The Apallic Syndrome / Vegetative State

One of the most severe neurological conditions

Exact diagnosis and modern treatment

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Pathophysiology of apallic syndrome (AS)

- Disconnection of cortical function to brain stem regulation centers
- Pallium, Latin term for old Greek overcoat Signalizing a functional disturbance
- Anatomical basis:
  - Lesion of the ascending reticular system
  - Discrete damage of cortical and sub-cortical regions (local, regional)
  - Severe damage of the cortex (laminar lesion) and/or diffuse or local damage of sub-cortical areas

Symptoms of AS/VS

- Coma vigile
- No recognition of the surroundings
- No contact to the surroundings
- No directed reaction to external stimuli
- Sleep-wake-rhythm regulated by fatigue
- Optomotoric disturbances
- Flexed-stretched position of extremities and trunk
- Rigido-spasticity
- Primitive motor patterns (oral, grasping, etc.)
- Dysregulation of the vegetative system

Etiology of apallic syndrome

1. After acute, severe brain injuries
   TBI, encephalitis, hypoxia, malignant stroke etc.
   Remission possible

2. After progredient, diffuse brain processes
   CJD, M. Alzheimer, M. Pick, Chorea Huntington etc.
   Final stage
   Remission not possible

3. Intoxication
   - Acute
     Exogenous (neuroleptics etc.)
     Endogenous (hepatic, uremic etc.)
     Full remission possible
   - Chronic
     Exogenous (Minamata disease etc.)
     Endogenous (hepatic, thyreotoxic etc.)
     Partial remission possible

Epidemiology of AS/VS Divergences in statistic evaluation

Prevalence 1.9/100.000 ppl./year in Austria (160 pat.)

Prevalence 1,7/100.000 ppl./year in Germany (1.500 pat.)

Prevalence in Italy and Belgium 0.9 – 2.0/100.000 ppl./year

Incidence USA 15.000-35.000 pat./year

Incidence Great Britain 1.500 pat./year

Incidence France 1.000-1.200 pat./year (post-traumatic)

Incidence Japan 10.000-17.000 pat./year

Persistent Vegetative State (VS) Critical aspects

- Vegetative State – Persistent Vegetative State: Term mixes diagnoses and prognoses, only sub-optimal rehabilitation is possible (B. Jennet, 2002)
- Vegetative State, a detailled neurological description and analysis is not existing, no description of initial stage, transitory stage, full stage and remission stage)
- Vegetative State: assumed as a static condition (B. Jennet, 2002)
- Vegetative State: no therapeutical concept (B. Jennet, 2002)
- Vegetative State: critics of international community and pro life committee of catholic bishops in the USA. The word vegetative can suggest the patient is a vegetable, therefore subhuman and discriminatory.
- Critics of English and American experts to use the term „wakeful unconscious state"(1995), „unresponsible wakefulness"(2012).

Location of lesons causing apallic syndrome after F. Gerstenbrand, 1967

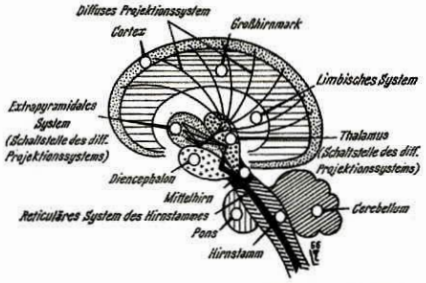


Abb. 67. Schematische Darstellung der verschiedenen Hirnformationen durch deren Ausfall das Symptomenbild des apallischen Syndroms entstehen kann. Einzeichnung des reticulären Systems im Hirnstamm und des diffusen Projektionssystems.

Apallic Syndrome Comparison with Anencephalus

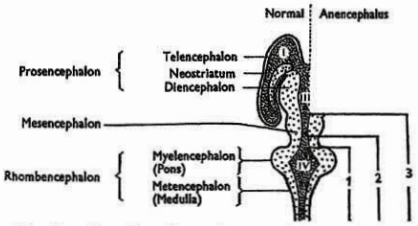
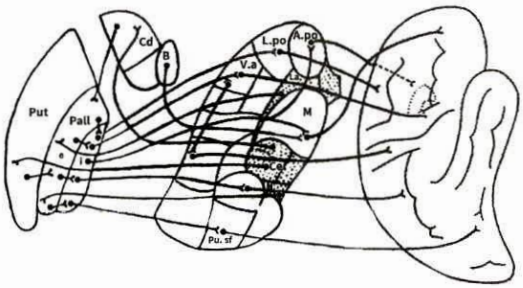


Abb. 69. Schematische Darstellung der 3 Typen des Anencephalus. 1. Rhombencephaler, 2. mesorhombencephaler, 3. mesencephaler Anencephalus (aus *M. Monnier*, Die Regulierung des Bewußtseins und ihre Störungen, in Bewußtseinsstörungen, Symp. vom 10. bis 12. I. 1961, St. Moritz, Schweiz, G. Thieme-Verlag, Stuttgart, S. 25).

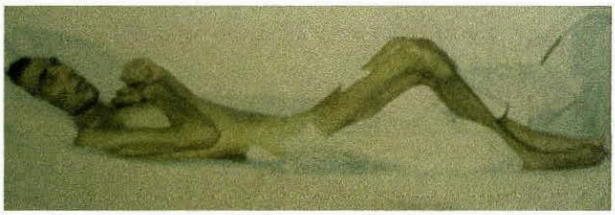
Different forms of anencephalus, after Monnier, 1961)

Unspecific Projection System of the Thalamus to the Cortex



Scheme of the connection mechanism between thalamus, the basal ganglia and the cortex. After: R. Hassler, 1964

Apallic syndrome, pat. G.B., 36ª traumatic brain injury, 1975



No modern treatment

Irreversible tertiary lesions and complications

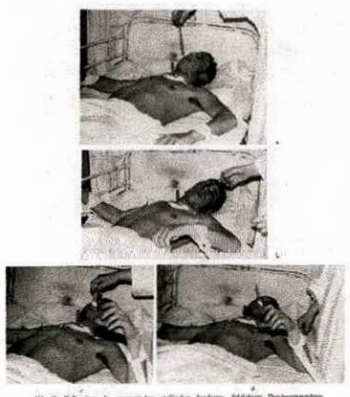
Exitus after 14 months

Apallic syndrome, pat. E.S., 19ª traumatic brain injury, 1992

Modern treatment program in special center for apallic syndrome patients, Innsbruck

No tertiary lesions, minimal complications

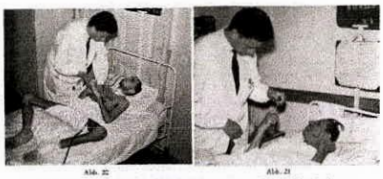
Remission after 5 months to minimal defect state



Pat. G.N., 39a

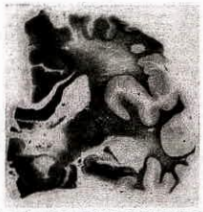
- Full stage, traumatic apallic syndrome
- Optic induced oral mechanism,
- Bulldogg-reflex

Apallic Syndrome
Full stage, traumatic aetiology



- Grasping reflex
  - Abb. 20: tonic
  - Abb. 21: phasic

Traumatic Apallic Syndrome, full stage



L.G., 32a, full stage, died 9 months after accident,
Diffuse lesion of the white matter fronto-temporal with local cystic necrosis, arterial compression necrosis in thalamus, cystic lesions peri-aquaeductal. (Heidenhain staining)

Apallic Syndrome after progredient, diffuse brain processes to a final stage

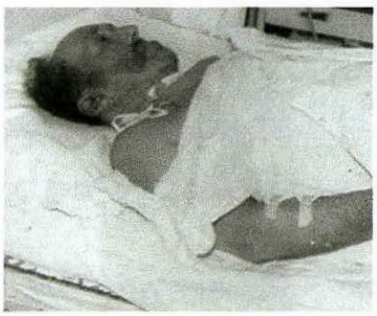
F. Gerstenbrand, 1967, 1977, F. Gerstenbrand, E. Rumpl, 1983

- Disintegration of higher and highest brain function
  (Diffuse organic psychosyndrome)
- Multilocular cerebral Symptoms
  Aphasia, Apraxia, motoric disabilities, etc.
- Klüver-Bucy Phase
  3 different stages
- Preapallic Phase
  called „dementia", motoric primitive patterns, mass movements, decerebrate rigidity, etc.
- Apallic Syndrome, Full Stage
  No remission signs

Apallic Syndrome after progredient, diffuse brain processes as final stage

- Disintegration of higher and highest brain function
  Diffuse organic psychosyndrome
- Multilocular cerebral Symptoms
  Aphasia, Apraxia, motor disabilities, etc.
- Klüver-Bucy Phase
  3 different stages
- Preapallic Phase
  „dementia", motoric primitive patterns, mass movements, decerebrate rigidity, etc.
- Apallic Syndrome, Full Stage
  No remission signs, End State

Apallic syndrome as a final stage



Symptoms of Locked-in syndrome
No real coma state

- Total paralysis of all extremities, trunk, neck and motor brain nerves
- Eye opening and vertical eye movements possible
- Consciousness and perception fully maintained
- Spontaneous respiration possible
- Impairment of swallowing

- Alpha-EEG

Etiology of Locked-In Syndrome Lesion in Pons

- Infarction caused by basilar thrombosis
- Hemorrhage
- Encephalitis
- Tumor
- Traumatic lesion

- Disconnection of the motor system, sensory connections undisturbed

Different Types of LIS (after Bauer et al, 1979)

- According to neurological symptoms
  - Classical Locked-In syndrome
  - Incomplete Locked-In syndrome
  - Total Locked-In syndrome
- According to time course
  - Chronic Locked-In syndrome
  - Transient Locked-In syndrome

Patient L.I.S , 45ª, female

Traumatic etiology

Defect state

Fully in need of care

Profound differences between apallic syndrome and locked-in syndrome

- Apallic syndrome
  Loss of all brain functions, reduction to the midbrain-level (coma vigile, no voluntary motor action, primitive motor patterns), irresponsible wakefulness

  temporary or permanent

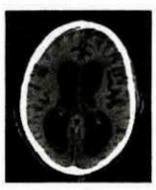
- Locked in syndrome
  Loss of all motoric abilities, except rest in optomotoric functions, undisturbed wakefulness, contact to the surrounding, normal body sensation

  temporary or permanent

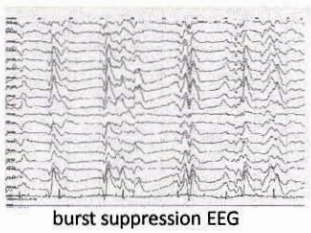
AS hypoxic, full stage

75 y, post-resuscitation state
Prolonged myoclonus symptoms

Sepsis and 10 additional diagnostic problems



cerebral CT

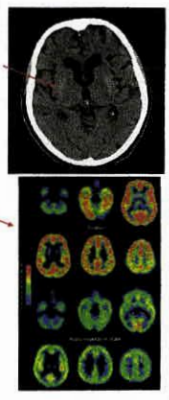


burst suppression EEG

Imaging in AS/VS

- CCT: Signal changes in basal ganglia,
  AS hypoxic
  remission stage IV

- PET: 11C-Flumazenil (Benzodiazepine receptor-ligand)-binding as sign for neuronal integrity
  AS/VS
  remission stage I

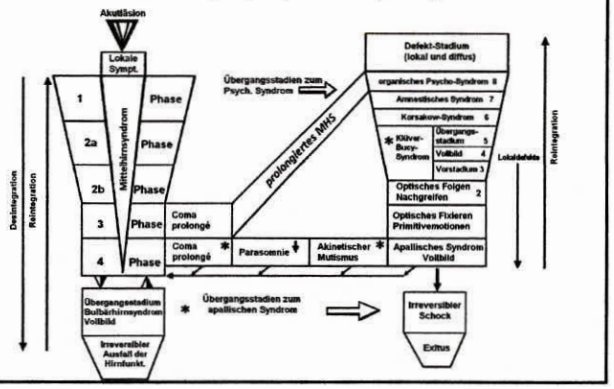


Apallic syndrome, after acute severe brain injury

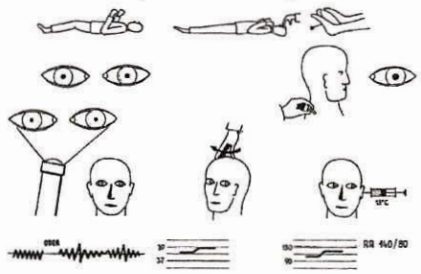
- Initial stage:
  - acute midbrain syndrome (central 5 phases, lateral 2 phases)
  - acute bulbar brain syndrome (2 phases)
- Transition stage (3 phases)
- Full stage of AS
- Remission stage (8 phases)
- Defect stage (multilocular lesions, regional lesions, diffuse lesions)

The course of apallic syndrome after acute brain damage

F. Gerstenbrand, 1967, 1977, F. Gerstenbrand, E. Rumpl, 1983



Midbrain syndrome phase III



Akutes traumatisches Mittelhirnsyndrom - Phase 3:
Schematische Darstellung. Nähere Erläuterung s. Text und Phase 1.
Aus: F. Gerstenbrand und C. H. Lücking,
Die akuten traumatischen Hirnstammschäden, 1970

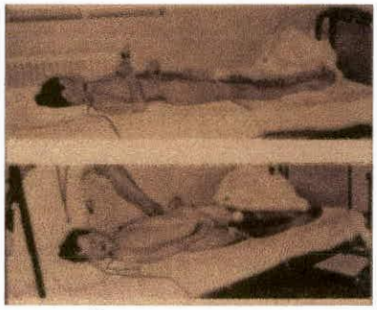
Phase III, Stretch-Flex position, disinhibition of autonomic system

Midbrain syndrome phase IV

- Coma
- Missing blink reflex and ocular movements
- Divergent position of bulbi
- Pupils reduced reaction to light
- Vestibulo-ocular reflexes disturbed
- Stretch position of the extremities
- Increased muscle tone, pyramidal signs
- Respiration machine – like rhythm
- Hyperthermia, tachycardia, increased blood pressure

Acute secondary midbrain syndrome

Traumatic brain injury, passager brain edema



Phase III, IV

STADIEN DER HIRNSTAMMSCHÄDEN NACH SUPRATENTORIELLER RAUMFORDERUNG / ZENTR. HERNIATION		MHS					BHS	
		I	II A	II B	III	IV	I	II
VIGILITÄT		SOMNOLENZ	SOPOR	COMA	COMA	COMA	COMA	COMA
REAKTION	AKUSTISCHE REIZE	GERING VERZÖGERT MIT ZUWENDUNG	VERZÖGERT OHNE ZUWENDUNG	FEHLEND	FEHLEND	FEHLEND	FEHLEND	FEHLEND
	SCHMERZREIZE	PROMPT GERICHTETE ABWEHR	VERZÖGERT UNGERICHTETE ABWEHR	RESTE UNGERICHTETER ABWEHR	BEUGE-STRECK-STELLUNG	STRECK-SYNERGISMEN	REST-STRECK-SYNERGISM.	FEHLEND
OPTOMOTORIK	-STELLUNG BULBUS -BEWEGUNG	NORMAL	NORMAL	BEGINNENDE DIVERGENZ	DIVERGENZ	DIVERGENZ	DIVERGENZ FIXIERT	DIVERGENZ FIXIERT
		PENDELND	SCHWIMMEND	DYSKONJUGIERT	FEHLEND	FEHLEND	FEHLEND	FEHLEND
	PUPILLENWEITE							
	LICHTREAKTION							
KÖRPERMOTORIK	KÖRPERHALTUNG							
	SPONTANMOTORIK	MASSEN- UND WÄLZ-BEWEGUNGEN	MASSENBEWEG. ARME STRECKBEWEG. BEINE	MASSENBEWEG. ARME STRECKBEWEG. BEINE	BEUGE-STRECK-HALTUNG	STRECK-HALTUNG	REST-STRECK-HALTUNG	SCHLAFFE HALTUNG
	TONUS	NORMAL	BEINE GERING ERHÖHT	BEINE ERHÖHT	ERHÖHT	STARK ERHÖHT	GERING ERHÖHT	SCHLAFF
	BABINSKI PHÄNOMEN	↓ ↓	↑ ↓	↑ ↓	↑ ↑	↑ ↑	↑ ↑	—
OBLIGAT	ATMUNG							—
VEGETATIV	PULS	LEICHT ERHÖHT	NORMAL	BESCHLEUNIGT	RESCHLEUNIGT	STARK BESCHLEUNIGT	BESCHLEUNIGT	VERLANGSAMT
NICHT OBLIGAT	RR	NORMAL	NORMAL	NORMAL	LEICHT ERHÖHT	ERHÖHT	NORMAL	ERNIEDRIGT
	KÖRPERTEMPERATUR	NORMAL	NORMAL	LEICHT ERHÖHT	ERHÖHT	STARK ERHÖHT	ERHÖHT	NORMAL ERNIEDRIGT

Prognosis of AS/VS

- Cannot be made in the first 6 weeks after an acute brain damage
- Within the first 6 months no decisions about ongoing of active treatment program can be made
- 80% of the patients with an traumatic apallic syndrome develop remission, same post encephalitic, post intoxication
- 60% of the patients with a hypoxic apallic syndrome show remission, mostly with severe defects

Apallic Syndrome - Remission Stages
Innsbruck Remission-Scale - 1

- Phase I: Optic fixation – reduce of Coma vigile, sopor
- Phase II: Optic tracking – sleep-wake-rhythm nomalising, stupor
- Phase III: Pre-Klüver-Bucy-Phase – combination in the primitive motor reflexes, hypersomnia – wakeful
- Phase IV: Klüver-Bucy-Phase – typical Klüver-Bucy reflexes, obnubilation

Apallic Syndrome - Remission Stages
Innsbruck Remission-Scale - 2

- Phase V: Post-Klüver-Bucy-Phase – hypersomnia, communication possible
- Phase VI: Korsakov syndrome – voluntary behavior, disorientation, confusional state
- Phase VII: Amnestic phase – emotional irritation, flat emotions
- Phase VIII: Psycho-organic syndrome – normal consciousness, aware

different local lesions with adequate neurological symptoms

Therapeutic strategies in apallic syndrome

- Initial phase: causal therapies
- Neurorehabilitation in special unit, individual neurorehabilitation program
  - Stimulation therapies (visual, haptic, acustic, basal stimulation)
  - Verticotherapy
  - Physiotherapy, specialized program
  - Logopedia, Ergotherapy
  - Special drug treatment (antispastics, anticonvulsants, ß-blockers, psychostimulants, etc.)

Therapeutic community relatives included

Special Treatment Program in Neurorehabilitation

- Activation of the proprioceptive system
  logomatics, cosmonaut trousers etc.
- Hyperbaric Oxygenation Treatment
- Surgical interventions of complications
  (joint contractions, hydrocephalus occlusus,
- Operation of periarticular ossification

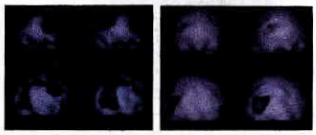
Case 2

MJ, 31ª, male, AS,
CO-intoxication, suicide,
remission state II-III during 12 years.

HBOT: 60 sessions
HBO home treatment: 350 sessions
1,5 ATA

Additional:
physio-therapy
logopedics

Marked improvement
minimal cognitive defects,
spastic signs



before HBO after HBO

Case 3

SPECT:

Marked improvement of perfusion

JN, 21ª, male, AS, traumatic
remission stage II-III
HBOT: 64 sessions
1.5 – 1.75 ATA

Additional treatment:
physio therapy

Significant improvement
Light defect symptoms: cerebellar, spastic symptoms, speech disturbances (pseudo-bulbar), cognitive deficits

Summarizing

- HBOT in apallic syndrome start
  - in full stage
    → as early as possible
  - in remission stage with temporary interruption state II-III
    → after 3 months
  - in later remission states and in defect stage without sufficient result of running rehabilitation
    → in any case
- Continuation of classic treatment and consequent neuro-rehabilitation program

Conclusion

Apallic syndrome and HBO-treatment:

Full stage: re-organization of cortical connections to brain stem centers supported by the activation of reticular system

Remission stage: Revitalization of the cortical network (idling neurons)

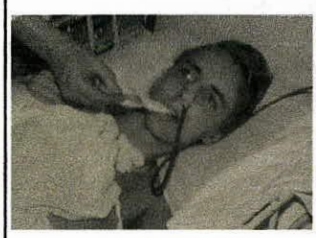
Revitalization of damaged axons

Defect stage: Re-activation of dendrite system

Ethical Considerations

- Every patient with an Apallic Syndrome/Vegetative State has to be treated in a special department, using an individual program
- The treatment has to be continued until a fixed defect state can be stated
- No connection with economic limitation
- No discussion for final of life decision
- Renunciation of maximal therapy is acceptable

AS Development (I)



Full stage of traumatic apallic syndrome

Early remission stage

AS Development (II)

Late remission stage

Full recovery

Terri Schiavo (USA)

Apallic syndrome/vegetative state, remission state II-III, contact with the surroundings

- Emotional reaction
- Optic fixation to her mother
- Turn towards
- Contact reaction
- Well-balanced body state
- Vegetative system regulated
- No artificial respiration
- Nutrition by PEG

End of life decision by court, withdrawal of liquid and nutrition.

Apallic syndrome – sindrome apallico (traumatic), Salvatore C., 38ª (I)

- Traumatic brain injury, August 2003
- late onset of remission
- Defect state with neurological deficits and orthopedic deficits

Patient could hear noises of the surroundings, felt pain and physical contact. Deep desperation.

Successful rehabilitation after AS/VS, traumatic, Fred A., 39ª (A)

- Car accident 1995 with 30 years
- Apallic syndrome in full stage in a special center for apallic patients over 6 months
- Remission phase over 2 years
- Treated in special rehabilitation center for apallic patients
- Continued rehabilitation with stepwise improvement
- Full Integrated in family life, father of a 3 years old daughter
- Only partial handicapped
- Strict aim to build up a normal professional condition