  - Studies of pre-pubertal and pubertal temperature effects in rodents and monkeys