



# PSYCHODERMATOLOGY: STRESS & ITCH PART 2

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# STRESS



- **STRESS DEFINITION:**
- IN **PHYSICS**, STRESS REFERS TO AN EXTERNAL **FORCE THAT CAUSES DEFORMATION** WHEN APPLIED TO THE SURFACE OF A MATERIAL
- HANS SELYE, A FAMOUS **ENDOCRINOLOGIST**, DEFINED STRESS AS “**THE NONSPECIFIC RESPONSE OF THE BODY TO ANY DEMAND MADE UPON IT**”.
- LAZARUS AND FOLKMANN REFERRED TO **PSYCHOLOGICAL** STRESS AS “**A RELATIONSHIP WITH THE ENVIRONMENT THAT THE PERSON APPRAISES AS SIGNIFICANT FOR HIS OR HER WELL-BEING AND IN WHICH THE DEMANDS TAX OR EXCEED AVAILABLE COPING RESOURCES**”.

# ITCH (PRURITUS)



- AN UNPLEASANT CUTANEOUS SENSATION WHICH PROVOKES THE DESIRE TO SCRATCH.
- IN A GERMAN STUDY POINT PREVALENCE OF CHRONIC PRURITUS REACHED **13.5 % IN GENERAL ADULT POPULATION, 16.4 % DURING 12-MONTH PERIOD AND 22.6 % LIFETIME PREVALENCE.**
- LATER POPULATION-BASED STUDY REPORTED **16.8 % PREVALENCE OF ITCH DURING PREVIOUS 6 WEEKS.**

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56 (65 of 257) 235%

**Table 6.1** The aetiological classification of pruritus according to the International Forum for the Study of Itch (IFSI) [11]

Category	Examples of diseases
I – Dermatological	Atopic dermatitis, urticaria, eczematous disorders, psoriasis, scabies
II – Systemic	Chronic kidney disease, primary biliary cirrhosis, Hodgkin's disease, drug-induced itch
III – Neurological	Multiple sclerosis, brain tumours, stroke, notalgia paresthetia
IV – Psychogenic	Depression, schizophrenia, hallucinosis, delusional parasitosis, psychogenic pruritus
V – Mixed	Several disorders form different groups
VI – Other	Senile pruritus

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Mac OS X dock with various application icons including Finder, Spotlight, Safari, Mail, Photos, Calendar, Notes, Reminders, App Store, and others.





# PRURITUS

- **PRURITUS** IS COMMON (**25.2 %**) IN SUBJECTS SUFFERING FROM **PSYCHIATRIC** DISORDERS.
- OVER **70 %** OF **DERMATOLOGY** INPATIENTS COMPLAINING OF **PRURITUS** WERE DIAGNOSED WITH AT LEAST ONE **PSYCHIATRIC** CONDITION.
- **DEPRESSIVE** SYMPTOMS SEEMED TO BE ASSOCIATED WITH MORE **PRONOUNCED PRURITUS**.
- SKIN DISORDERS CAUSE A SIGNIFICANT BURDEN FOR HEALTH SYSTEMS WORLDWIDE, PLACING **4TH** IN THE RANKING OF YEARS LOST DUE TO DISABILITY (**YLD**) IN 2010. HIGHER BURDEN WAS ATTRIBUTED TO LOW BACK PAIN, MAJOR DEPRESSIVE DISORDER AND IRON-DEFICIENCY ANEMIA (PLACED 1ST, 2ND AND 3RD, RESPECTIVELY).
- **PRURITUS** WAS REGARDED AMONG 50 MOST PREVALENT DISEASES WORLDWIDE AND WAS ASSOCIATED WITH **HIGHER YLD** VALUES ESPECIALLY IN THE **ELDERLY** POPULATION.
- RECENTLY IT HAS BEEN ESTIMATED THAT **PRURITUS GLOBAL THERAPEUTICS MARKET** WILL HAVE EXCEEDED **16 BILLION USD** BY 2025.

# ITCH & STRESS



- THE RELATION BETWEEN ITCH AND STRESS IS HIGHLY COMPLEX.
- IN GENERAL, **STRESS** MAY BE REGARDED AS A **CONSEQUENCE** OF THE UNDERLYING **DISEASE**, INCLUDING THOSE ACCOMPANIED BY PRURITUS. STRESS MAY COEXIST WITH PRURITUS, BOTH STEMMING FROM THE PRESENCE OF THE DISEASE.
- **PRURITUS** ITSELF IS SO BOTHERSOME THAT IT ALSO **INCREASES STRESS** LEVELS.
- RESEARCHES INVESTIGATING HEALTH RELATED QUALITY OF LIFE (HRQOL) HAVE PROVEN THAT **STRESS** IS A MAJOR PROBLEM IN NUMEROUS DISEASES, ESPECIALLY IN **DERMATOLOGICAL** DISORDERS THAT MANIFEST WITH **PRURITUS**.
- ON THE OTHER HAND, HIGH **STRESS** LEVELS FREQUENTLY CONTRIBUTE TO THE **DEVELOPMENT AND EXACERBATION** OF ACUTE AND CHRONIC DISEASES. ANALOGICALLY, THESE OBSERVATIONS ALSO HOLD TRUE FOR **DERMATOLOGICAL** CONDITIONS, ESPECIALLY THOSE PRESENTING WITH **ITCH**.
- THEREFORE, A COMPOSITE NETWORK OF ASSOCIATIONS SEEMS EVIDENT WHEN ANALYZING THE CAUSAL LINK BETWEEN STRESS AND ITCH.

# THE PATHOGENESIS OF PRURITUS

- PRURITUS CAN BE INTERPRETED AS A **DEFENSE** MECHANISM DIRECTED AGAINST DANGEROUS ORGANISMS OR STIMULI.
- THESE COMPRISE PARASITES, INSECTS, SHARP OBJECTS, IRRITANTS AND ALLERGENS. VARIOUS STIMULI ARE TRANSMITTED
- FROM SKIN THROUGH CUTANEOUS **SENSORY** UNMYELINATED C-NERVE FIBERS BUT ALSO VIA THINLY MYELINATED A $\Delta$  FIBERS.
- THE TRANSMISSION PROCEEDS THROUGH DORSAL ROOT GANGLIA INTO THE SPINAL CORD, THEN DUE TO LAMINA I NEURONS THROUGH THE SPINOTHALAMIC TRACT, THALAMUS AND EVENTUALLY REACHES CEREBRAL CORTEX. SEVERAL AREAS OF CORTEX ARE ACTIVATED, BOTH SENSORY AND MOTORIC.



# THE PATHOGENESIS OF PRURITUS

- NEUROTRANSMITTERS IN THE SKIN ARE SYNTHESIZED BY NERVE FIBERS AND **NUMEROUS CELLS** INCLUDING MERKEL CELLS, LANGERHANS CELLS, KERATINOCYTES, MELANOCYTES, GRANULOCYTES, LYMPHOCYTES, MONOCYTES- MACROPHAGES AND MAST CELLS.
- PRURITUS TRANSMISSION IS DIVIDED INTO **HISTAMINIC AND NON- HISTAMINIC**. THE LATTER IS ASSOCIATED WITH MEDIATORS SUCH AS ACETYLCHOLINE (ACH),  $\alpha$ -MELANOCYTE-STIMULATING HORMONE ( $\alpha$ -MSH), BETA-ENDORPHINE, CATECHOLAMINES, CALCITONIN GENE RELATED PROTEIN (CGRP), ENDOTHELIN 1 (ET-1), GASTRIN-RELEASING PEPTIDE (GRP), INTERLEUKIN 31 (IL-31), NERVE-GROWTH FACTOR (NGF), NEUROKININ A (NKA), OPIOIDS, PROSTAGLANDINS, PROTEASES, SUBSTANCE P (SP) AND VASOACTIVE INTESTINAL PEPTIDE (VIP)

# THE PATHOGENESIS OF PRURITUS

- ADMINISTRATION OF VARIOUS **DRUGS** MAY ALSO ELICIT PRURITUS, ESPECIALLY ANTIMALARIAL, OPIOIDS AND HYDROXYETHYL STARCH (HES).
- ALTHOUGH SELECTIVE SEROTONIN REUPTAKE INHIBITORS (**SSRI**) MAY BE USED AS A **TREATMENT** MODALITY IN SEVERAL FORMS OF PRURITUS, THEY MAY ALSO **ELICIT** PRURITUS IN CERTAIN SITUATIONS.
- **IATROGENIC** TYPES OF PRURITUS MAY OCCASIONALLY RESULT FROM THE DERMATOLOGIC TREATMENT ITSELF, FOR EXAMPLE DUE TO CONTACT **IRRITANT** REACTION (HIGH CONCENTRATIONS OF TOPICAL MODALITIES) OR **PHOTOTHERAPY**.



# CONTAGIOUS PRURITUS

- THE CONTAGIOUS PRURITUS IS AN EXAMPLE OF A “**NOCEBO** EFFECT” IN WHICH A SUBJECT EXPECTS A CERTAIN FORM OF REACTION FROM THE ORGANISM BASED SOLELY ON A SUGGESTION.
- THE SOCIAL CONTAGION OF ITCH IS A **NORMATIVE** RESPONSE, BEING EXPERIENCED BY MOST PEOPLE.
- AREAS OF THE **BRAIN** RESPONSIBLE FOR EXPERIENCING AND RESPONDING TO ITCH WERE ANTERIOR INSULA, PREMOTOR CORTEX, PRIMARY SOMATOSENSORY CORTEX AND PREFRONTAL CORTEX.
- **NEUROTICISM** AS A PERSONALITY TRAIT WAS ALSO POSTULATED AS FACTOR INFLUENCING THE ITCH CONTAGION.

# BANDURA THEORY

- CERTAIN INTRINSIC PERSONALITY FACTORS COMBINED WITH STRESSFUL LIFE EVENTS MAKE AN INDIVIDUAL MORE PRONE TO DEVELOP PRURITUS.
- **SELF-EFFICACY** WHICH IS DEFINED AS PEOPLE'S BELIEFS ABOUT THEIR CAPABILITIES. THESE BELIEFS DETERMINE FEELINGS, THOUGHTS, MOTIVATION AND BEHAVIOR. IN CONSEQUENCE, PERCEIVED SELF-EFFICACY MAY INFLUENCE THE WAY IN WHICH AN INDIVIDUAL COPE WITH DIFFICULT SITUATIONS AND STRESS.
- ADOLESCENT INDIVIDUALS WITH **POOR SELF-EFFICACY** COMPLAINED **OF ITCH TWICE** AS OFTEN IN HIGHLY STRESSFUL SITUATIONS AS THOSE WITH HIGH SELF-EFFICACY (30 % VS. 15 %;  $P = 0.072$ ).
- ITCH MAY POSSIBLY BE ALLEVIATED BY PSYCHOTHERAPEUTIC INTERVENTIONS THAT STRENGTHEN THE GENERAL COPING MECHANISMS.

# ITCH INHIBITION

- **THERMAL AND MECHANICAL** COUNTER STIMULI MAY **INHIBIT HISTAMINE-ASSOCIATED PRURITUS** IN HUMAN SUBJECTS.
- **SPINAL INTERNEURONS** RELEASING **GLYCINE AND GAMMA-AMINOBUTYRIC ACID (GABA)** CONTRIBUTE TO THIS PHENOMENON.
- RECENTLY, THE ROLE OF **SPINAL B5-INTERNEURONS AND KAPPA-OPIOID AGONIST DYNORPHIN** AS AN ITCH INHIBITING NEUROMODULATOR HAS BEEN REPORTED IN MICE.
- **GLUTAMATE** RELEASE ASSOCIATED WITH **VGLUT-2 TRANSPORTER AND TRPV-1 RECEPTORS** GENERATES PAIN AND INHIBITS PRURITUS.
- **TROPOMYOSIN-RECEPTOR KINASE A (TRKA)** FUNCTIONING AS NGF RECEPTOR HAS RECENTLY BEEN **TARGETED BY NOVEL CT327 ANTAGONIST**.



# ITCH AND STRESS: WIDE SPECTRUM OF ASSOCIATIONS

- **STRESS** EXERTS ITS INFLUENCE ON DERMATOLOGICAL DISORDERS AND ITCH ITSELF DUE TO RELEASING **NEUROPEPTIDES** AND **HORMONES**.
- **MEDIATORS** RELEASED LOCALLY OR SYSTEMATICALLY **INCREASE SENSORY INNERVATION, PROMOTE THE SYNTHESIS OF PRURITOGENIC SUBSTANCES, STIMULATE NEUROGENIC INFLAMMATION AND LOWER THE THRESHOLD OF ITCH.**
- AN **IMPAIRED PARASYMPATHETIC RESPONSE** POSSIBLY LINKS CHRONIC STRESS AND ITCH.
- STRESS INFLUENCES ITCH WHEREAS ITCH RESULTS IN ADDITIONAL STRESS. THUS, VICIOUS “**ITCH-SCRATCH-ITCH**” CYCLE APPEARS AND PERPETUATES ITSELF.

# ATOPIC DERMATITIS



- ATOPIC DERMATITIS (AD) IS A COMMON CHRONIC OR RECURRENT INFLAMMATORY SKIN DISEASE AFFECTING **15–20 % OF CHILDREN AND 1–3 % OF ADULTS WORLDWIDE.**
- **PRURITUS IS A KEY FEATURE OF AD** INCLUDED IN THE CLASSIC DIAGNOSTIC CRITERIA PROPOSED BY HANNIFIN AND RAJKA AND BY UK WORKING PARTY. THE PATHOGENESIS OF ITCH IN AD IS MULTIFACTORIAL.
- **PRURITUS THRESHOLD IS DIMINISHED** AND VARIOUS FACTORS TRIGGER ITCH IN LOWER CONCENTRATIONS THAN IN HEALTHY SUBJECTS.
- **EPIDERMAL BARRIER DYSFUNCTION** MEASURED BY INCREASE IN TRANS EPIDERMAL WATER LOSS (TEWL) WAS REPORTED.
- ALTERED PATTERN OF CUTANEOUS INNERVATION WAS OBSERVED IN SKIN SPECIMENS. THE **DENSITY OF EPIDERMAL AND DERMAL NERVE FIBERS WAS HIGHER..**
- PLASMA CONCENTRATIONS OF **SP, CGRP, NPY, BETA-ENDORPHINE, NGF, BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF)** WERE ALTERED IN PATIENTS WITH AD. **INCREASED LEVELS OF HISTAMINE** WERE REPORTED IN PLASMA AND SKIN OF PATIENTS SUFFERING FROM AD. **HISTAMINE INDUCED EXTRAVASATION OF PROTEINS WAS LOWER IN ATOPIC SUBJECTS,** IMPLYING THAT OTHER MEDIATORS MAY ELICIT PRURITUS IN THIS GROUP OF PATIENTS. THIS ISSUE WAS REFLECTED BY INCONSISTENT EFFECTIVENESS OF ANTIHISTAMINES IN REDUCING ITCH. INTERLEUKINES WERE ALSO INVESTIGATED IN THE CONTEXT OF ITCHING, SUCH AS IL-2, IL-6, IL-13 OR IL-31

# ATOPIC DERMATITIS



- **87 %** SUBJECTS SUFFERING FROM AD EXPERIENCED PRURITUS ON A **DAILY BASIS**. THE WORST ITCH INTENSITY REACHED  $9.0 \pm 1.2$  POINTS (**VAS**).
- **91 %** SUBJECTS EXPERIENCED PRURITUS AT LEAST **ONCE EVERY DAY**, WHEREAS MEAN ITCH INTENSITY WAS 8.3/10 (**LIKERT SCALE**).
- THE **SEVERITY OF ITCH INCREASED DUE TO STRESS IN 71 % RESPONDENTS; 22 % IDENTIFIED STRESS AS THE MOST COMMON FACTOR INITIATING THE ONSET OF PRURITUS**
- **PRURITUS INTENSITY** (VAS) WAS POSITIVELY CORRELATED WITH **STATE-ANXIETY** AND **TRAIT-ANXIETY** VALUES ( $R = 0.573$ ;  $R = 0.525$ ; RESPECTIVELY).
- SUBJECTS WITH **ANXIETY AND PRURITUS** LEVELS PRESENTED WITH MORE INTENSE **NPY AND NGF** IMMUNOHISTOCHEMICAL STAINING.

# ATOPIC DERMATITIS



- **INTENSITY OF PRURITUS** ASSESSED WITH VAS (MEAN  $7.9 \pm 2.2$ ) WAS RELATED TO THE **STRESS** EXPERIENCED BY AD PATIENTS **PRIOR TO DISEASE EXACERBATION** ( $P = 0.37$ ,  $P < 0.001$ ) [105].
- STRESS WAS EVALUATED UTILIZING SOCIAL READJUSTMENT RATING SCALE AND STRESS SELF-ASSESSMENT SCALE.
- **PRURITUS** INTENSITY WAS **HIGHER** IN SUBJECTS PRESENTING WITH SYMPTOMS POSSIBLY ASSOCIATED WITH **DEPRESSION**

# ATOPIC DERMATITIS



- SIGNIFICANT POSITIVE **CORRELATION** BETWEEN **ITCH AND NGF+ NEUROFILAMENTS IN NON-LESIONAL SKIN** AND BETWEEN **ITCH AND NF-MAST CELL CONTACTS IN LESIONAL SKIN** IN SUBJECTS SUFFERING FROM AD WHO HAD PERFORMED TSST TRIER SOCIAL STRESS TEST).
- HEART RATE VARIABILITY (HRV) WAS MEASURED AFTER ELICITING HISTAMINE INDUCED ITCH, AFTER ARTIFICIAL SCRATCHING THE ITCHY AREA OF THE SKIN USING CYTOLOGY BRUSH AND AFTER PERFORMING TSST. **AD PATIENTS PRESENTED HIGHER HEART RATES THAN HEALTHY SUBJECTS, MARKED SYMPATHETIC RESPONSE TO ITCH AND SCRATCHING AND DYSFUNCTIONAL PARASYMPATHETIC RESPONSE TO ITCH AND SCRATCHING.**



# PERSONALITY TRAITS AND DEPRESSION ON ITCH

- THE QUESTIONNAIRE MEASURES PERSONALITY TRAITS DEFINED AS NEUROTICISM, EXTRAVERSION, OPENNESS TO EXPERIENCE, AGREEABLENESS AND CONSCIENTIOUSNESS)
- AD SUBJECTS WITH HIGH **HADS** SCORES WERE PRONE TO EXPERIENCE MORE PRONOUNCED **ITCH**, WHEREAS THE INCREASE IN THE NUMBER OF **SCRATCH MOVEMENTS** WAS ASSOCIATED WITH **HIGH PUBLIC SELF-CONSCIOUSNESS AND LOW AGREEABLENESS**
- A RECENT STUDY ATTEMPTED TO DETERMINE THE ROLE OF COPING AS A POSSIBLE MEDIATOR INFLUENCING THE RELATIONSHIP BETWEEN STRESS AND PRURITUS:
- THE RESULTS SUPPORTED THE HYPOTHESIS THAT **PRURITUS-RELATED STRESS LEADS TO UNFAVORABLE COPING MECHANISMS WHICH FURTHER PERPETUATE THIS BOTHERSOME PHENOMENON.**

# PSORIASIS

- PSORIASIS IS A CHRONIC INFLAMMATORY DISORDER AFFECTING APPROXIMATELY **0.73–2.9 %** OF EUROPEAN POPULATION. AMONG ADULTS AGED 20–59 YEARS IN THE US, THE PREVALENCE OF PSORIASIS IN CAUCASIANS, AFRICAN AMERICANS AND HISPANICS WAS 3.6 %, 1.9 % AND 1.6 %, RESPECTIVELY. FREQUENCY OF **PRURITUS** IN PSORIASIS PATIENTS RANGES FROM **67 TO 96.6 %**

# NEUROGENIC INFLAMMATION

- **INCREASED** NUMBER OF **SP-POSITIVE** NERVES IN THE PERIVASCULAR AREA, INCREASED NUMBER OF **NGF IMMUNOREACTIVE KERATINOCYTES** AND INCREASED **NGF** SKIN CONCENTRATION WAS FOUND
- HIGH AFFINITY RECEPTOR FOR NGF (**TRKA**) WAS OBSERVED IN THE **EPIDERMIS AND DERMAL NERVE FIBERS**, WHILE PROTEIN GENE PRODUCT 9 (**PGP-9.5**) **IMMUNOREACTIVE NERVE FIBERS** WERE MORE PREVALENT IN THE **EPIDERMIS AND UPPER DERMIS**. THESE ASPECTS WERE **CORRELATED** WITH ITCH **INTENSITY** AS WELL.
- **E-SELECTIN** IMMUNOREACTIVE **VESSELS** AS WELL AS ENDOTHELIAL LEUCOCYTE ADHESION MOLECULE 1 (**ELAM-1**) DENSITY IN **VENULES** CONTRIBUTE TO THE PATHOGENESIS OF ITCH.

# NEUROGENIC INFLAMMATION

- MADEJ EMPHASIZED THE ROLE VASCULAR ADHESION PROTEIN-1 (**VAP-1**).
- PRURITUS INTENSITY MAY BE CORRELATED WITH **HIGH CGRP AND LOW NPY** PLASMA LEVELS.
- **DECREASED** LEVEL OF **SEMAPHORINE-3A** **UPREGULATES NGF EXPRESSION**, FURTHER RESULTING IN **HYPER INNERVATION OF C-FIBERS**.
- **DOWNREGULATION OF KAPPA OPIOID RECEPTOR** IN EPIDERMIS WAS ALSO OBSERVED IN PSORIASIS.
- GAMMA-AMINOBUTYRIC ACID (**GABA**) AND ITS RECEPTOR (**GABAR** ) PARTICIPATE IN PATHOGENESIS OF PSORIASIS AND DEVELOPMENT OF PRURITUS IN THESE INDIVIDUALS.

# ITCH SCORE IN PSORIASIS

- INDIVIDUALS SUFFERING FROM PSORIASIS REGARD **PRURITUS** AS THE **MOST BOTHERSOME** SYMPTOM. THE INTENSITY OF PRURITUS IN PSORIASIS IS REGARDED AS **MODERATE**
- MEAN VAS SCORES OF  $4.2 \pm 2.4$ , THE WORST VAS SCORES REACHED  $6.4 \pm 2.5$ .



# RELATIONSHIP BETWEEN STRESS AND PRURITUS IN PSORIASIS

- 67 % OF RESPONDENTS DEEMED STRESS AS AN AGGRAVATING FACTOR OF PRURITUS; **PRURITUS INTENSITY AND STRESS** WERE POSITIVELY **CORRELATED**.
- **PRURITUS NEGATIVELY** IMPACTED **QOL** OF PARTICIPANTS: **60 %** COMPLAINED OF **MOOD** DISTURBANCES, WHEREAS PROBLEMS CONCERNING **CONCENTRATION, SLEEP, SEXUAL** DESIRE AND **APPETITE** WERE DECLARED BY **47 %**, **35 %**, **21 %** **AND 11 %** OF PARTICIPANTS, RESPECTIVELY.
- PATIENTS SUFFERING FROM HEAVY OR EXTREMELY **HEAVY STRESS** (AS ASSESSED BY SOCIAL READJUSTMENT RATING SCALE AND SELF-ASSESSMENT METHOD) WERE MORE SUSCEPTIBLE TO THE OCCURRENCE OF **ITCH** ( $P < 0.05$ ). THE SEVERITY OF STRESS AND THE INTENSITY OF PRURITUS WERE POSITIVELY CORRELATED ( $P = 0.015$ ).
- MODERATE CORRELATION BETWEEN STRESS REACTIVITY AND THE DEGREE OF ITCHING IN A LARGE GROUP OF NORDIC SUBJECTS
- OVER **70 %** OF PATIENTS HAD EXPERIENCED AT LEAST **ONE STRESSFUL EVENT WITHIN 1 MONTH** BEFORE EXACERBATION OF THE DISEASE.
- REGARDING STRESS LEVELS, NO DIFFERENCES WERE OBSERVED BETWEEN PATIENTS EXPERIENCING PRURITUS AND THOSE WHO DID NOT

# PSORIASIS

- PRURITUS WAS EXACERBATED BY EMOTIONAL STRESS IN OVER 49 % OF KOREAN OUTPATIENTS.
- THE AUTHORS PERFORMED SKIN BIOPSIES AND HISTOLOGIC EXAMINATION ALONG WITH IMMUNOFLUORESCENT STAINING. SPECIMENS FROM **LESIONAL**, ITCHY SKIN PRESENTED WITH MORE PRONOUNCED STAINING FOR **TRKA PARTICLES (HIGH AFFINITY RECEPTOR FOR NGF)**, SP-RECEPTORS (**SPR**) AND CGRP RECEPTORS (**CGRPR**) WHEN **COMPARED** TO **HEALTHY** AREAS OF SKIN AND **LESIONAL, NO PRURITIC** AREAS.
- ANOTHER STUDY: PRURITUS INTENSITY MEASURED WITH VAS WAS NOT CORRELATED NEITHER WITH THE NUMBER OF SP POSITIVE FIBERS AND SP POSITIVE CELLS, NOR WITH SALIVARY CORTISOL LEVELS.

# PSORIASIS

- **STRESS** IS THE MOST IMPORTANT FACTOR **INDUCING** AND **AGGRAVATING ITCH** IN PSORIASIS (**49 %** AND **61 %** OF PATIENTS), RESPECTIVELY.
- **PRURITUS SEVERITY** (10-POINT SCALE) WAS CORRELATED WITH **DEPRESSION SCORES** (CARROLL RATING SCALE FOR DEPRESSION; CRS D) AMONG OUTPATIENTS SUFFERING FROM **PSORIASIS, ATOPIC DERMATITIS AND CHRONIC IDIOPATHIC URTICARIA**.
- THE AUTHORS SUGGESTED THAT DEPRESSIVE SYMPTOMS MAY BE REGARDED BOTH AS A PRIMARY FEATURE OF THE SKIN DISORDER OR AS ITS CONSEQUENCE.
- ELEVATED LEVELS OF **CORTICOTROPIN RELEASING FACTOR** ASSOCIATED WITH **DEPRESSION** COULD **INTENSIFY ITCH PERCEPTION** BY INCREASING OPIATE LEVELS IN CNS.

# URTICARIA

- **0.3 TO 11.3 %** OF POPULATION.
- AMONG GERMAN SUBJECTS REPORTED LIFETIME PREVALENCE OF ANY URTICARIAL LESIONS AND CHRONIC URTICARIA (CU) REACHING 8.8 % AND 1.8 %, RESPECTIVELY.
- POSSIBLY UP TO 20 % OF POPULATION WILL EXPERIENCE AT LEAST ONE EPISODE OF ACUTE URTICARIA (AU) DURING THEIR LIFETIME. IN 40 % CASES ANGIOEDEMA IS ALSO PRESENT.
- ACUTE FORMS OF URTICARIA SUBSIDE WITHIN 6 WEEKS (MOST COMMONLY WITHIN 24 H), WHEREAS CHRONIC FORMS LAST LONGER THAN 6 WEEKS.
- IN CHRONIC IDIOPATHIC URTICARIA (CIU) LESIONS APPEAR SPONTANEOUSLY DUE TO KNOWN OR UNKNOWN CAUSES.

# URTICARIA

- ITCHING IN URTICARIA IS ALMOST INVARIABLE;
- PRURITUS IS DESCRIBED AS **PRICKING** OR **BURNING** IN QUALITY AND **EXACERBATES** IN THE **EVENING** OR DURING **NIGHT**.
- ALTHOUGH THE LESIONS ARE ITCHY, PATIENTS TEND TO **RUB THE SKIN RATHER THAN SCRATCH IT**.
- THE NHP (NOTTINGHAM HEALTH PROFILE) SCORES OBTAINED DURING THE STUDY WERE **COMPARED** TO NHP SCORES AMONG PATIENTS SUFFERING FROM **ISCHEMIC HEART DISEASE**. **CU PATIENTS PRESENTED ALMOST IDENTICAL SCORES CONCERNING ENERGY, SOCIAL ISOLATION, EMOTIONAL REACTIONS AND HIGHER SLEEP DISTURBANCE**.



# URTICARIA

- **PRURITUS INTENSITY** (VAS) AT ITS WORST STATE WAS MORE **PRONOUNCED** IN PATIENTS THAT FELT **DEPRESSED** AND **ANXIOUS**. 25 % RESPONDENTS CLAIMED THAT **STRESS INCREASED THE PERCEIVED PRURITUS INTENSITY**.
- COMPARED TO HEALTHY SUBJECTS, BOTH **CIU & PSORIASIS** GROUPS WERE CHARACTERIZED BY HIGHER **EMOTIONAL DISTRESS, DEPRESSION AND ANXIETY**.
- **ANGER TRAIT AND ANGER STATE VALUES** WERE ALSO MORE PRONOUNCED IN THE LATTER GROUPS.
- **IN TERMS OF PRURITUS SEVERITY, STATE ANGER WAS A SIGNIFICANT PREDICTOR** ACCOUNTING FOR 19 % OF ITS VARIANCE AMONG THE **URTICARIA GROUP**.
- AMONG SUBJECTS SUFFERING FROM **PSORIASIS, DEPRESSION WAS THE ONLY SIGNIFICANT PREDICTOR RESPONSIBLE FOR 12 % VARIANCE IN PRURITUS SEVERITY**.

# ACNE VULGARIS

- AMONG ADOLESCENTS WITH ACNE VULGARIS **36.1 %** SUBJECTS COMPLAINED OF **PRURITUS** THAT HAD OCCURRED WITHIN THE ACNE LESIONS IN THE **PAST**, WHILE **13.9 %** PARTICIPANTS REPORTED THAT THEIR ACNE LESIONS WERE **PRURITIC** AT THE **TIME OF EXAMINATION**.
- THE LATTER GROUP EXPERIENCED PRURITUS INTENSITY REACHING APPROXIMATELY  $3.1 \pm 2.9$  POINTS (VAS). THE MAXIMAL INTENSITY OF PRURITUS WITHIN ACNE LESIONS IN THE PAST HAD REACHED  $4.0 \pm 2.5$  POINTS.
- **ITCH AGGRAVATION ASSOCIATED WITH STRESS** WAS REPORTED BY **33.3 %** OF SUBJECTS.




# SEBORRHEIC DERMATITIS

- 90 % SUBJECTS COMPLAINED OF PRURITUS
- 76.4 % RESPONDENTS REPORTED THAT **DISEASE OUTBREAK** WAS TRIGGERED BY FACTORS SUCH AS **STRESS, DEPRESSION OR FATIGUE**





# HAND DERMATOSES

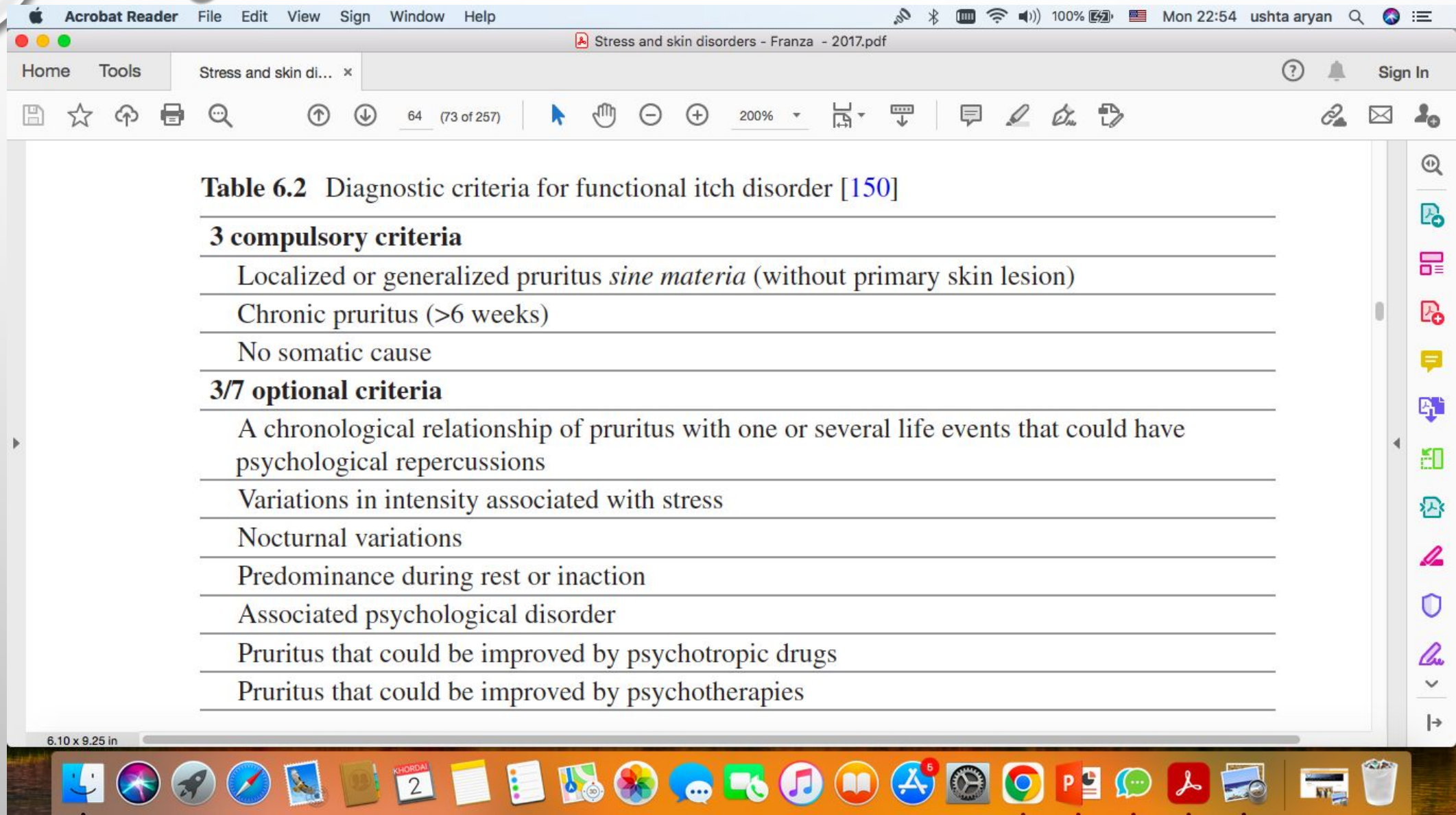
- **HIGH STRESS RESPONDERS** EXPERIENCED **MORE SEVERE PRURITUS** INTENSITY THAN LOW STRESS RESPONDERS
  - **HIGH STRESS RESPONDERS** WERE MORE LIKELY TO PRESENT **SOCIAL ANXIETY AND AVOIDANCE, VICIOUS CIRCLE OF ITCHING OR SCRATCHING, HELPLESSNESS AND ANXIOUS-DEPRESSIVE MOOD**
- 

# WOUND HEALING

- CERTAIN STUDIES REVEALED THAT WOUND HEALING IS **IMPAIRED** BY PSYCHOLOGICAL FACTORS INCLUDING **STRESS**. ON THE OTHER HAND, **PRURITUS** IS A SERIOUS ISSUE IN PATIENTS SUFFERING FROM **BURN** INJURIES.
- AT **3 MONTHS POSTBURN**, **87 %** SUBJECTS SUFFERED FROM MILD TO SEVERE **ITCHING**. AT **1 AND 2 YEARS** POSTBURN THE PERCENTAGES DROPPED TO **70 % AND 67 %**, RESPECTIVELY.
- **ITCH INTENSITY DECREASED** FROM  $2.8 \pm 1.8$  AT 3 MONTHS POSTBURN, THROUGH  $1.8 \pm 1.8$  AT 1 YEAR POSTBURN AND EVENTUALLY  $1.5 \pm 1.6$  POINTS AT 2 YEARS POSTBURN.
- THE **ITCHING** COMPLAINTS SEEMED TO BE **RELATED** TO **EARLY POST-TRAUMATIC STRESS SYMPTOMS**.
- IT IS POSSIBLE THAT **PRURITUS** EXPERIENCED BY PATIENTS SUFFERING FROM **CHRONIC WOUNDS** MAY NOT ONLY **STEM FROM THE UNDERLYING DISEASE** BUT ALSO **INDUCE ADDITIONAL STRESS** AND THEREFORE IMPAIR THE HEALING PROCESS.

# PSYCHOGENIC PRURITUS

- “ITCH DISORDER, WHERE ITCH IS AT THE CENTER OF THE SYMPTOMATOLOGY, AND WHERE PSYCHOLOGICAL FACTORS PLAY AN EVIDENT ROLE IN THE TRIGGERING INTENSITY, AGGRAVATION OR PERSISTENCE OF THE PRURITUS”



# PSYCHOGENIC PRURITIS

- IN A GERMAN STUDY 195 **DERMATOLOGICAL OUTPATIENTS** WERE EVALUATED. **SOMATOFORM PRURITUS** WAS DIAGNOSED IN OVER **10 %** SUBJECTS.
- AN INTERESTING STUDY WAS CONDUCTED BY KRETZMER ET AL.. AMONG 100 **PSYCHIATRIC WARD INPATIENTS** **IDIOPATHIC PRURITUS** WAS DIAGNOSED IN **42 %** OF THE SUBJECTS, **MORE FREQUENTLY AMONG FEMALES** (58 % VS. 34 %;  $P = 0.03$ ).
- THE DIAGNOSIS SEEMED TO BE ASSOCIATED **WITH PSYCHOSOCIAL STRESS AS IT WAS ESTABLISHED IN 48.5 % AND 29 % PATIENTS WITHOUT AND WITH ADEQUATE SOCIAL SUPPORT, RESPECTIVELY** ( $P = 0.02$ ).
- **IDIOPATHIC PRURITUS** WAS DIAGNOSED IN **76 % OF PATIENTS REGULARLY RECEIVING OPIOIDS**.
- ADDITIONALLY, THE DIAGNOSIS WAS **MORE FREQUENT** IN PATIENTS WITH HIGHER SCORES ON **THE ANGER-TRAIT MEASURE** ( $P = 0.02$ ), **ANGRY TEMPERAMENT MEASURE** ( $P = 0.02$ ) AND **RUMINATIVE CATASTROPHIZATION** ( $P = 0.04$ ).



# THERAPEUTIC RECOMMENDATIONS


- FACTORS THAT INCREASE **SKIN DRYNESS** SHOULD BE AVOIDED, ESPECIALLY IN AD INDIVIDUALS. THESE INCLUDE DRY CLIMATE, HEAT, EXCESSIVE WASHING AND BATHING.
- LIKEWISE, CONTACT WITH **IRRITANTS, ALLERGENS, HOT AND SPICY MEALS, HOT BEVERAGES, ALCOHOL AND STRESSFUL SITUATIONS** IS UNADVISABLE.
- **WASHING** SHOULD BE PROMPT, PERFORMED WITH MILD, NON-ALKALINE SOAPS OR SYNDETS AND FOLLOWED BY **EMOLLIENT** APPLICATION.
- THE LATTER NEED TO BE PRESCRIBED IN ADEQUATE AMOUNTS (E.G. 250 G PER WEEK) AND IDEALLY ADMINISTERED **LIBERALLY AND FREQUENTLY**

# THERAPEUTIC RECOMMENDATIONS

- **FIRST GENERATION ANTIHISTAMINES** (HYDROXYZINE, CLEMASTINE) MAY IMPROVE SLEEP DUE TO THEIR SEDATIVE PROPERTIES. ACCORDING TO RANDOMIZED CONTROLLED TRIALS SECOND GENERATION ANTIHISTAMINES PROVED SOMEWHAT DISAPPOINTING IN RELIEVING PRURITUS INTENSITY IN AD PATIENTS.
- THEY ARE, HOWEVER, UTILIZED AS A **TREATMENT OF CHOICE IN CHRONIC URTICARIA**.
- NOVEL THERAPEUTIC MODALITIES IN **AD (DUPILUMAB)** OR **PSORIASIS** PATIENTS (**APREMILAST**) ALSO SIGNIFICANTLY REDUCE ITCH.
- AS **DEPRESSION** SYMPTOMS FREQUENTLY ACCOMPANY **CHRONIC PRURITUS** INDIVIDUALS (10 %), **SSRI** THERAPY SEEMS ADVISABLE IN SELECTED CASES.
- **PAROXETINE** PROVED USEFUL IN PATIENTS WITH **POLYCYTHAEMIA VERA, PARANEOPLASTIC PRURITUS OR PRURITUS ASSOCIATED WITH PSYCHIATRIC DISEASES, WHILE SERTRALINE WAS EFFECTIVE IN CHOLESTATIC PRURITUS AND UREMIC PRURITUS**.



# THERAPEUTIC RECOMMENDATIONS

- CONCERNING THE ROLE OF STRESS IN ITCH DEVELOPMENT **PATIENT EDUCATION, STRESS MANAGEMENT AND RELAXATION TECHNIQUES ARE BENEFICIAL.**
  - **HABIT REVERSAL THERAPY (HRT)** IS A SUBTYPE OF COGNITIVE THERAPY ENCOMPASSING AWARENESS TRAINING, INDUCING RESPONSES REPLACING DYSFUNCTIONAL BEHAVIOR AND INCREASING THE MOTIVATION TO CONTROL THE HABITS. **AD PATIENTS UTILIZING HRT EXPERIENCED AN IMPROVEMENT IN SKIN STATUS AND REDUCTION IN SCRATCH BEHAVIOR**
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# NEVER FORGET

- 3% OF DERMATOLOGY PATIENTS HAVE A PRIMARY PSYCHIATRIC DISORDER
- 8% HAVE SECONDARY PSYCHOPATHOLOGY DUE TO SKIN DISORDERS
- 14% HAVE PSYCHOLOGICAL CONDITION EXACERBATING THEIR DERMATOSIS
- 17% NEED INTERVENTION TO DEAL WITH PSYCHOSOCIAL ISSUES 2NDRY TO SKIN DISEASE
- 85% SAY PSYCHOLOGICAL ASPECTS OF DERMATOSIS IS A MAJOR COMPONENT
- “THE BRITISH ASSOCIATION OF DERMATOLOGISTS’ WORKING PARTY”
- MARSHALL C, TAYLOR R, BEWLEY A. PSYCHODERMATOLOGY IN CLINICAL PRACTICE: MAIN PRINCIPLES. ACTA DERM VENEREOL. 2016;96(217):30-4.



Thanks for your attention

A PODCAST BY MICHELE PANA

# SKIN SOUL & PSYCHE

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Psychosomatic medicine may be a necessity for  
Dermatology residents.