

# **PRURITUS (ITCH) IN CHOLESTASIS**

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- **PSC results in cholestasis**
  - **impaired secretion of bile**
  - **Accumulation in blood of substances that are secreted in bile normally**
  - **Pruritus is a symptom experienced in cholestasis (e.g. PSC)**

# **PROBLEM OF THE PRURITUS OF CHOLESTASIS**

- **Etiology unknown**
- **Treatments not satisfactory**
- **Indication for liver transplantation**

# **PERCEPTION OF PRURITUS IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS**

- **Aims:**
  - To identify patterns in the perception of pruritus (and fatigue)
  - To learn how symptoms were evaluated and treated
- **Subjects:**
  - Members of the PBCers Organization who have PBC
- **Methods:**
  - On-line survey from June to September 2002.

# RESULTS

Sensation N= 164 / 242		Interferes with sleep	Worse at night	Worse after meals	Worse pre menses
Bugs crawling	58 (35%)	120 (73%)	107 (64%)	31 (19%)	13 (25%)
Deep itch	48(29 %)				
Relieved by scratching	12 (7%)				
Worsened by heat	69 (41%)				

# Evaluation and management

- **104/156 (67%)** stated that doctor does not evaluate their itch in any way.
- **47 (28%)** of those with itch were not given medication
- **72 (43%)** were prescribed cholestyramine, **74 (44%)** antihistamines, **39 (23%)** a cream, **22 (13%)** an antidepressant and **7 (4%)** an opiate antagonist.

# RESPONSE TO TREATMENT

- **Most effective treatment**
  - 27 (16%) - antihistamines,
  - 14 (8%) - cholestyramine,
  - 16 (10%) - some cream
  - 13 (7%) - ursodeoxycholic acid
  - **19 (11%) - nothing.**

# Conclusions

- The pruritus of cholestasis
  - interferes with sleep
  - it is worse at night
- No consistent therapeutic plan is followed
  - Thus, pruritus merits scientific investigation

# Approach to the Pruritus of Cholestasis

## Measurement of plasma substances

- non-specific approach
- availability of assays
- relevance of substances unclear

# **The Problem with Bile Acids**

- **Skin concentration may be irrelevant**
- **Relief of pruritus independent from changes in bile acids**
- **Increase plasma concentrations of bile acids**
- **Bile acids can be high in patients who do not report itch**

# **The Problem with Histamine**

- **No characteristics skin findings**
- **No response to antihistamines**

# Miscellaneous Therapies for the Pruritus of Cholestasis

- Removal of pruritogens
  - Charcoal hemoperfusion, plasmapheresis
  - Partial external diversion
  - Cholestyramine
- Hepatic enzyme inducers
  - Phenobarbital
  - Antibiotics (Rifampicin, metronidazole)
- Antihistamines
- Others
  - Ultraviolet light to the skin

# APPROACH TO THE PRURITUS OF CHOLESTASIS

- **Antiquated**
  - **Measurements of non-specific substances**
- **Alternative**
  - **Behavioral approach**

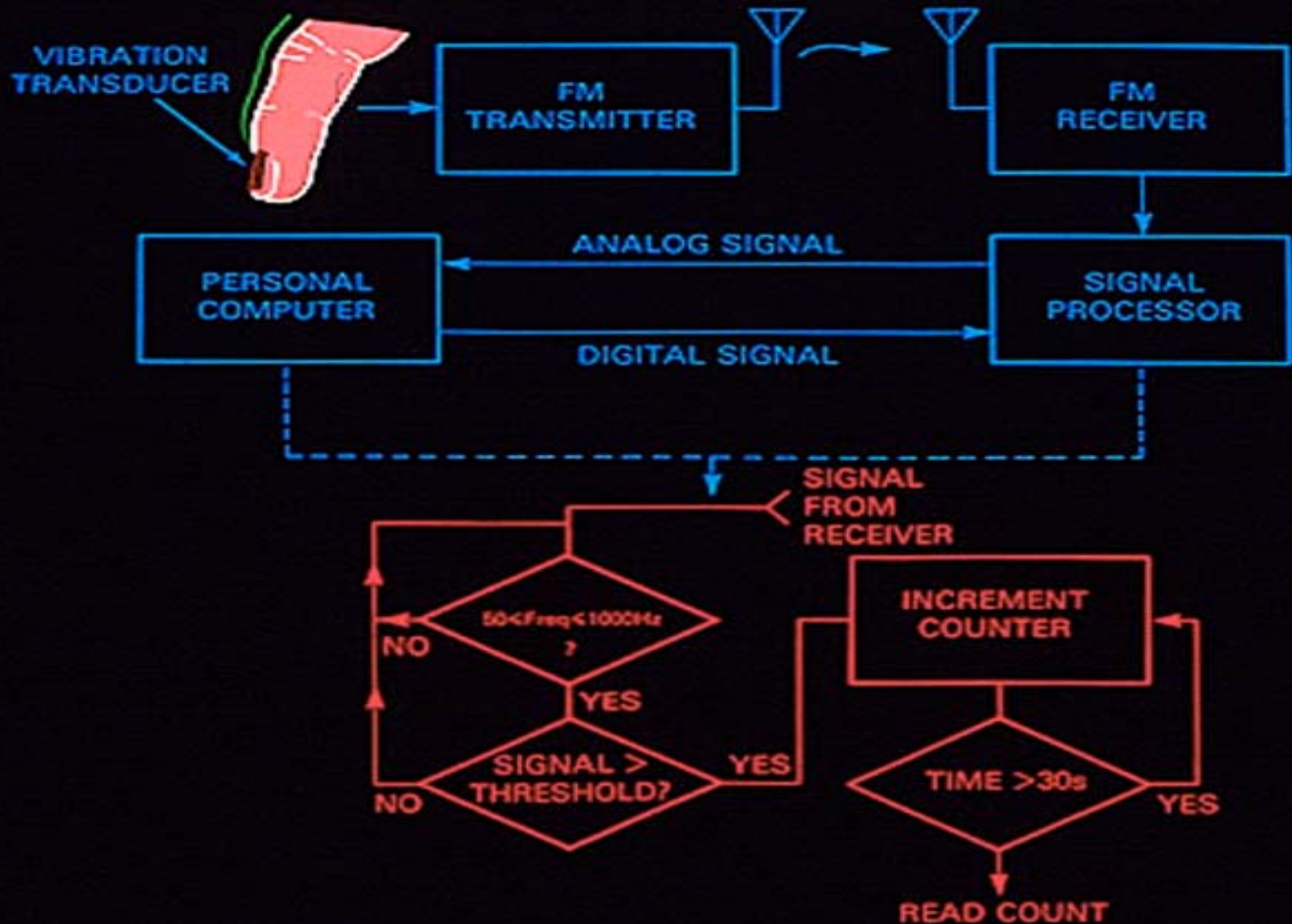
## THE BRAIN AND PRURITUS

- **Central administration of opiate drugs (e.g. morphine) associated with:**
  - pruritus in human beings
  - scratching behavior in animals
- **Opiate antagonists are effective in the treatment of opiate-induced pruritus**

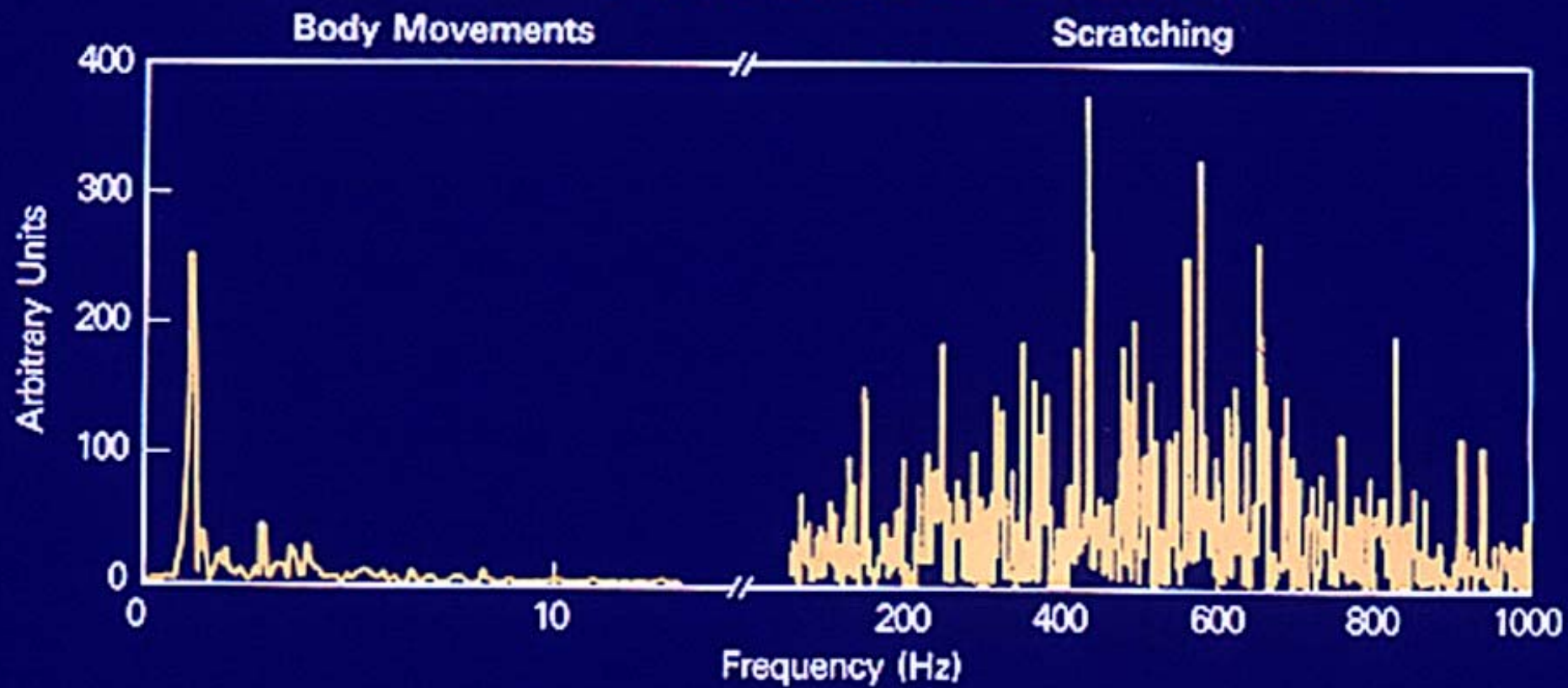
# METHODOLOGY

- **Pruritus: an unpleasant sensation that elicits the need to scratch**
- **Scratching activity: the behavioral manifestation of pruritus**

# BLOCK DIAGRAM OF MONITORING SYSTEM WITH FLOW CHART

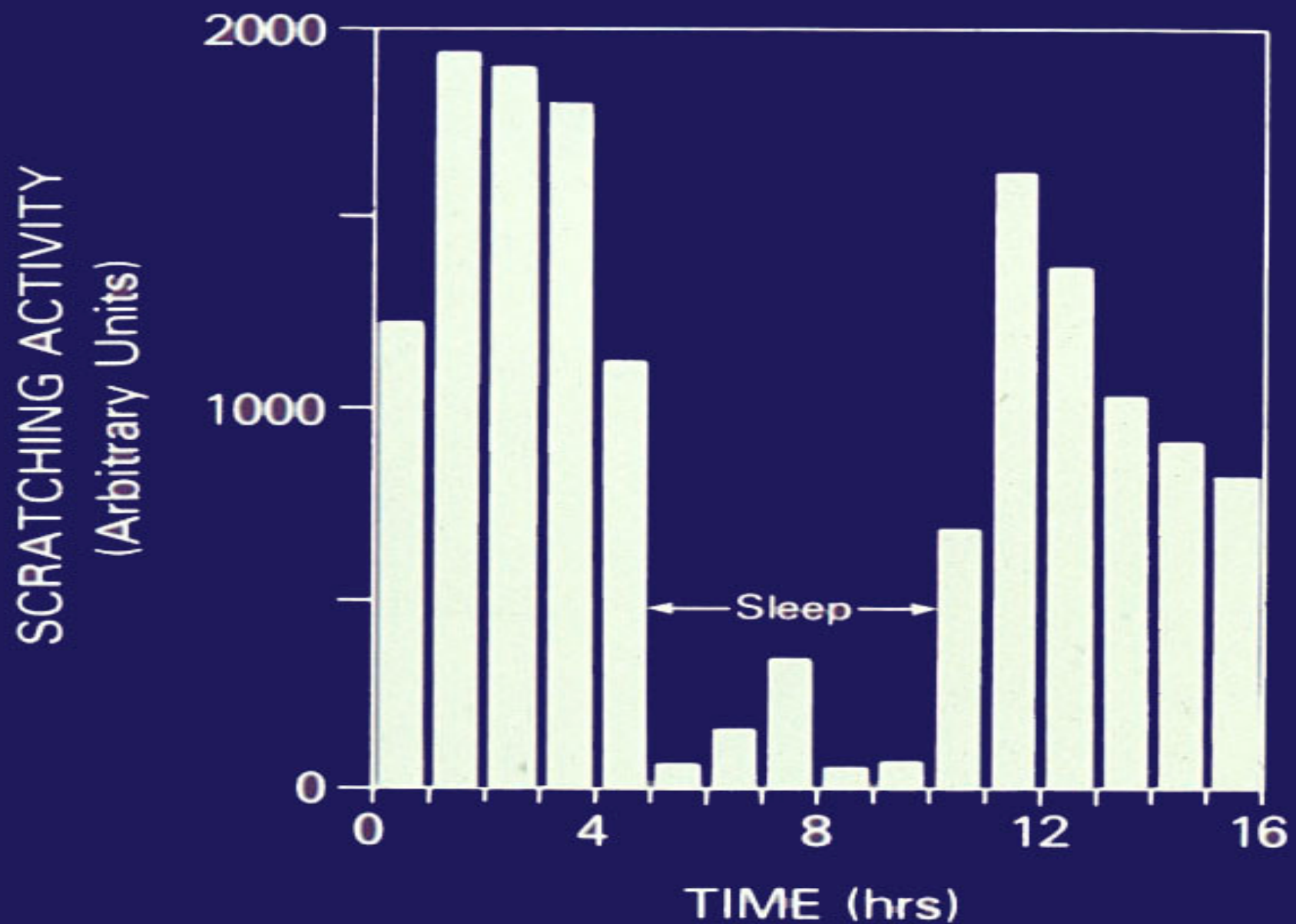


## FOURIER ANALYSIS OF DEMODULATED SIGNALS

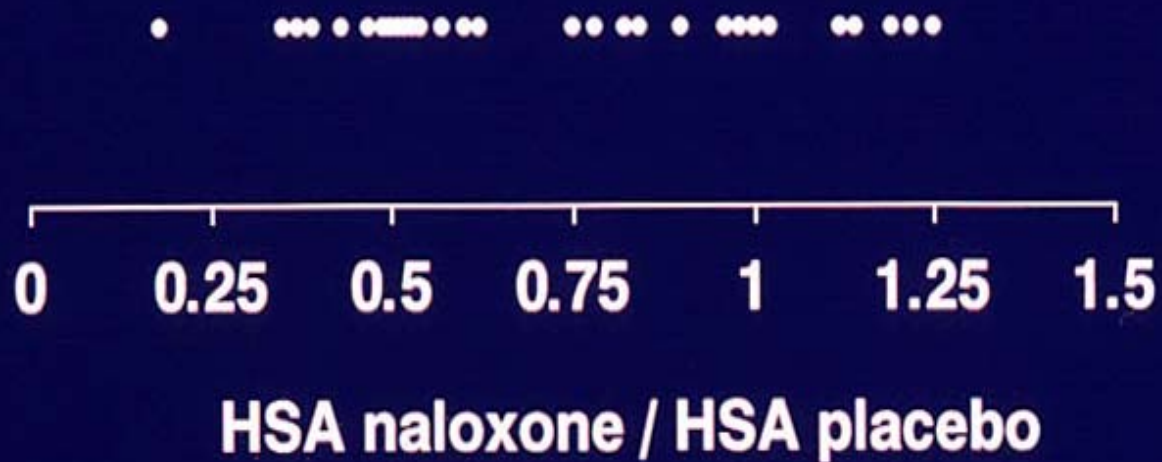




## SCRATCHING ACTIVITY RECORD OF A PRURITIC PBC PATIENT



# EFFECT OF NALOXONE THERAPY ON HOURLY SCRATCHING ACTIVITY



Adapted from Bergasa et al. Ann Int Med 1995;123:161-7

# Evolution in the Study of the Pruritus of Cholestasis

- Peripheral to central origin (i.e. skin to brain)
- Bile acids to endogenous opioids and other neurotransmitters
- Empirical to specific therapy
- Measuring of “pruritogens” in blood to behavioral studies
  - Quantitative methodology
    - Scratching activity monitoring system (SAMS)
      - Recording of scratching activity **independent** from gross body movements
        - » well-defined end-points in clinical trials

# Neurotransmitters and Pruritus

- **Serotonin**            **ondansetron, sertraline**
- **Cannabinoid**        **dronabinol**
- **Gabaergic**           **gabapentin**
- **Opioids**              **butorphanol**

# Summary

- **Effective treatments for liver diseases associated with cholestasis and their complications are needed**
- **Referral to clinical trials is necessary**
- **International Society for the Study of Itch**