CHAPTER 11
FEVER

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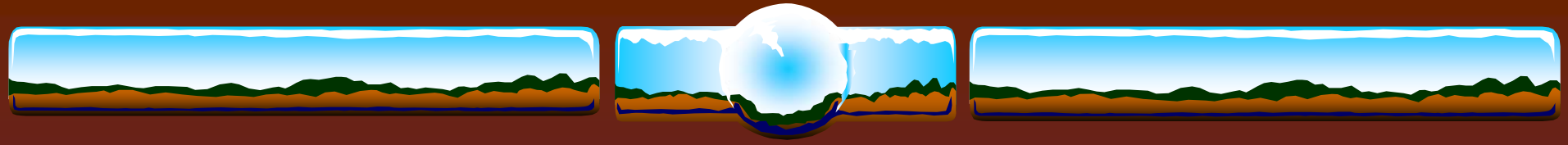
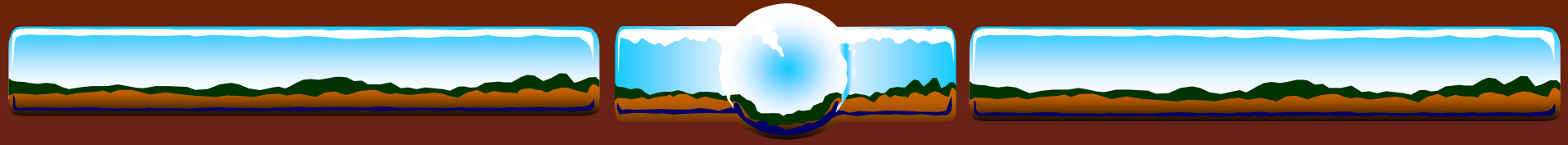


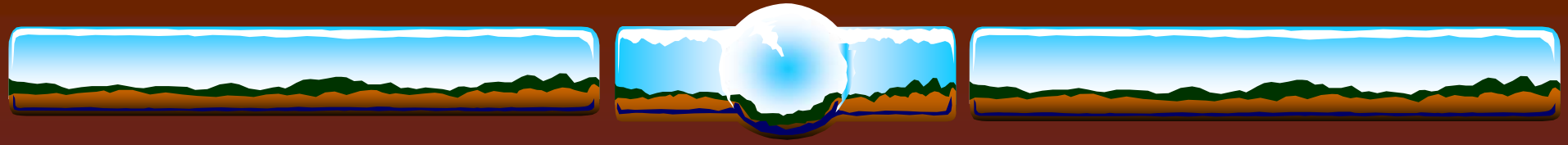
DEFINITION OF FEVER

- Fever is an elevation of body temperature that exceeds the normal daily variation, in conjunction with an increase in hypothalamic set point



VARIATION IN TEMPERATURE

- Anatomic variation
- Physiologic variation:
  - Age
  - Sex
  - Exercise
  - Circadian rhythm
  - Underlying disorders



NORMAL BODY TEMPERATURE

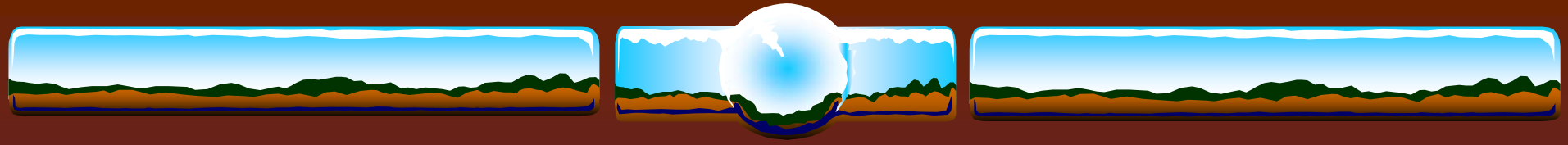
- Maximum normal oral temperature
  - At 6 AM : 37.2
  - At 4 PM : 37.7

PHYSIOLOGY OF FEVER

- Pyrogens:
  - Exogenous pyrogens:
    - Bacteria, Virus, Fungus, Allergen,…
  - Endogenous pyrogen
    - Immune complex, lymphokine,…
- Major EPs: IL1, TNF, IL6

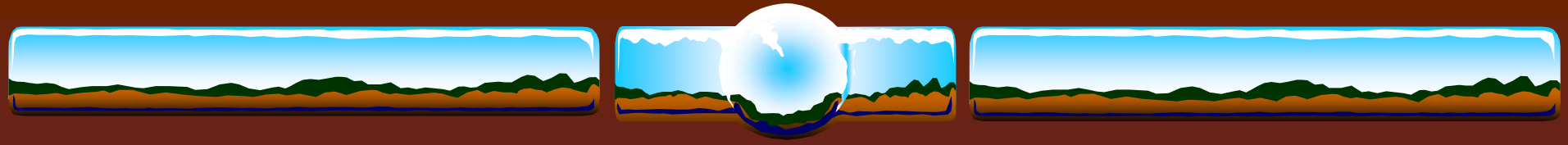
PHYSIOLOGY OF FEVER

- Exogenous pyrogen → Activated leukocytes → Endogenous pyrogen(IL1,TNF,…)
- → Acute Phase Response
- Preoptic area of anterior hypothalamus (PGE2) increase of set point =>
  - Brain cortex
  - Vasoconstriction → heat conservation
  - Muscle contraction → heat production → **FEVER**



ACUTE PHASE RESPONSE

- Metabolic changes
  - Negative nitrogene balance
  - Loss of body weight
- Altered synthesis of hormones
- Hematologic alterations
  - Leukocytosis
  - Thrombocytosis
  - Decreased erythrocytosis
- Altered hepatocyte function (**Acute phase reactants**)
  - C reactive protein(increased)
  - Serum amyloid A(increased)
  - Fibrinogen(increased)
  - Fibronectin(increased)
  - Haptoglobin(increased)
  - Ceruloplasmin(increased)
  - Ferritin(increased)
  - Albumin(decreased)
  - Transferrin(decreased)



HYPERTHERMIA

- Heat production exceeds heat loss, and the temperature exceeds the individuals set point

CAUSES OF HYPERTHERMIA SYNDROME

- Heat stroke: Exercise, Anticholinergic
- Drug induced: Cocaine, Amphetamine,MAO inh.
- Neuroleptic malignant syndrome:Phenothiazine
- Malignant hyperthermia: Inhalational anesthetics
- Endocrinopathy: throtoxicosis, pheochromocytoma

DIAGNOSIS OF HYPERTHERMIA

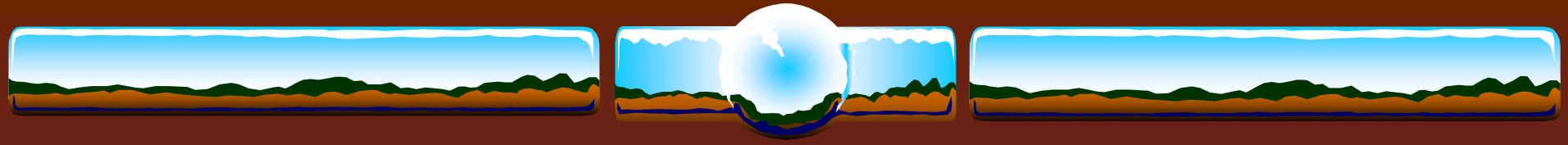
- History
- Antipyretics are not effective
- Skin is hot but dry

TREATMENT OF FEVER

- Most fevers are associated with self-limited infections, most commonly of viral origin.

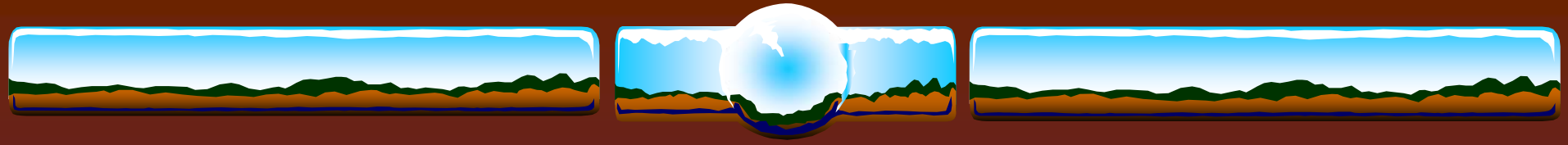
TREATMENT OF FEVER

- Reasons not to treat fever:
  - The growth and virulance of some organisms
  - Host defense-related response
  - Fever is an indicator of disease
  - Adverse effect of antipyretic drugs
  - Iatrogenic stress
  - Social benefits



DISCOMFORT DUE TO FEVER

- For each 1 °C elevation of body temperature:
  - Metabolic rate increase 10-15%
  - Insensible water loss increase 300-500ml/m2/day
  - O2 consumption increase 13%
  - Heart rate increase 10-15/min

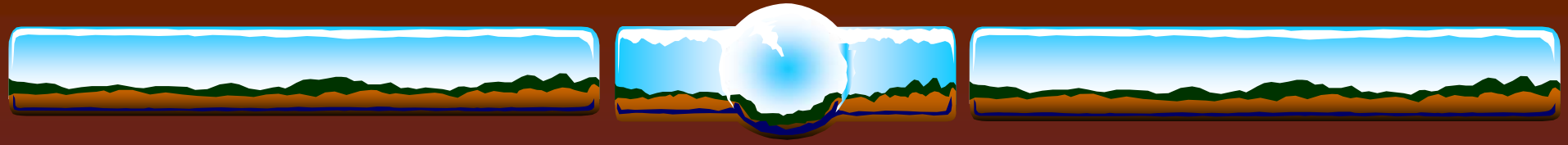


TREATMENT OF FEVER

- Reasons to treat fever:
  - The elderly individual with pulmonary or cardiovascular disease
  - The patient at additional risk from the hypercatabolic state (Poor nutrition, Dehydration)
  - The young child with a history of febrile convulsions
  - Toxic encephalopathy or delirium
  - Pregnant women (contraversy)
  - For the patient comfort
  - Hyperpyrexia

Treatment Strategies

- **Acetaminophen is generally a first-line antipyretic due to being well tolerated with minimal side effects.**
- Pediatric dose: 10-15mg/kg q4-6h (2400mg/day); adult: 650mg q 4 h(4000mg)
- Can be hepatotoxic in high doses; can upset stomach



Clinical Pearls

- Don’t give aspirin to children under 18 years (Reye’s Syndrome)
- Try water sponge bath; remove blankets and heavy clothing; keep room at comfortable temp

ATTENUETED FEVER RESPONSE

- Fever may not be present despite infection in:
  - Newborn
  - Elderly
  - Uremia
  - Significant malnourished individual
  - Taking corticosteroids

DRUG FEVER

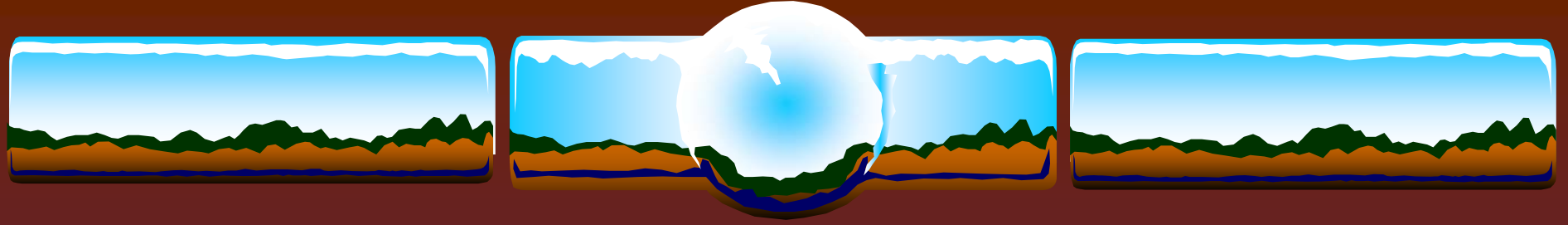
- PATHOGENEGIS
  - Contamination of the drug with a pyrogen or microorganism
  - Pharmacologic action of the drug itself
  - Allergic (hypersensitivity) reaction to the drug

DRUG FEVER

- Fever out of proportion to clinical picture
- Associated findings:
  - Rigor (43%), Myalgia (25%), Rash (18%), Headache (18%),
  - Leukocytosis (22%), Eosinophilia (22%), Serum sickness,Proteinuria Abnormal liver function test

DRUG FEVER

- Onset and duration:
  - Onset: 1-3 weeks after the start of therapy
  - Duration: remits 2-3 days after therapy is stoped



APPROACH TO THE PATIENT WITH FEVER

ACUTE FEBRILE ILLNESS

APPROACH TO FEVER

- Personal History:
  - Age
  - Occupation
  - Place of origin,Travel History
  - Habits
    - Sexual Practices
    - Injection Drug Abuse
    - Excessive Alcohol Use
    - Consumption of Unpasteurized Dairy Products

APPROACH TO FEVER

- Underlying Diseases:
  - Splenectomy
  - Surgical Implantation of Prosthesis
  - Immunodeficiency
  - Chronic Diseases:
    - Cirrhosis
    - Chronic Heart Diseases
    - Chronic Lung Diseases

APPROACH TO FEVER

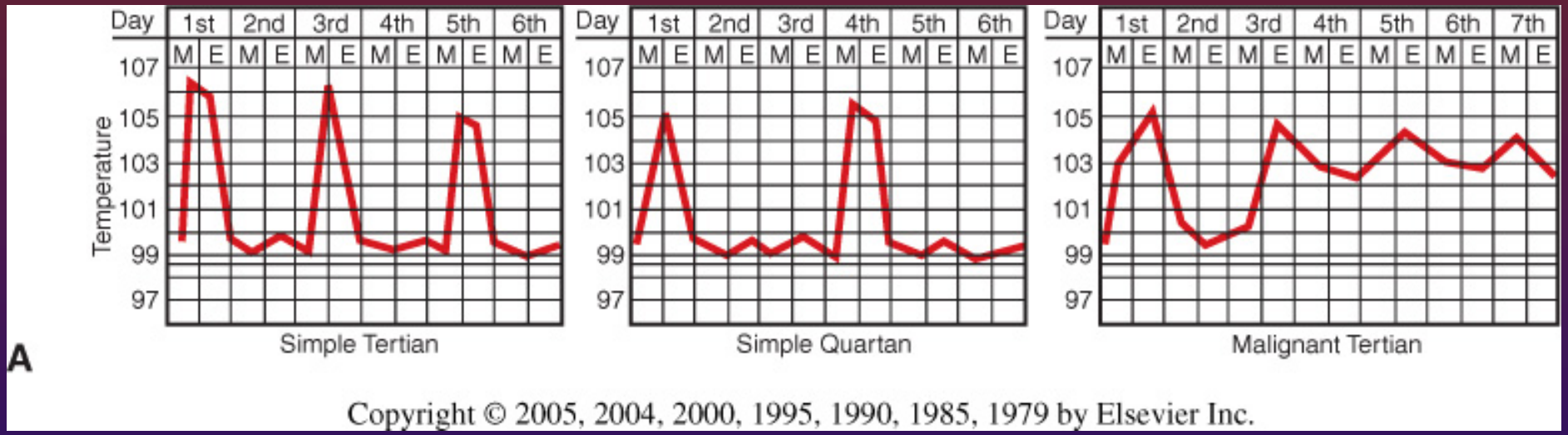
- Drug History:
  - Antipyretics
  - Immunosuppressants
  - Antibiotics
- Family History:
  - TB in the Family
  - Recent Infection in the Family

APPROACH TO FEVER

- Associated Symptoms:
  - Shaking chills
  - Ear pain,Ear drainage,Hearing loss
  - Visual and Eye Symptoms
  - Sore Throat
  - Chest and Pulmonary Symptoms
  - Abdominal Symptoms
  - Back pain, Joint or Skeletal pain

PATTERN OF FEVER

- Sustained (Continuous) Fever
- Intermittent Fever (Hectic Fever)
- Remittent Fever
- Relapsing Fever:
  - Tertian Fever
  - Quartan Fever
  - Days of Fever Followed by a Several Days Afebrile
  - Pel Ebstein Fever
  - Fever Every 21 Day



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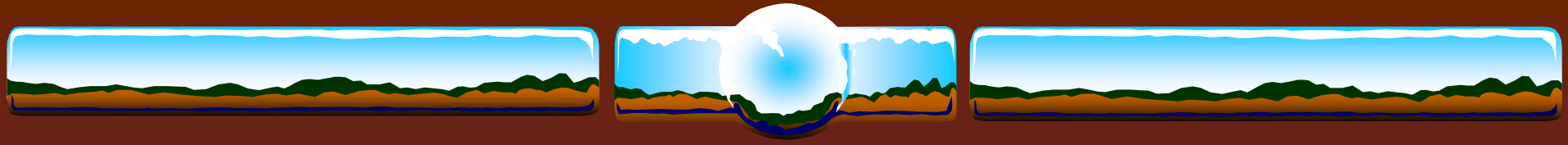

Date		1st week							2nd week							3rd week							4th week						
Day of disease		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Pulse	Temp.																												
170	108																												
160	107																												
150	106																												
140	105																												
130	104																												
120	103																												
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Respirations																													
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Temperature

Pulse

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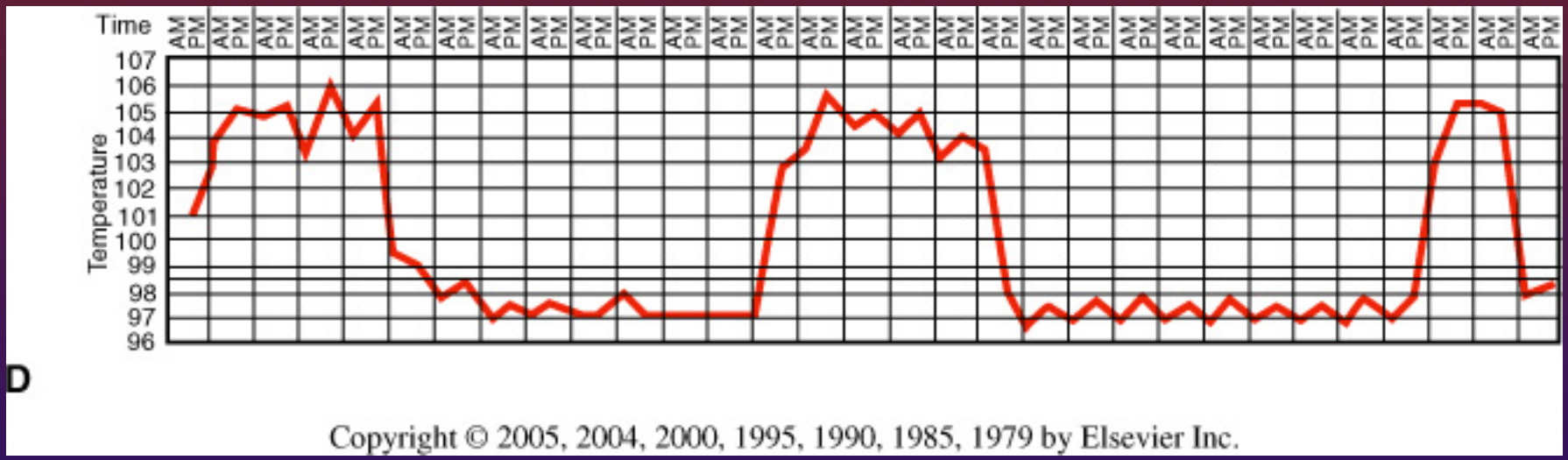

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APPROACH TO FEVER

- Physical Examination:
  - Vital Signs
  - Neurological Exam.
  - Skin Lesions,Mucous Membrane
  - Eyes
  - ENT
  - Lymphadenopathy
  - Lungs and Heart
  - Abdominal Region (Hepatomegaly,Splenomegaly)
  - Musculoskeletal

LABORATORY STUDY

IN PATIENT WITH FEBRILE ILLNESS

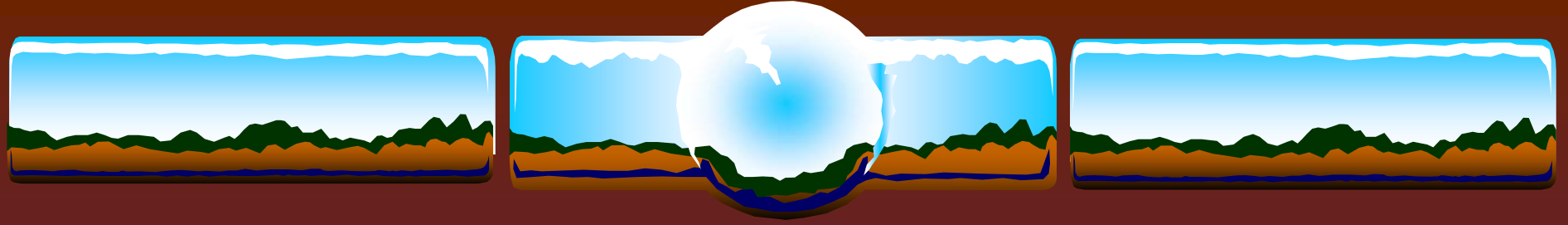
- Assess the extent and severity of the inflammatory response to infection
- Determine the site(s) and complications of organ involvement by the process
- Determine the etiology of the infectious disease

Initial Laboratory Evaluations in **UNEXPLAINED PROLONGED FEVER**

- CBC (diff.)
- PBS for Malaria and borelia
- Two Blood Culture in 30 min. Interval
- CXR
- U/A
- L.F.T. in selected patients
- Wright in selected patients

INDICATIONS OF HOSPITALISATION IN PATIENT WITH FEBRILE ILLNESS

- Persons who are clinically unstable or are at risk for rapid deterioration
- Major alterations of immunity
- Need for IV Antimicrobials or other fluids
- Advanced age



FUO

FEVER OF UNKNOWN ORIGIN

FUO

- Classic FUO
- Nosocomial FUO
- Neutropenic FUO
- HIV-Associated FUO

Classic FUO

- Definition:
  - Fever of 38.3 C or higher on several occasions
  - Fever of more than 3 weeks duration
  - Diagnosis uncertain, despite appropriate investigations after at least 3 outpatient visits or at least 3 days in hospital

Nosocomial FUO

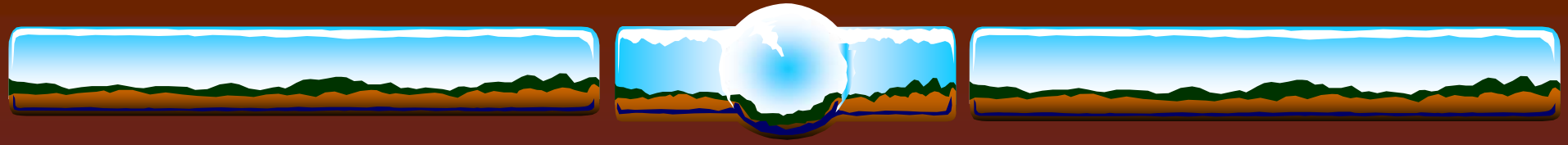
- Definition:
  - Fever of 38.3 or higher on several occasions
  - Infection was not manifest or incubating on admission
  - Failure to reach a diagnosis despite 3 days of appropriate investigation in hospitalized patient

Neutropenic FUO

- Definition:
  - Fever of 38.3 or higher on several occasions
  - Neutrophil count is <500/mm3 or is expected to fall to that level in 1 to 2 days
  - Failure to reach a diagnosis despite 3 days of appropriate investigation

HIV-Associated FUO

- Definition:
  - Fever of 38.3 or higher on several occasions
  - Fever of more than 3 weeks for outpatients or more than 3 days for hospitalized patients with HIV infection
  - Failure to reach a diagnosis despite 3days of appropriate investigation



Causes of classical FUO

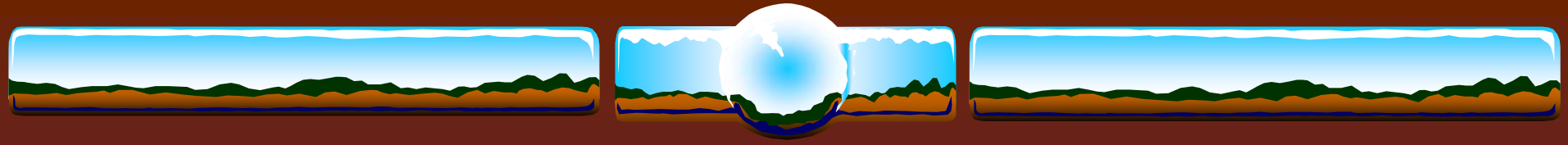
Infections	22-58%
Neoplasms	up to 30%
Noninfectiouse inflammatory diseases	up to 25%
Miscellaneous causes	up to 25%
Undiagnosed	up to 30%

Infections commonly associated with FUO

- Localized pyogenic infections
- Intravascular infections
- Systemic bacterial infections (Tuberculosis, Brucellosis,…)
- Fungal infections
- Viral infections
- Parasitic infections

Malignancies commonly associated with FUO

- Hodgkin’s disease
- Non-hodgkin’s lymphoma
- Leukemia
- Renal cell carcinoma
- Hepatoma
- Colon carcinoma
- Atrial myxoma



Noninfectious inflammatory diseases with FUO

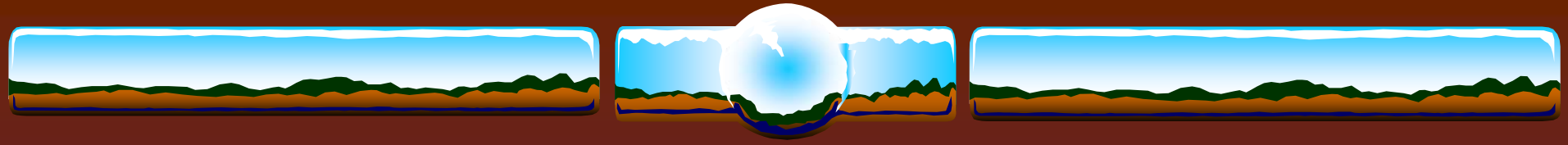
- Collagen vascular/ hypersensitivity diseases
  - Lupus
  - Still's disease
  - Temporal arteritis (Giant cell arteritis)
- Granulomatouse diseases
  - Crohn's disease
  - Sarcoidosis
  - Idiopathic granulomatouse disease

Miscellaneous causes of FUO

- Drug fever
- Factitious fever
- FMF
- Recurrent pulmonary emboli
- Subacute thyroiditis

FACTITIOUS FEVER

- Diagnosis should be considered in any FUO, especially in:
  - Young women
  - Persons with medical training
  - If the patients clinically well
  - Disparity between temperature and pulse
  - Absence of the normal diurnal pattern



Causes of FUO lasting > 6 month

Undiagnosed	19%
Miscellaneous	13%
Factitious	9%
Granulomatouse hepatitis	8%
Neoplasm	7%
Infection	6%
No fever	27%

Approach to FUO

- Determine whether the patient has a true FUO
- Workup of true FUO:
  - Careful history
    - Serial follow-up histories
  - Careful physical examination
    - Physical examination should be repeated

Laboratory examination:

- CBC(diff)
- PBS
- ESR
- U/A
- S/E
- Culture of blood, urine,…
- Skin test
- Serology
- ANA

Imaging:

- CXR
- Ultrasonography
- Radiographic contrast study
- Radioneuclide scan
- CT or MRI

Invasive Procedures

- Biopsies:
  - Bone marrow
  - Skin lesion
  - Lymph node
  - Liver
  - Temporal artery


WEBSHOTS