APALLIC SYNDROME / VEGETATIVE STATE TREATMENT WITH HYPERBARIC OXYGENATION

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The Apallic Syndrome/Vegetative State (AS/VS) is one of the severest neurological conditions and an absolutely tragic health condition. The term Apallic Syndrome is used mainly in Europe, also because of misunderstanding for "Vegetable State" (Shanghai Daily Com. 19.12.2005). With modern therapeutic strategies 60% of AS/VS patients can at least partially recover, 25% of them are possible to be resocialized. The results are better in patients after a traumatic brain damage. In the Apallic Syndrome, initial stage, remission stage and the full stage have to be differentiated; the remission stage shows 8 different phases. Patients in full stage and the first 3 phases of remission especially after hypoxia in a third are without further improvement. Most of these patients without any signs of recovery have to stay in special nursing homes or must be cared at home, even for years. Previously, some of Apallic patients evoked large scale media interest, like the patient Terri Schiavo. Medico legal discussion and the accusation offalling back to Middle Age or in the time of "forced euthanasia "(Zwangs-Euthanasie) came up.

The number of patients with an AS/VS is growing worldwide because of better equipped intensive care units and an there are increasing numbers even in not well medically developed countries. Patients after severe traumatic brain injury or anoxia of different origin are maintained a life and can develop an AS/VS. Really experienced and special equipped neuro-rehabilitation centres for patients with Apallic Syndrome are rare. The main demand for a patient developing an Apallic Syndrome is, to give the chance for a modern treatment beginning as early as possible, with a special treatment programme, if possible in the initial stage of the acute midbrain syndrome (Gerstenbrand, Lücking, 1970), the late diencephalic syndrome (Plum and Posner 1971). Besides the use of different drugs aiming to avoid a secondary brain damage in the penumbra in the early phase, there are other pharamceutical or electrophysiological means in the later course to activate the propriozeptive system and the reticular tract. The method of Hyperbaric Oxygenation (HBO) seems to provide new therapeutic opportunities for Apallic patients.

HBO has already successfully been used as an adjunct therapeutic tool in a number of diseases. Hohlbach et al (1976) could show an improvement in patients with early and chronic stroke states using clinical and EEG control. Borromei et al (1996) reported positive results in patients with severe Parkinson's Syndrome. Similar results where published by Hoggard et al in a case report (2002). Ya Neretin et al (1998) had treated 64 Parkinson patients with akinetic-rigide form successfully with HBO. An improvement in patients with frontal Leukoariosis was published by Balcarce et al (1998). A positive influence for

cognitive disturbances was observed by Alex et al (2005). An antidepressive effect was found in animal experiments by Somen-Secgin et al (2005).

Wassmann et al (1999) used HBOT in a randomized group of 99 patients with acute midbrain syndrome as a possible initial state of an Apallic Syndrome. In the HBO group 53% up to74% had a positive outcome, the remaining were dying or developed Apallic Symptoms. 33% toward 6% showed a complete recovery. From the Shanghai centre directed by Liu Quingle came a report about a young women with an Apallic Syndrome treated with HBO with an impressively positive result after 6 months. The method should be used in other Apallic patients. Positive results were also reported by Rockswold at al (1992) in patients with severe brain injury using HBOT method.

In the Ocean Hyperbaric Centre, Fort Lauderdale, 5 patients with an Apallic Syndrome, 3 after a traumatic brain injury, 2 after anoxia were treated with HBO. The treatment results were proved by single photon emission computerized tomography (SPECT). Better results were seen in the traumatic brain injured patients, including an 89 year old woman. In a 23 year old woman after a cardiac arrest with anoxia transferred from the Netherlands to the USA, the result was surprisingly good. This young patient was similar to the case of Mrs. Terri Schindler-Schiavo who was suffering from an Apallic Syndrome in the early remission stage following the analysis of the published videotape and written reports about the young woman. Three years before her dramatic death Mrs. Schiavo's husband had refused a treatment with HBOT.

The exact mechanisms of HBO related neuroprotective effects are yet to be further defined. But in AS/VS patients with only a very limited number of therapeutic options clinicians shall consider HBO as a possibly helpful treatment.

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ABSTRACTS

JULY 18-22, 2006 FORT LAUDERDALE, FLORIDA

The 1st International Symposium For The Use Of Hyperbaric Oxygenation In Neurosciences

Presented by

HB O_2 Ocean Hyperbaric Neurologic Center
Hyperbaric Oxygenation Treatment

Co-Sponsor: World Federation of Neurology,
Research Group on Space and Underwater Neurology,
Subdivision Hyperbaric Oxygenation.

Apallic Syndrome / Vegetative State Treatment with Hyperbaric Oxygenation

F. Gerstenbrand, R. Neubauer, V. Neubauer, A. Günther, W. Struhal

The 5th International Symposium For Hyperbaric Oxygen and the Recoverable Brain

Fort Lauderdale, Florida, USA

July 19-22, 2006

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

Aetiology of apallic syndrome

1. After acute, severe brain injuries
   TBI, encephalitis, hypoxia, malignant stroke etc.
   Possibility of remission
2. After progredient, diffuse brain processes
   CJD, M.Alzheimer, M.Pick, Chorea Huntington etc.
   Final stage
   Remission not possible
3. Intoxication
   3a Acute
   Exogenous (neuroleptics etc:)
   Endogenous (hepatic, uremic etc.)
   Full remission possible
   3b Chronic
   Exogenous (Minamata disease etc.)
   Endogenous (hepatic, thyreotoxic etc.)
   Partial remission possible

Epidemiology of AS/VS Divergences in statistic evaluation

Prevalence 1.9/100000 pop./year in Austria (160 pat.)

Prevalence 1,7/100000 pop./year in Germany (1.500 pat.)

Prevalence in Italy and Belgium 0.9 – 2.0/100000 pop./year

Incidence USA 15000-35000 pat./year

Incidence Great Britain 1500 pat./year

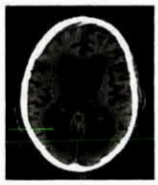
Incidence France 1000-1200 pat./year (post-traumatic)

Incidence Japan 10000-17000 pat./year

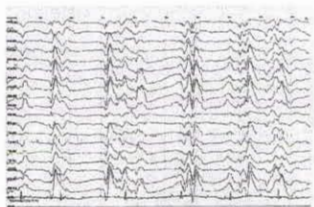
AS hypoxic full stage

75 y, post-resuscitation state
Prolonged myoclonus

sepsis and 10 additional diagnoses



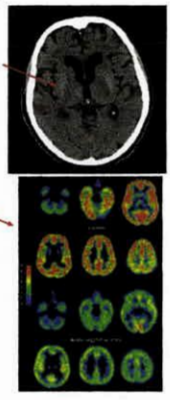
cerebral CT



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



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 commitee of catolic bishops in the US. The word vegetative can suggest the patient is a vegetable, therefore subhuman and discriminatory
- Critics english and american experts to use the term „the wakeful unconscious state" (1995)

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

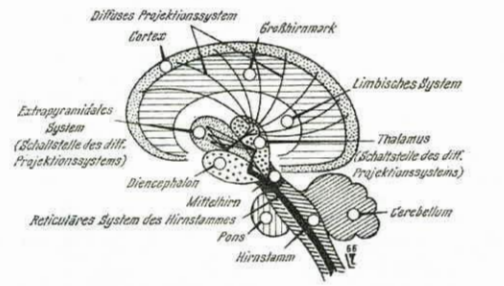


Abb. 67. Schematische Darstellung der verschiedenen Hirnformationen durch deren Ausfall das Symptomenbild des apallischen Syndroms entstehen kann. Einzeichnung des reticulären Systems im Hirnstamm und des diffusen Projektionssystems.

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

No modern treatment

Irreversible tertiary lesions, 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

No tertiary lesions, minimal complications

Remission after 5 months to minimal defect state

Terri Schiavo (USA)

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

- 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 surrounding and felt pains and physical contact. Deep desperation.

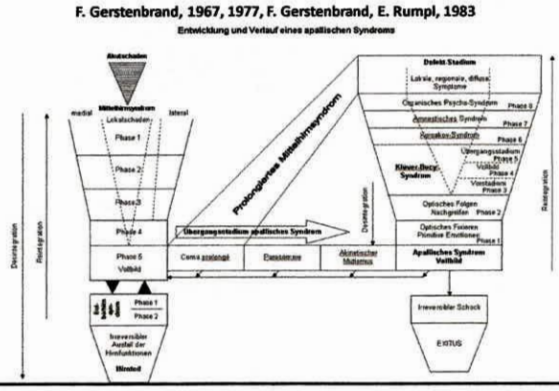
Successful rehabilitation after AS/VS, traumatic, Fred A., 39ª (A)

- 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

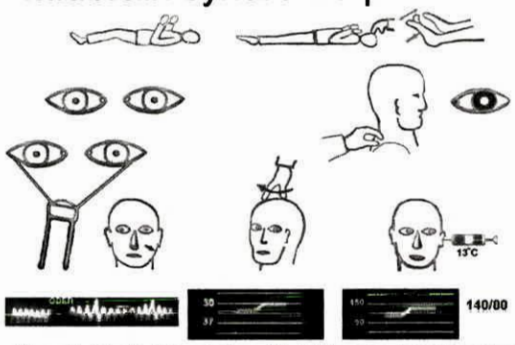
Apallic syndrome, after acute severe brain injury

- 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 leasons, regional leasons, diffuse leasons)

The course of apallic syndrome after acute brain damage



Midbrain syndrome phase III



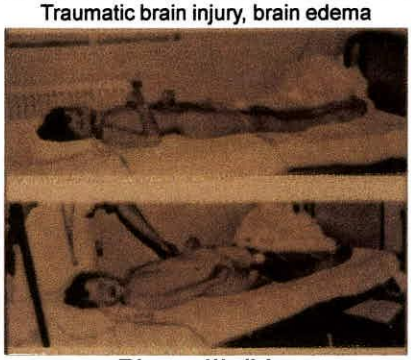
Phase III, Stretch-Flex position, disinhibition of autonomic system

Midbrain syndrome phase IV

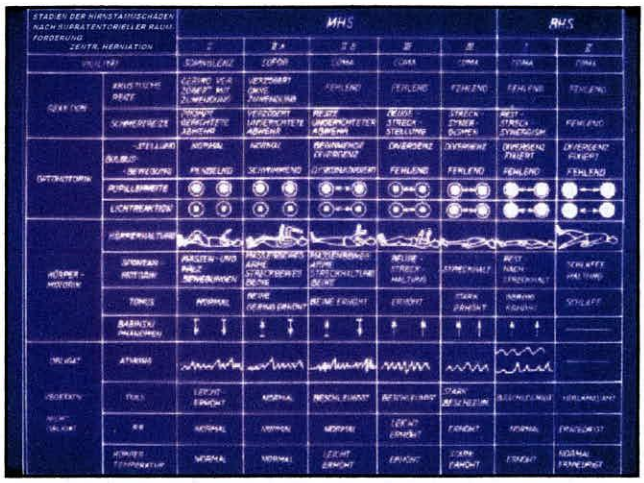
- Coma
- Missing blink reflex and ocular movements
- Divergent position of bulbi
- Pupils reduced reaction to light
- Vestibuloocular reflexes disturbed
- Stretch position of the extremities
- Increased muscle tone, pyramidal signs
- Respiration – machine like rythmus
- Hyperthermia, tachycardia, increased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

Acute secondary midbrain syndrome

Traumatic brain injury, brain edema



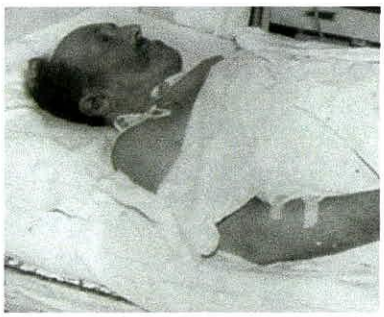
Phase III, IV



Apallic Syndrome after progredient, diffuse brain processes as final stage

- Desintegration of higher and highest brain function
  Diffuse organic psychosyndrome
- Multilocular cerebral Symptoms
  Aphasia,Apraxia,mot.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

Apallic syndrome as a final stage



Therapeutic strategies in apallic syndrome

- Causal therapies in the initial phase
- Special drug treatment (antispastics, Anticonvulsants, ß-blockers, psychostimulants, etc)
- Stimulation therapies (visual,haptic,acustic, basal stimulation)
- Verticotherapy
- Physiotherapy, ergotherapy, logopedia, Cognitotherapy
- Therapeutic community relatives included

Decisions to make during the treatment of patients with AS/VS

- Decide, whether an active rehabilitation program has to be continued in a special center, or the patient can be transferred to a nursing home with long term activating program
- Decide, whether to minimize special medical treatment, renunciation of MAXIMALTHERAPIE and continuation in nursing care

„End of life decision", realization in Austria and in most other European countries not possible, equate active euthanasia, regulated by crime law.

Prognosis of AS/VS

- Can't be made in the first 6 weeks after an acute brain damage
- Within the first 6 months there cannot be made any decisions about ongoing of active treatment program
- 80% of the patients with an traumatic apallic syndrome develop remission, same post-encephalitic
- 60% of the patients with a hypoxic apallic syndrome show remission, mostly with severe defects

AS Development (I)

Full-stage of traumatic apallic syndrome

Early remission stage

AS Development (II)

Late remission stage

Full recovery

Case 1

MP, 23ª, male, AS, traumatic
remission stage IV
HBOT: 1997 – 1999: 208 sessions, 1.5 – 1.75 ATA
HBOT: since April 2002: 600 sessions

Additional treatment: physio-therapy

Most light defect symptoms as spasticity, pseudo-bulbar symptoms, emotional irritability, frontal lobe symptoms
Full ability for self decisions

GCS: 6; Final GCS: normal

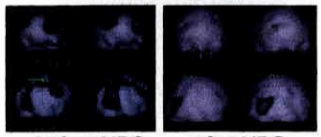
Case 2

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

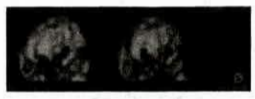
Additional:
physio-therapy
logopedics

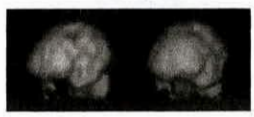
Marked improvement
minimal cognitive defects,
spastic signs



before HBO after HBO

Case 3





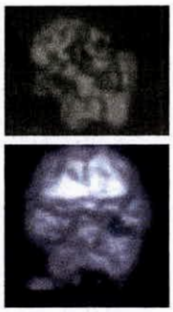
SPECT:

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



SPECT

Marked improvement of perfusion

Case 4

MAB, 89a, female, AS, traumatic, full stage

HBOT: 38 sessions,
1.1 ATA (1 hour each session)
Treatment stopped because disallowed

One week after start improvement: spasticity and encephalopathy reduced, mobilization possible, walking with help, speech understandable

Improvement to marked amelioration of quality of life with good contact to surrounding and less demand of nursing care.
Mild encephalopathy as rest state.

Case 5

NM, 23a, female, AS, hypoxic,
remission stage II-III, temporary interruption of further remission
(similar situation to Mrs. Terri Schiavo)

HBOT: 400 sessions over the course of a year, 1.5 ATA

Improvement of the apallic symptoms state II to VI.
Contact to the surrounding, marked reduction of spasticity, diminishing of encephalopathy
Removing of gastrotomy tube, oral feeding possible, partly eating by her own.
Continuation of rehabilitation program, including sensory stimulation, cognitive stimulation.

Defect stage of AS: spasticity, cerebellar symptoms, speech disturbance, cognitive impairment, rest of complications
GCS: 7, final GCS: 14

Overview

Pat.	age	sex	Aetiology	AS state	HBOT-sess.	ATA	Add. treatm.	GCS	Defect stage
MP	23	m	traumatic	rem.IV	208/600	1.5-1.75	phys.th.	6-15	light motoric, cog.imp.
MJ	31	m	CO-intox.	rem.II-III	410	1,5	phys.th., logoped		min. mot., cogn.impair.
JN	21	m	traumatic	rem.II-III	64	1.5-1.75	phys.th.		spastic, cerebellar, speech dist., cog.def.
MAB	89	f	traumatic	full stage	38	1,1	phys.th.		enceph., mot.impairm.
NN	23	f	hypoxic	rem.II-III	400	1.5	phys.th, logoped.	7-14	spasticity, cog.imp.

Literature, HBOT in neurology (I)

- Hohlbach et al (1976)
  - Improvement: stroke, early and chronic state
- Borromei et al (1996)
  - Positive results in patients with severe Parkinson syndrome
- Hoggard et al (2002)
  - Positive results in patients with Parkinson syndrome
- Ya Neretin et al (1998)
  - Parkinson syndrome, rigid-akinetic type (64 cases), positive results
- Balcarce et al (1998)
  - Encephalopathy frontal accent, improvement

Literature, HBOT in neurology (II)

- Alex et al (2005)
  - Encephalopathy, positive results,
- Wassmann et al (1999)
  - Acute midbrain syndrome, initial state of AS, randomized study, positive outcome
- Somen-Secgin et al (2005)
  - Animal experiments „anti-depressive effect"
- Rockswold at al (1992)
  - Severe traumatic brain injury, positive results
- Liu Qingle (2005)
  - Apallic syndrome, case report

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:	Re-vitalization of the cortical network (idling neurons)
	Revitalization of damaged axons
Defect stage:	Re-activation of dendrite system

Greetings from Vienna!

Stephansdom by night

Wolfgang Amadeus Mozart
1756 – 1791
„Eine kleine Nachtmusik"