

Journal of Alternative Medicine Research

Volume 1, Issue 1

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Journal of Alternative Medicine Research

The *Journal of Alternative Medicine Research* is a peer-reviewed journal published by Nova Science Publishers aimed at the scientific community interested in the broad area of integrative, complementary, and alternative medicine. This Journal provides an international, multidisciplinary forum with a holistic approach to health issues, health and medicine, social policy, service aspects, developmental aspects, epidemiology, rehabilitation, social issues, quality of life, and all other aspects of human development over the whole age spectrum. The *Journal of Alternative Medicine Research* covers all aspects of health and human development in the form of review articles, original articles, case reports, short communications, letters to the Editor, and book reviews. Manuscripts will be reviewed from disciplines all over the world. The international Editorial Board is dedicated to producing a high-quality scientific journal of interest to researchers and practitioners from many disciplines.

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Alternative medicine: A new peer-reviewed international journal with a mission

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Introduction

Alternative medicine is medicine that is not biomedicine, but alternative to it, so this is a new journal with a different focus and to some extent a focus on non-drug medicine, but we will accept any sound paper after peer-review in the field of integrative, alternative or complementary medicine. In the context of this editorial we want to define non-drug medicine in the broadest possible way, as interventions that induce healing, or as Aaron Antonovsky (1923-1994) called it with a fancier word saying basically the same: salutogenesis. Salutogenesis as the reverse process of pathogenesis, so it is not a mysterious concept, it simply means getting well again.

In our own personal focus of interest we would like to receive research papers on any kind of talk and touch therapy that really helps the patients. In the context of non-drug medicine we are not that interested in therapy that is strongly connected to a specific culture, i.e. Native American Medical rituals like the sweat lodge ritual, or Chinese medicine with needles or burning ashes, as we doubt that they will do the same for people from Europe and the rest of the world in general, but we do most definitely acknowledge, that these procedures works wonders in the USA and China. Neither will we exclude traditional psychoanalysis and similar therapies, in spite of lack of documentation of very good results for almost a hundred years. Inefficient cures, however well established, are not our primary focus and interest, but they might be developed into something very efficient, and an important factor is, that they are know to be safe already. In our own research and practice we want to focus on therapy that effectively induces healing of man regardless if the healing happens in body, mind, feelings, sexuality, spirit, or

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the whole human existence, the latter being the better of cause.

What we hope to see in this journal

We want to receive good papers documenting improved health – physically and mentally, socially and spiritually. We want to see studies that document outcomes like improved global quality of life, life satisfaction, happiness (QOL being the most important outcome), self-rated and objective physical and mental health (self-rated health being the second most important outcome), social ability, sexual ability, working ability, or studying ability (sexual and working ability being the third most important outcomes).

We want to present fine science from philosophy, theory, tools for therapy and research, and documentation of effect. We accept both clinical randomized trials (CRTs) and clinical studies, where the chronic patients serve as their own control, which is of equal value as documentation. Actually we believe that the latter is better, as we then know for sure that these people were really helped, and it makes research simple minimizing bias. Case reports are also welcome.

We want to see relevant cures for the sufferings that torment the modern man: Poor quality of life, low working ability, chronic pains, social dysfunction, recidivate infections, allergy, sexual dysfunctions, mental diseases like depression, borderline personality, and schizophrenia, all kinds of deterioration of health and ability – from myopia and caries to dementia - and of cause serious somatic diseases like cancer and coronary heart disease.

We want to bring medicine for the sick to the physicians and therapists of the world today and tomorrow. We want to bring tools for personal development of the people, who did not successfully complete their personal and psychosexual development, and ended up useless for other people and society. We want to document that we human beings can help each other, when we come as therapists that work from our hearts. We want to work to bring change and hope to medicine and build a bridge between the good old traditional medicine and the new biomedicine in order to help the patients to

achieve full potential and good health, even when suffering from a chronic illness or disease.

Primum non nocera

In Wikipedia you will find that the origin of the above phrase is not widely known and contrary to popular belief, the phrase is not in the Hippocratic Oath. However, it is often described as a Latin paraphrase by Galen of a Hippocratic aphorism (despite the fact that Galen also wrote in Greek rather than Latin). The closest approximation to the phrase that can be found in the Hippocratic Corpus is "to help, or at least to do no harm," taken from Epidemics, Bk I, Sect V.

It seems that *primum non nocere* was introduced into American and British medical culture by Worthington Hooker (1806-1867) in his 1847 book "Physician and patient", where he attributed it to the Parisian pathologist and clinician Auguste François Chomel (1788–1858), the successor of René-Théophile-Hyacinthe Laënnec (1781-1826), the inventor of the stethoscope in 1816, in the chair of medical pathology. Apparently, the axiom was part of Chomel's oral teaching. Others have traced the expression back to an attribution to Thomas Sydenham (1624–1689) in a book by Thomas Inman (1860), but the fact is that it has for the past several hundred of years been one of the basic principles of medicine and should continue to always be in the mind and practice of every physician treating patients.

We want medicine to be harmless and affordable for everybody. Good medicine is cheap and without side effects. We know today that most drugs only cure one patient out of five, 10 or 20 patients (NNT=number need to treat=5-20). We know that there are drugs that give serious adverse effects more often than they actually cure, while other drugs are able to help patients and for many patients with chronic disease drugs are not able to cure or rehabilitate them. It is therefore essential that medical practice continue to uphold the concept of "primum non nocera-first do no harm" also with the new biomedical drugs that are introduced and monitoring and utilization should be ethical and conform to the high standard of not doing harm.

Drugs and the industry

We would also want to contribute to save the world or at least do our part as best as we can. Many of the financial problems we see in our world today are somehow related to the high cost of biomedicine. It seems that the large US-automobile industry is thus failing apart, because health insurance for the workers have become so expensive, that the US industry cannot compete. Many US hospitals now charge uninsured patients 7,000 USD for one day for treatment, forcing everybody to have an insurance. There has been several indications also that the insurance companies work together with pharmaceutical industry and this way they are able to dictate the use of drugs. European countries with socialized medicine and non-drug medicine has been repressed systematically during the last decades, so complementary medicine must be paid by the patients themselves. The consequence is that only 10 % or so of the national health budget goes to complementary treatments, where a few thousand dollars or Euros evidently could help a large number of diseases and illnesses that drugs cannot cure - chronic pain being an example. 50 or so CRTs have already documented the effect of physical therapy.

We have seen on a small scale that touch therapy and talk-therapy, for people with illness treated before this treatment by biomedical specialists unable to help the patients, have been able to help 50% of the patients. The last decades of research in complementary medicine give us reason to believe that many diseases can be helped or maybe even in some instances cured this way. We need to be aware of the political and financial issues in medicine. We know that there are huge commercial interests and have seen examples of suppression and systematic misinformation about non-drug medicine, so we are not happy that science is related to politics and financial interests, but we know very well that it is.

Invitation

We invite every therapist, researcher and even philosophers, economists, human rights people and many more to contribute with reviews, original research, case reports and short communications, but would also be interested in providing space for special issues over time with the following topics:

- Methods for the documentation of efficacy of non-drug medicine
- Efficacy of non-drug medicine
- Side effects of non-drug medicine
- Non-drug medicine for somatic diseases - chronic pain, allergies,
- infections, autoimmune diseases
- Non-drug medicine for cancer and coronary heart disease
- Non-drug medicine for mental diseases and schizophrenia
- Non-drug medicine for sexual dysfunctions
- Repression of non-drug medicine, medical knowledge, and non-drug
- therapist's human rights
- Power in medicine - money and politics in medicine
- Sexology, the tradition of the sexological examination, and new tools for manual sexology

We are open for other ideas concerning special issues and if you contact us we will explain the procedure and practical aspects. Besides from special issues we also hope that we people in the field will take up the glove and submit good papers for peer-review and publication.

Functional brain model: A nested hierarchical and parallel organization during development and evolution

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Abstract

A functional brain model is proposed, based on neurobiology, nested hierarchy and parallel organization, evident during animal development and evolution. The drive for behavior is survival of the individual and genes (species). Brain has evolved to better serve these goals. Based on this model, behaving brain is classified into: I) Invertebrate brain, II) a) Vertebrate Oro-Pharyngeal Brain, b) Cephalo-Truncal Brain, and c) Neo-Cortical Brain. Seven postulates are discussed for the evolutionary development of 1) medullo-spinal region, 2) visceral networks, 3) somatic networks, 4) sensory-motor integration, 5) memory, 6) attentive facing, and 7) creativity. A behavioral hierarchy results in reflex, conditioned, sensory-guided, memory-guided, rule-based, self-generated, and creative behaviors with emergence of cognition, speech, imagery, self-consciousness, creativity and altruism. The proposed brain model is based on the functional behavior development and evolution of invertebrate and vertebrate animals including humans. It is founded on a hierarchy of simple, essential to more complex, creative behaviors in all animals. The more simple behaviors include ionic-osmotic homeostasis, respiration, swallowing, feeding, sleeping and waking. Whereas, the more complex behaviors include vocalizing, communicating by verbal and nonverbal gestures, symbols, language, memory, mentation, self-awareness, intention/volition with purposeful actions, decision making, planning, social-emotional intelligence, creativity and altruism. Understanding this brain model will enhance our understanding of animal and human behavior and conscious mentation.

Keywords: Brain models, bauplan, pharyngeal arches, oro-pharyngeal brain, cephalo-truncal brain, neo-cortical brain, vertebrate brain, invertebrate brain, neurology.

Introduction

Traditionally, the brain is anatomically divided into I) rhombencephalon, which includes myelencephalon

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and metencephalon, II) mesencephalon and III) prosencephalon, which includes diencephalon and telencephalon. This current division does not correctly fit the complex hierarchy of animal behavior and human self-consciousness. A unified behavioral brain model is currently lacking. Thus, we are left with a sense of awe, facing a daunting complexity of countless interactive neurons with innumerable connections and neural networks with the manifestation of a variety of simple and complex animal behaviors and mentations. The wondrous unfolding of brain and behavior during animal development and evolution are even more perplexing.

In this article, a Functional Brain Model (FBM) is proposed, which is based on nested hierarchy and parallel organization (NHPO). Seven specific postulates are described in details. Based on this model, behaving brain is classified into: I) Invertebrate brain, II-a) Vertebrate Oro-Pharyngeal Brain (OPB), II-b) Cephalo-Truncal Brain (CTB), and

II-c) Neo-Cortical Brain (NCB). OPB includes medullary and caudal ponto-cerebellar regions. CTB includes rostral pons, midbrain and limbic-allocortical regions and NCB includes telencephalic, hemispheric and bi-hemispheric, global networks. The NHPO organization operates at all functional brain levels. The parallel processing operates within a single NHPO level, whereas, nested hierarchy manifests between the five vertical levels. This functional brain model is illustrated in the Figure and its structural and behavioral details are given in tables 1-4.

This brain model is based on sound principles of behavioral neurobiology (1), which not only deals with how brain works and how animals behave, but also why they behave, the way they do. Every animal has a behavioral body plan or a bauplan. The bauplan depends on animal's genetic make-up and its mode of living in the environment.

Nested Hierarchical & Parallel Organization of Brain & Behavior

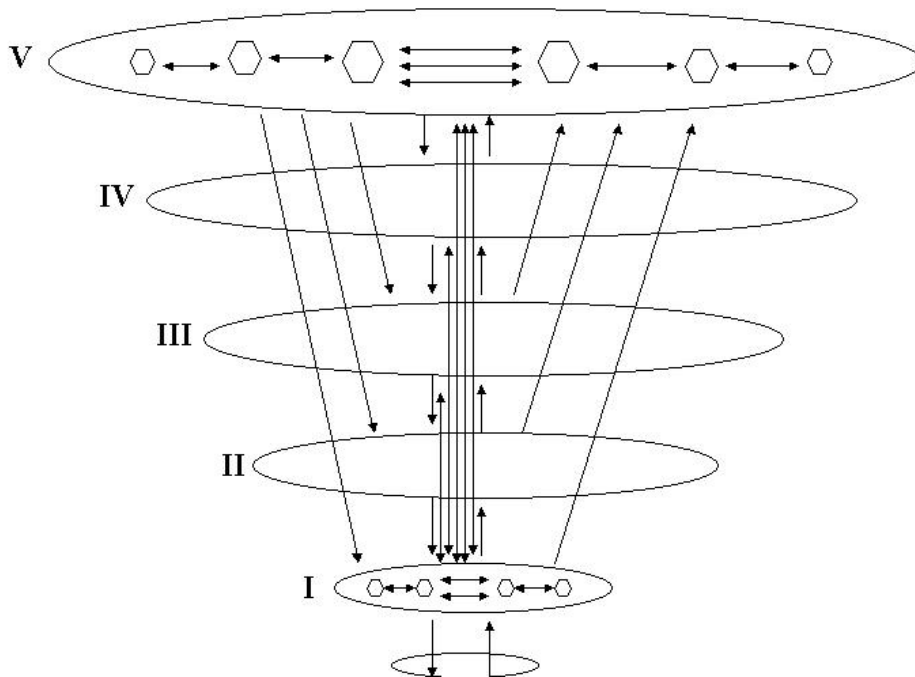


Figure 1. Nested hierarchy and parallel organization (NHPO) of brain and behavior. I-V represent NHP organizational levels. The lowest ellipse represents the spinal cord. Level I: medulla, Level II: pons-cerebellum, Level III: mid brain, Level IV: limbic-allocortex and Level V: multimodal neocortex. Hexagons represent neuronal ensembles and cortical functional modules. Single arrows show the direction of afferent and efferent connections and triple arrows represent commissural connections between cerebral hemispheres and subcortical structures.

Table 1. The invertebrate brain and behavior

Invertebrate Phyla	Invertebrate Brain structures	Invertebrate Behavior
Porifera: Sponges.	Neuroid system: No true nervous systems but these organisms have generalized contractile ability through the syncytial trabecular tissue.	Any mechanical stimulus anywhere on the epithelium spreads by electrotonic conduction with a diffuse motor response. Epithelial conduction velocity 3-35 cm/s
Cnidaria: Hydra, Jellyfish, Sea Anemones, Hydromedusae.	Nerve nets: Diffuse two-dimensional plexus of two or multipolar neurons. Sensory ganglia and giant fiber nerve net for global motor response.	Behaviors include feeding, swimming, climbing, burrowing and intra-species aggression. Neural conduction velocity 10-100 cm/s. Chemical neurotransmission including dopamine, 5-Hydroxytryptamine.
The Worms, Platyhelminthes, Nematoda and Annelida: Flatworms, Flukes Tapeworms, and Segmented worms, Earthworms, Leeches.	Suprapharyngeal and Subpharyngeal ganglia connected by circum pharyngeal connectives or ring. Orthogonal pattern of paired nerve cords and commissures.	Subpharyngeal ganglion mediates behaviors like feeding, but the suprapharyngeal ganglion receives and integrates sensory information and makes an appropriate behavioral decision and takes action in the given circumstance.
Arthropoda, Brachipoda: Arthropods, Trilobites, Shrimps, Crabs, Spiders, Scorpions, Millipedes, Centipedes and Insects.	Suprapharyngeal complex with a) Protocerebrum with Neurosecretory cells and Optic lobes, b) Deutocerebrum with antennal nerves and c) Tritocerebrum. Subpharyngeal ganglion and Hypocerebral ganglion	Suprapharyngeal complex modulates the activities of the Subpharyngeal and Hypopharyngeal ganglia, based on sensory input and its integration. Subpharyngeal ganglia control mouthparts, local musculature and salivary glands. Hypocerebral ganglion controls endocrine functions, growth and metamorphosis. Memory and associative learning in Honeybees.
Mollusca, Gastropoda, Cephalopoda: Molluscs, Snails and Slugs, Clams, Shells, Squids, Nautilus and Octopuses.	The brain of an Octopus consists of 15 structurally and functionally distinct pairs of structures including cerebral lobes viz. optic, vertical, frontal, buccal, brachial and pedal.	Modality specific pathways and associative learning, e.g. visual, tactile. Memory traces plus formation of a coded representation of a situation with the ability to generalize from one subject to a similar one.

Table 2. The vertebrate oro-pharyngeal brain (OPB) and behavior

NHP Organizational Level and Neural Structures	Related Cranial Nerves	Mediated Functional Behavior	Motor Responses and Actions	Sensory and Memory Guidance
I Medulla, Myelencephalon-Rhombencephalon, Medullary Reticular Formation (MRF) Hypoglossal n, Dorsal Vagus n, Ambiguus n, Gracile n, Cuneatus n, Raphe n.	Hypoglossal, Accessory, Vagus and Glossopharyngeal Nerves	Reflex Behavior: Regulation of Energy intake, Homeostasis: Cardiovascular, Respiratory and Swallowing behavior, Reflex Phonation and vocalization	Central Autonomic Regulation with Sympathetic and Parasympathetic Responses. Reflex Movements of Pharynx Esophagus and Tongue	Chemosensory Guidance of Behavior: O ₂ , CO ₂ , pH, Water, Salt, Electrolytes, Glucose, Toxins, Taste and Thirst
II Cerebellum-Pons, Metencephalon-Rhombencephalon, Pontine Reticular Formation (PRF) Vestibular n Cochlear n, Facial n,	Vestibulo-Cochlear, Facial, Abducent and Trigeminal nerves	Conditioned Behavior: Startle response. Reflex and Coordinated Movements of head, face, Lips, ears, and eyes, jaws, trunk and Limbs in relation to gravity. Micturition, Sexuality, REM Sleep and	Whole body, Locomotor response including Stance and Gait. Attentive facing with Directed Head, face, ears and eyes, Jaw,	Sensory-guided behavior: Behavioral guidance by Pain, Touch, Temperature, Proprioception,

Table 2. (Continued)

NHP Organizational Level and Neural Structures	Related Cranial Nerves	Mediated Functional Behavior	Motor Responses and Actions	Sensory and Memory Guidance
Abducent n Trigeminal motor and Sensory n, Salivary n, Fastigial n, Interposed n Dentate n, Raphe n.		Basic Wakefulness. Reflex and Coordinated Vocalization	Body and Limbs. Basic reflex Sexuality	Lateral line receptors, Vestibular, and Auditory.

Table 3. The vertebrate cephalo-truncal brain (CTB) and behavior

NHP Organizational Level and Neural Structures	Related Cranial Nerves	Mediated Functional Behavior	Motor Responses and Actions	Sensory and Memory Guidance
III Midbrain Mesencephalic Reticular Formation (MRF) Periaqueductal gray, Tectum Tegmentum, Troclear n, Oculomotor n, Red n. Raphe n.	Troclear, Oculomotor and Optic nerves and Tracts.	Sensory-Guided Behavior: Central pain/pleasure. Reflex Orientation to visual, auditory and Sensory stimuli. Locomotion, Micturition, Sexuality, Wake-Sleep Arousal, Appetite-Satiety	Conditioned orientation, facing, gazing, listening, Behavioral approach or escape. Sexual behavior.	Vision plus the integration of all of the lower level sensory inputs
IV Limbic- Allocortical Hypothalamus-Pituitary, Thalamus, Basal Ganglia, Paleo-Cortex, Arche- Cortex, Limbic System	Olfactory nerves and tracts, Multiple subcortical white matter fiber tracts and connections.	Memory-Guided Behavior Automatic learned, Subconscious, implicit behavior. Affective/Emotional behavior. Hypothalamo-Pituitary- Adrenal stress response. Active smelling, sniffing, Sexuality. Wake-Sleep regulation and Neocortical arousal, Species-Specific Vocalizations and Subcortical Language and motor processing.	Survival and Stress responses, Fight, Flight or Fright, Circadian rhythms, Wake- Sleep cycle, Appetite-Satiety, Conditioned Subconscious Sexuality	Smell plus complex multisensory integration or gestalts. Affective/emotional memories and stereotyped and memory-guided perceptions and experiences. Conditioned fear, hatred, anger, pain and pleasure, joy and happiness. Group mentality and insecurity resulting in fierce Territoriality.

The main drive for animal behavior is survival of the individual and its genes i.e., species. Both animal form and behavior have evolved to best serve these goals. For survival of the individual, various essential neural mechanisms have evolved, which regulate a) ionic-osmotic homeostasis, b) respiration, c) feeding,

d) locomotion, e) defense, f) reproduction, and g) purposeful behavior. All animals, being thermodynamically open systems, have to continuously exchange energy, biomolecules and information with their environments, for survival, growth and fecundity.

Table 4. The vertebrate neo-cortical brain (NCB) and behavior

NHP Organizational Level and Neural Structures	Related Fiber Tracts	Mediated Functional Behavior	Expressive Actions and Behavior	Perceptual, Memory-Guided and Self-Generated Experiences
Va Neocortical-Left and Right Hemispheric Neocortical Left and Right Hemispheres with Primary Sensory-Motor and Unimodal Associative Visual, Auditory, Somatosensory areas and Language dominant Hemisphere	Primary Somato-Motor and Somato-Sensory, Visual, Auditory, Gustatory and Olfactory pathways, Hemispheric white matter connections.	Rule-Based Behavior Primary Hemispheric Sensory-Motor Integration and Unimodal and multimodal, associative, learned behaviors. Oral and Written language Communication in the dominant hemisphere. Stroop and Wisconsin card sorting test	Situational, Skillful, Voluntary, Intentional actions and Motivated behaviors, directed or attentive behaviors and actions or voluntary inattention to a stimulus or situation.	Complex, multisensory, Situational and Memory-Guided Perceptions, Feelings and self-generated Experiences.
Vb Neocortical-Global: Prefrontal, cingulate and temporo-occipitoparietal (TOP) multimodal associative neural network Both cerebral hemispheres connected through corpus callosum and other commissural fibers, working together in parallel and synchronous processing mode.	Profuse convergent and divergent white matter neural pathways connecting tertiary cortical areas from both hemispheres to other cortical areas, subcortex, brainstem and Spinal cord.	Self-Guided, Executive Behavior: Self-generated actions, internal speech and cognition. Working Memory. Situationally adaptive, and Flexible, Conscious Decision Making and Execution of behavior. Anticipatory planning, Volition, Intentionality and Sense of Self. Cognitive Modeling of Environment, Self and others. Creative Problem-solving and creative innovation	Voluntary, Intentional and Planned actions. Skillful and Creative actions and anticipatory behaviors. Go/No-Go abilities with Selective and Purposeful activation or inhibition of cortex, subcortex, brainstem and spinal cord. Complex sexual behavior. Empathy and altruism.	Global situational perceptions and on-going personality. Conscious cognitive and emotional experiences. Self-generated scenarios. Images of self and others. Feelings of hatred, love, fear, anxiety, expectations of the future. Feelings of awe and wonder. Awareness and acceptance of aging and death.

Hierarchical organization of complex metazoan animals has evolved in five progressive stages: a) protoplasm, b) cell, c) tissue, d) organ, and e) the system. The NHP organization of the invertebrate brain and behavior is summarized in Table 1. In vertebrates, behavioral hierarchy and parallel processing are evident in the functions of swallowing (2), hypothalamo-pituitary-adrenal stress response (3), primate basal ganglia activity (4), human olfaction, visual, auditory and somatosensory functions (5,6,7), cognition, working memory (8), and language (9)

In vertebrates, the first nested, hierarchical and parallel organizational level regulates most of the simple, essential behaviors for survival. This Oro-Pharyngeal Brain (OPB) regulates the pharyngeal arches and their derivatives. The next two divisions, Cephalo-Truncal Brain (CTB), and Neo-Cortical

Brain (NCB) have adaptively evolved to favorably move and relocate the oro-pharyngeal apparatus for successful sensing, capturing prey, feeding, mating and escape etc. CTB organizes all activities of vertebrate head, trunk and limbs, together and independently. NCB evolved as the highest integrative level for emotions, perception, cognition, consciousness, memory, intentions, planning and creativity. During evolution, OPB is relatively conserved, whereas, CTB and NCB have evolved extensively for the optimization of behavior, mentation and self-consciousness.

In NHP organization, rostral neural networks exercise an overriding influence on the spontaneous activities of caudal neural networks. For instance, in invertebrates, suprpharyngeal ganglion modulates the subpharyngeal ganglion, which coordinates

swallowing behavior. In vertebrates, CTB modulates OPB and NCB modulates both CTB and OPB. The CTB and NCB are of recent origin in animal ontogeny and phylogeny.

The first postulate

The first postulate is about the bidirectional embryonic development that starts at the medullo-spinal region. The development of neural tube begins at this region and proceeds both rostrally and caudally (10). From ontogenic and phylogenic perspective, cranial nerves appear in the reverse order i.e. the XIIth cranial nerve, the hypoglossal appears earlier than the Ist the olfactory nerve. Therefore, they are better understood in the reverse order as they appear during embryogenesis. The numbering of pharyngeal arches and rhombomeres is also better understood in the reverse order. From this perspective, the tongue, which is innervated by the hypoglossal nerve, is the true rostrum of all animals, like chameleons, snakes, frogs and bats. The tongue is also a vital, multifunctional organ, in many terrestrial animals.

The pharyngeal arches develop early during embryogenesis. They form tongue, stomodeum, mouth, face, head and related brain structures (11, 12, 13). During evolution, animal oropharynx and head became adaptively specialized, e.g. the evolution of hardened bills in birds, turtles and mammals due to deposition of keratin in lips; the evolution of tongue to better serve functions like handling food, taste, temperature control, capturing prey, an accessory olfactory organ and human speech modulation.

The second postulate

The second postulate is that the development of Visceral Nervous System (VNS) precedes the development of Somatic Nervous System (SNS) (14). VNS mediates vital functions including alimentation, swallowing (15,16), breathing (17), cardiovascular regulation (18), thermal and ionic homeostasis and procreation.

The third postulate

The third postulate is about the role of Somatic nervous system (SNS) in varied environments, when there is a need for an animal to quickly move towards an opportunity and away from danger. This is achieved by somato-visceral coordination resulting in efficient relocation of body, head and mouth, either together or independently, towards food, energy and mates and away from dangers like heat of volcano or fire, acidity, toxic substances like sour or bitter foods, precipitous heights and predators. Various locomotor systems (19, 20, 21) evolved, which enabled animals to swim, crawl, walk, run and fly. Such activities require coordination of body, head and limbs, with guidance from sensory organs, like skin, face, tongue, whiskers, lateral line receptors, vestibular organs, ears, eyes, nose and memory.

Initial progravity, side-to-side movements were followed by antigravity movements like vertical stance, gait and rotatory movements of head (22), and eyes (23, 24, 25). This enabled animals to swim, stand, walk, run, climb and fly vertically. These developments depended on the evolution of neural networks, integrating vestibular, cerebellar, oculomotor and midbrain reticular nuclei. The mesencephalic, basal ganglia and cerebellar locomotor circuits are well documented.

The fourth postulate

The fourth postulate is about sensory-motor integration. The neuromotor system evolved for stronger and faster locomotion and skillful movements of head, mouth, lips, tongue, larynx, hands and fingers, for better gestural and vocal communication (26,27). Communicative abilities reached their pinnacle in human oral and written languages, performing arts and sports (28).

The neurosensory system integrates information from various receptors including tactile, vibration, chemo-, baro-, thermo-, geo- (gravity), proprio-, phono- and photo-receptors. The neurosensory system evolved in two major divisions. The contact senses (CS), which include taste, touch, temperature, pain, vibration, pressure, proprioception and vestibular sense and the distance senses (DS), which include

auditory, visual and olfactory (29). Both CS and DS guide animal behavior. The CS are involved in reflex responses of pharynx, tongue, lips, mouth, face, head, hands and feet, whereas, DS are involved in long-distance, whole body movements, like locomotion, swimming, walking, running, jumping, flying, gesturing and vocal communication.

The fifth postulate

The fifth postulate is about memory. The initial memory was probably due to an intense painful or pleasurable event, leaving a trace in the limbic system (30, 31, 32). Intuitively, it is adaptive for an animal to register, store and recall significant events, for the guidance of future behavior, avoiding pain and pursuing pleasure. Emotional memories are established through classical conditioning by reward or punishment and are subconsciously mediated by the limbic-allocortical networks.

The “on-line” working memory is a function of the most recently evolved prefrontal and posterior parietal-occipital-temporal (TOP) associative cortices. This amazing ability makes it possible for us to register, hold and manipulate information/representation of an event or an episodic memory, as a conscious content. There is sufficient evidence that working memory is mediated by dorso-lateral prefrontal cortex and the long-term, semantic memories are stored in the TOP associative cortices. By interaction between the dorso-lateral prefrontal and the TOP associative cortices, meaningful experiential stories are built. The evolution of such cognitive ability is crucial for purposeful decision-making, symbol-language processing, story-telling, creative arts and sciences (33, 34).

The sixth postulate

The sixth postulate is about attentive facing, which is the turning of body, head, face, mouth, ears and eyes towards pleasant stimuli like food, air, water, warmth and friends and away from unpleasant stimuli like excessive heat or cold, foul smell, toxins and predators. Attentive facing is adaptive for security, comfort, pleasure and communication. For instance,

flock of birds and mammals prefer to face wind, light and to stay within their group. Attentive facing helps to communicate by gestures, grimacing, vocalizations and language (35). Decorating one’s face for better communication and relationships with others has evolved in several birds, mammals and humans.

Attentive facing conveys emotions like fear, anger, joy, sadness, disgust, humor, peace and happiness. These expressions can be reflex at oropharyngeal brain level, automatic at cephalo-truncal brain level and intentional at neocortical brain level. There is evidence of deliberate ignoring of a stimulus and even falsifying facial expressions to hide emotions. Facing behavior forms the beginning of human attentiveness. Just as evolution of binocular vision improved visual acuity, attentional behavior has increased our capacity to gather, process, store, and communicate multimodal information from environment and past experience. Further expansion of such cognitive ability and working memory, probably resulted in the emergence of human self-reflective consciousness (36-38).

The seventh postulate

The seventh postulate is about creative neocognition, which is the ability to generate and use new and appropriate information. Such information may be a new perception, understanding, movement, speech, writing or any discovery. Human cognition is defined as the ability to attend, perceive, comprehend, manipulate, integrate and maintain information; to intend to or to act and communicate (39). Human executive function is defined as the ability to abstract, plan, organize, shift set and adapt current and past knowledge to future behavior (40).

Human creativity is well developed. Creativity is defined as: “The ability to produce work that is novel, original, spontaneous and appropriate, useful and adaptive” (41, 42, 43). It has given us an enormous advantage over our environment and other animals. Spontaneous as well as intentional creativity is useful for making cognitive models of self and environment. Such ability gives us capacity to simulate and anticipate future, based on our past experiences. Such a mind is capable of complex decision-making, creative thinking and altruistic behavior (44).

Recently, rostro-lateral prefrontal cortex was shown to be activated in explicit processing of self-generated information in humans. The lateral Brodmann's area 10 was recruited during cognitively oriented tasks and medial Brodmann's area 10 was recruited during emotionally oriented tasks (45).

Creativity was further defined as an understanding and expression of novel orderly relationships (46). Such innovation may occur when there is co-activation and communication between prefrontal and TOP associative cortices, in a relatively low norepinephrine arousal state, with a vast knowledge of the subject stored in multimodal cortices, in a motivated individual. Innovative cognition requires us to attend, reflect, imagine, model and predict by participating actively in our ever-changing situations. This promotes active exploration of new environment for security, profit, pleasure and curiosity. It is the very basis of an astronomical progress made in human knowledge, languages, communications, sciences, technologies, space-explorations and creative arts. There is an endless opportunity for us to learn, innovate, invent, explore, discover, understand, express and share our unique human experience of this amazing and apparently endless universe.

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Submitted: November 01, 2008.

Revised: December 19, 2008.

Accepted: December 24, 2008.

Bryophytes: Potential medicinal natural products

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Abstract

Liverworts and mosses are small, low-growing plants, which constitute the phylum bryophyta. Bryophytes, which are phylogenetically placed between vascular plants and algae, form a unique division in the plant kingdom. There exist more than 22,000 members of the mosses (Bryophyta) in the world. They are now increasingly used for diverse purposes including pollution control and as new sources of pharmaceuticals. One of the reasons for exploring biological compounds in bryophytes is the potential for medical use. Bryophytes contain numerous bioactive constituents as shown in investigational studies. However, much work still remain in order to link medical effects with specific bryophyte species. Traditional medical claims need to be justified by pre-clinical and clinical research.

Keywords: Homeopathic medicine, bryophytes.

Introduction

Liverworts and mosses are small, low-growing plants, which constitute the phylum bryophyta. Bryophytes, which are phylogenetically placed between vascular plants and algae, form a unique division in the plant kingdom (1).

There exist more than 22,000 members of the mosses (Bryophyta) in the world. They are now increasingly used for diverse purposes including pollution control and as new sources of pharmaceuticals (2). The Napralert database at the University of Illinois establishes ethno medicinal uses for about 9200 of 33,000 species of monocotyledons, dicotyledons, gymnosperms, lichens, pteridophytes, and bryophytes (3).

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Bryophytes in traditional systems of medicine

There is no historical record, explaining use of liverworts and mosses in Ayurveda, the Indian system of medicine. A research claims that the mosses like species of *Barbula*, *Fissidenc*, *Minium*, *Thuidium* and species of liverworts like *Asterella*, *Dumortiera*, *Marchantia*, *Pellia*, *Plagiochasma* and *Stephenrencella-Anthoceros* were present in the vicinity of Shilajit (*Asphaltum punjabianum*) exuding rocks and these bryophytes are responsible for formation of Shilajit. The bryophytes reveal occurrence of minerals and metals in their tissue such as copper, silver, zinc, iron, lead etc, which are similar to the elements present in Shilajit (4).

Chinese traditional medicine named 40 kinds of bryophytes used to treat cardiovascular diseases, tonsillitis, bronchitis, cystitis and skin infections (5). Some species of *Fissidens* and *Polytrichum* were utilized as diuretic and hair growth stimulating drugs in China more than 400 years ago. *Marchantia polymorpha* is used in the treatment of liver diseases like jaundice and hepatitis (6). In China, *Rhodobryum giganteum* (Schwaegr.) Par and *R. roseum* (Hedw) Limpr are used in the treatment of heart ailments (7).

North American Indians used *Bryum*, *Mnium*, *Philonotis* spp., and *Polytrichum juniperinum* to heal burns, bruises, and wounds (8). The Seminole people in North America were reported to use *Barbula unguiculata* Hedwig, *Bryum capillare* T. Bickley and *Octoblepharum albidum* (L.) Hedw as febrifuge and anodyne (9). Willow moss, *Fontinalis antipyretica* Hedw was once reputed as febrifuge (documented in Journal of Linnaeus). Dried *Sphagnum* were used extensively as surgical dressing during the First World War (10). In France, *Marchantia polymorpha* was used to promote diuresis (11). In Himalayas, *Riccia* spp were used in the treatment of Tinea (ringworm) infestations.

The use of bryophytes as antibacterial or disinfectants agents deserves special mention. *Sphagnum teres* (Schimp.) Ångstr is used in ophthalmologic diseases (12). In China and Bolivia, *Fissidens osmundoides* Hedwig is used an antibacterial agent to treat inflammatory condition of the pharynx and larynx. *Haplocladium microphyllum* (Hedw) Broth is used as demulcent medicine in

inflammatory conditions like bronchitis, cystitis, tonsillitis and tympanitis (13). *Philonotis fontana* (Hedw) Brid is used by Go suite native people as soothing preparation for healing burns (9).

Phytochemistry of bryophytes

Extracts of many species of Bryophytes are known to contain phenolic compounds (14). Sterols, isoflavonoids, flavonoids, and bioflavonoids have been reported (1,14,15). Terpenoids, phenolics and volatile constituents have also been investigated in some bryophytes (15). *Rhodobryum giganteum* is reported to contain volatile oil, lactone and amono acid (7). Essential oil of *Plagiomnium undulatum* (Hedw) T Kop is reported to contain butenolides (16). Quercetin, luteolin and apigenin have been identified as major flavonoids in *Marchantia convoluta* Gao et KC Zhang (17).

Marchantia polymorpha Linn from Japan has been reported to accumulate eicosapentaenoic acid (18). Diterpenoids have been reported from New Zealand liverwort *Jungermannia* species (19). *Isotachis japonica* Steph is reported to contain aromatic esters (20). *Anoetangium bicolor* Renaud and Cardot has been reported to contain highest amount of neurotransmitter, acetylcholine (ACh), among bryophytes (21).

Pharmacological investigations

The antifungal and antifeedant activity of bryophytes is widely known, but mainly from *in vitro* studies. Recent exapalraty studies done in Germany, Peru and Bolivia have demonstrated that extracts derived from native bryophyte species have significant effects on human pathogenic fungi and may cure skin diseases (22). Several Indian bryophytes have been identified as potential source of antimycobacterial agents (23). As pointed out, *Anoetangium bicolor* is rare bryophyte with anti cholinesterase activity (21). A brief account of pharmacological investigations carried out on bryophytes is summarized below:

Antifungal activity

Fractionation of the ethanolic extract of *Homalia trichomanoides* (Hedw) B. S. G. lead to isolation of 3 β -methoxyserrat-14-en-21 β -ol, atranorin, and methyl 2, 4-dihydroxy-3, 6-dimethylbenzoate as antifungal compounds active against *Candida albicans* (24). *Pallavicinia lyellii* (Hook) Carruth is known to have antifungal activity against *Aspergillus fumigatus* under *in vitro* conditions (25). Further investigations lead to the discovery of steroid as the antifungal compound from *P. lyellii* The compound was found to be effective against aspergillosis-induced mortality in immuno-compromised mice (26).

Hypnum cupressiforme Hedwig has significant antifungal effects. *Herbertus aduncus* subsp. *hutchinsiae* (Gottsche) R.M.Schust. has antifungal activity against *Botrytis cinerea*, *Pythium debaryanum* and *Rhizooctonia solani*. (-) α -herbertenol, (-) β -herbertenol, and (-) α -formylherbertenol were identified as antifungal constituents (27).

Bioassay-directed fractionation of the MeCOEt extract of the American liverwort, *Porella cordeana* (Hueben.) Evans yielded drimenin and aristolone which were moderately toxic towards DNA-repair-deficient mutant of *Saccharomyces cerevisiae* (28).

Antibacterial activity

An acetone extract of the Chinese moss, *Pleurochaete squarrosa* (Brid.) Lindb. was reported to be active against some gram-negative strains (29). The acetone and methanol extracts of *Palustriella commutata* (Hedw.) Ochyra (native to Turkey) were studied for antibacterial activity. The acetone extract had a potential activity against gram-negative and gram-positive bacteria (30). Acetone extracts of the moss, *Rhynchostegium riparioides* (Hedw) C Jens has significant antibacterial activity against gram-negative bacteria (31).

Sanionins A and B isolated from the moss *Sanionia georgico-uncinata* Ochyra, (collected on the Antarctic Livingston Island) showed activity against important Gram-positive pathogens, such as mycobacteria, multiresistant staphylococci, and

vancomycin resistant enterococci. Sanionins A and B showed anti-inflammatory activity and low cytotoxicity along with antibacterial activity (32). The extract of Stringy Moss, *Leptodictyum riparium* (Hedw.) Warnst. inhibited activity against conventional antibiotic-resistant *Pseudomonas aeruginosa* (33). *Dicranum scoparium* Hedw. has strong antibacterial activity against gram negative bacteria.

Anti-cancer activity

Extracts of *Polytrichum juniperum* Hedw were reported to have anticancer activity against Sarcoma 37 (34). Diplophyllin, an ent-eudesmanolide isolated from *Diplophyllum albicans* (L) Dum and *D taxifolium* (Wahlenb) Dumort showed significant anticancer activity against human epidermoid carcinoma (35).

Sesquiterpenoids, costunolide and tulipinolide, isolated from *Conocephalum supradecompositum* (Lindb.) Steph, *Frullania monocera* *Frullania monocera* (Hook f and Tayl) Gottsche, Lindenb and Nees, *F. tamarisci* (L) Dumortier, *Machantia polymorpha*, *Porella japonica* (Sande Lac) Mitt. and *Wiesnerella denudata* (Mitt) Steph, *Lepidozia vitrea* Steph and *Plagiochila semidecurrans* Lehm et Lindenb demonstrated anticancer activity against carcinoma of the nasopharynx (27,36-41).

Marchantin A from *Marchantia palacea* Bertal, *M polymorpha* L and *M tosana* Steph demonstrated anticancer activity against KB cells. Perrottetin E isolated from *Radula perrottetti* and riccardin isolated from *Riccardia multifida* (L) Gray showed anticancer activity similar to marchantin (36). Benzonaphthoxanthenones (ohioensin A- E) isolated from *Polytrichum ohioense* Ren et Card, following bioassay-directed fractionation and three novel benzonaphthoxanthenones (1-O-methyl ohioensin B, 1-O-methyldihydroohioensin B and 1,14-di-O-methyldihydroohioensin B) and two novel cinnamoyl bibenzyls (pallidisetin A and B) isolated from the ethanol extract of *Polytrichum pallidisetum* Funck showed cytotoxicity against 9PS and several human tumor cell lines (42).

Crude methanolic extracts of mosses, *Isothecium subdiversiforme* Broth. and *Thamnobryum sandei*

(Besch.) Iwatsuki seen commonly in South Japan demonstrated *in vitro* cytotoxicity against P-388 lymphocytic leukemia cells. Mayatansinoids are active cytotoxic principles of the two mosses (43).

Claopodium crispifolium Hook) Ren and Card and *Plagiomnium venustum* (Mitt) T Kop were found to have P-388 activity against P-388 lymphocytic leukemia cells (44). *Bazzania trilobata* (L) S Gray, a liverwort from New Hampshire, showed KB activity and is reported to contain lignans (45). *Atrichum undulatum* (Hedw) PBeauv has broad spectrum antibacterial activity. *Barbula* and *Timmiella* species have been reported to have significant antibacterial activity (21).

Cardio protective activity

An ether extract of *Rhodobryum giganteum* (Schwaegr) Par. was reported to have cure angina (chest-pain) and reduce the oxygen resistance by increasing the rate of flow in the aorta by over 30% (7).

Miscellaneous activity

In Britain, sphagnol, a derivative of *Sphagnum* is used to relieve the itch of insect bites (46). Sphagnol is recognized as an useful application in eczema, psoriasis, pruritus, hemorrhoids, chilblains, scabies and acne.

Conclusions

One of the reasons for exploring biological compounds in bryophytes is the potential for medical use. Bryophytes contain numerous bioactive constituents as shown in investigational studies. However, much work remains to link medical effects with specific bryophyte species (47). Traditional medical claims need to be justified by pre-clinical and clinical research.

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Submitted: October 02, 2008.

Revised: December 19, 2008.

Accepted: December 24, 2008.

Zootherapy as an alternative therapeutic in South America

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Abstract

The healing of human ailments by using therapeutics based on medicines obtained from animals or ultimately derived from them is known as zootherapy. The use of animal-derived medicines as an alternative therapeutic has also been recorded in different parts of the globe, yet little attention has been paid to the cultural, medical, or ecological significance of zootherapeutic practices, even in countries, where the use of medicinal animals is well established. Despite their importance, studies on the therapeutic use of animals and animal parts have been neglected, when compared to plants. This paper discusses some related aspects of the use of animals or parts thereof as medicines in South America, and their implications for public health, ecology and economy. Our review revealed that at least 322 species of animals belonging to 157 families are used in traditional folk medicine in South America. The use of medicinal animals is a fundamental component within traditional health systems and medical practice in South America. Besides being influenced by cultural aspects, the relations between humans and biodiversity in the form of zootherapeutic practices are conditioned by the social and economic relations.

Keywords: Zootherapy, traditional medicine, alternative medicine, public health.

Introduction

Although recent advances in molecular biology and physiological chemistry have greatly enhanced our understanding and treatment of diseases, a large segment of the population still relies on traditional medicine or so-called alternative medicine as the preferred form of health care (1). The World Health Organization (WHO) estimates that as many as 80% of the world's more than six billion people rely primarily on animal and plant-based medicines (2,3).

Medicinal plants and animals, since times immemorial, have been used in virtually all cultures as a source of medicine (2,4-9). Traditional human

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populations have a broad natural pharmacopoeia consisting of wild plant and animal species. Ingredients sourced from wild plants and animals are not only used in traditional medicines, but are also increasingly valued as raw materials in the preparation of modern medicines and herbal preparations (10).

Due to the extensive use of plant materials, traditional medicine is associated with herbalism. However, animal-based medicines also play a significant role in healing practices of many societies. Several authors (4,5,11-18) have showed that animals and products derived from different organs of their bodies have constituted part of the inventory of medicinal substances used in various cultures since ancient times.

The healing of human ailments by using therapeutics based on medicines obtained from animals or ultimately derived from them is known as zootherapy (2,19). As Marques (20) states, "all human culture which presents a structured medical system will utilize animals as medicines". The phenomenon of zootherapy is marked both by a broad geographical distribution and very deep historical origins. In modern societies, zootherapy constitutes an important alternative among many other known therapies practiced worldwide (2).

The use of biological resources for various therapies has been documented in many different parts of the world - but largely in remote regions, where traditional medicines provide a *de facto* alternative to "modern" health care systems (5,21-24). It is well established that traditional medicine plays a crucial role in health care for a large part of the population living in developing countries. In fact, for centuries, traditional medicine was the only health care system available to the prevention and treatment of diseases in different cultures. The interfaces among public health, traditional medicine and biodiversity encompass a number of relevant and contemporary issues, which are seldom dealt with in an integrated fashion by policy makers (25).

The South America region is remarkably heterogeneous in terms of climate, ecosystems, human population distribution, and cultural traditions. South America's rich biological and cultural diversity makes it an exceptional location in which to examine and increase our knowledge of faunistic resources

used as in traditional folk medicine, and to draw attention to the need to their importance for public health, protect traditional knowledge and biodiversity. In that context, the aim of this work was to provide an overview of the use of medicinal animals in South America, identify those species used as folk remedies, and discuss the implications of public health.

Methods

In order to examine the diversity of animals used in traditional medicine in South America, all available references or reports of folk remedies based on animal sources were examined. Only taxa that could be identified to species level were included in the database. Scientific names provided in publications were updated according to the ITIS catalogue of life: 2007 annual checklist (26) and the sources were analyzed (5,24-65).

Results and discussion

The medicinal fauna South America has been the focus of some ethnozoological research over the last two decades, mainly in countries such as Brazil and Bolívia. These studies have been showed the importance of zootherapy to traditional communities in various socio-cultural environments (5,31,35). This is not a surprise, considering the rich biological resources and cultural of the region, that generated invaluable local knowledge systems that include extensive information on animal uses in general and medicinally useful species in particular (5,66).

Our review revealed that at least 322 species of animals belonging to 157 families were used in traditional folk medicine in South America. The taxonomic group with the largest number of animal species fishes [with 85 species], followed by mammals [73], birds [44], reptiles [43] and insects [36]. Other groups mentioned by the interviewees were crustaceans [16], molluscs [13], echinoderms [7], amphibians [3] and cnidarians [2] (see table 1 and figure 1). Similarly to the results obtained in previous studies (24,28,35,37,40,62,63,67-69), in our review the taxonomic groups with the largest number of medicinal species documented were vertebrates.

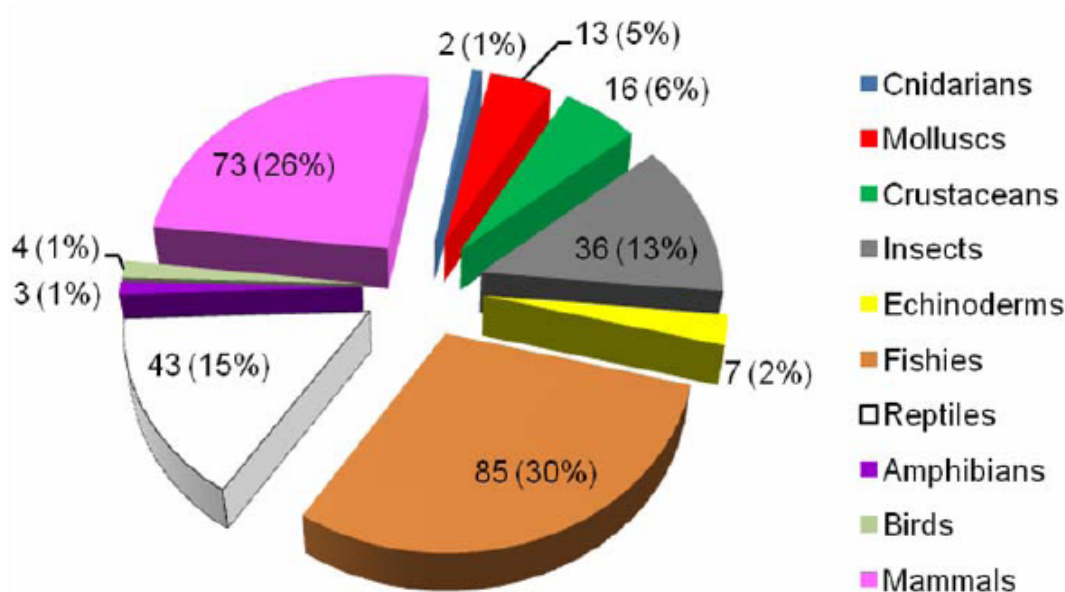


Figure 1. Representativeness of animals taxonomic groups used in South America traditional medicine.

Table 1. Animal Taxa Recorded as Having Medicinal Properties

Family / Species / local name	Conditions to which remedies are prescribed
CNIDARIANS	
Mussidae	
<i>Mussismilia harttii</i> (Verril, 1868) – “Coral”	Vaginal discharge, diarrhoea
Physaliidae	
<i>Physalia physalia</i> (Linnaeus, 1758) -Portuguese-man-of-war, “jellyfish”	Asthma
MOLLUSCS	
Ampullariidae	
<i>Pomacea lineata</i> (Spix, 1827) - Snail, “Clam”	Asthma, sprains, boils, ulcer
Cassidae	
<i>Cassis tuberosa</i> (Linnaeus, 1758) - “Conch”	Asthma
Littorinidae	
<i>Littorina angulifera</i> (Lamarck, 1822) - Periwinkle snail	Chesty cough, shortness of breath
Lucinidae	
<i>Lucina pectinata</i> (Gmelin, 1791) – “Shellfish”	Sexual impotence
Melongenidae	
<i>Pugilina morio</i> (Linnaeus, 1758) – “Conch”	Sexual impotence
Mytilidae	
<i>Mytella charruana</i> (Orbigny, 1842) – Mussel, “Shellfish”	Ophthalmological problems
<i>Mytella guyanensis</i> Lamarck (1819) - Mussel, “Shellfish”	Weakness
Ostreidae	

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Crassostrea rhizophorae</i> (Guilding, 1828) “Mangrove oyster”	Osteoporosis, pneumonia, stomach ache, cancer, flu, weakness, pain relief in injuries caused by the dorsal fin spine of a species of catfish, anaemia, tuberculosis
Strombidae	
<i>Strombus pugilis</i> Linnaeus, 1758 – “West Indian fighting conch”	Sexual impotence
Teredinidae	
<i>Neoteredo reynei</i> (Bartsch, 1920) “Shipworm”	Anaemia, tuberculosis
<i>Teredo pedicellata</i> Quatrefages, 1849	Tuberculosis
Vasidae	
<i>Turbinella laevigata</i> (Anton, 1839) – “Conch”	Sexual impotence
Veneridae	
<i>Anomalocardia brasiliana</i> (Gmelin, 1791) – Clam, “shellfish”	Asthma, flu, stomach ache
CRUSTACEANS	
Calappidae	
<i>Calappa ocellata</i> Holthuis, 1958 – “Ocellate box crab”	Asthma, osteoporosis
Gecarcinidae	
<i>Cardisoma guanhumii</i> Latreille, 1825 – “Blue land crab”	Asthma, bronchitis, wounds, boils
Grapsidae	
<i>Goniopsis cruentata</i> (Latreille, 1802) – “Mangrove root crab”	Epilepsy, venereal disease
<i>Plagusia depressa</i> (Fabricius, 1775) - “Tidal spray crab”	Epilepsy
Hippidae	
<i>Emerita portoricensis</i> Schmitt, 1935 - “Puerto Rican sand crab”	Earache
Ocypodidae	
<i>Ocypode quadrata</i> (JC Fabricius, 1787) – “Ghost crab”	Asthma, haemorrhage in women, flu, to alleviate the symptoms of intoxication with poison of ‘niquim’ (Pisces, Batrachoididae)
<i>Ucides cordatus</i> (Linnaeus, 1763) – “Swamp Land crab”	Hemorrhage in women, incontinence, osteoporosis, cough, asthma, tuberculosis, womb disorders, arthrosis, bronchitis
<i>Uca maracoani</i> (Latreille, 1802) – “Fiddler crab”	Asthma, whooping cough
Palaemonidae	
<i>Macrobrachium carcinus</i> (Linnaeus, 1758) – “Bigclaw river shrimp”, “Painted river prawn”	Amnesia
<i>Macrobrachium acanthurus</i> (Wiegmann, 1836) – “Cinnamon river shrimp”	Irritation when milk teeth are erupting

Family / Species / local name	Conditions to which remedies are prescribed
<i>Macrobrachium borellii</i> (Nobili, 1896) – “Freshwater shrimp”	Irritation when milk teeth are erupting
Penaeidae	
<i>Xiphopenaeus schmitti</i> (Burkenroad, 1936) – “Southern white shrimp”	Irritation when milk teeth are erupting, skin spots
<i>Xiphopenaeus kroyeri</i> (Heller, 1862) – “Atlantic seabob”	Irritation when milk teeth are erupting, skin spots
<i>Pseudosquilla</i>	
Cloridopsis dúbia (H. M. Edwards, 1837) – “Mantis shrimp”	Asthma
Armadillidiidae	
<i>Armadillidium vulgare</i> (Latreille, 1804) – “Pillbug”	Asthma
Sesarmidae	
<i>Aratus pisoni</i> (H. Milne Edwards, 1837) – “Mangrove crab”	Epilepsy, to alleviate the symptoms of intoxication with poison of <i>Colomesus psittacus</i> (a species of pufferfish)
INSECTS	
Apidae	
<i>Apis mellifera</i> (Linnaeus, 1758) – “Africanised honey bee”	Cough, flu, rheumatism, tuberculosis, bronchitis, hoarseness, ulcer, diabetes, verminosis, headache, giddiness, backache, wounds, burns, mumps, varicose veins, arthrosis, cellulitis, amoebiasis, sore throat, asthma, anaemia
<i>Cephalotrigona capitata</i> (Smith, 1854) - “Bee”	Snake bite (antidote)
<i>Frieseomelitta silvestrii</i> (Friese, 1902) - “Stingless bee”	Flu
<i>Melipona compressipes</i> (Fabricius, 1804) – “Stingless bee”	Asthma, cough
<i>Melipona mandacaia</i> Smith, 1863 – “Stingless bee”	Wounds
<i>Melipona quadrifasciata</i> Lapeletier, 1836 “Neotropical stingless bee”	Snake bite
<i>Melipona scutellaris</i> (Latreille, 1811) – “Stingless bee”	Headache, migraine, stroke, verminosis, stomach ache, tuberculosis, haemorrhage, cataracts, mycosis in the mouth, flu, cancer, asthma, bronchitis, intestinal disorders, cough, sexual impotence, ophthalmological problems, weakness, thrombosis, amoebiasis, snake bite (antidote), rabies, sinusitis
<i>Melipona subnitida</i> (Ducke, 1910) - “Honey bee”	Flu, sore throat
<i>Partamona Cupira</i> (Smith, 1863) – “Stingless bee”	Sore throat, swelling, headache, thrombosis, stroke
<i>Plebeia cf. emerina</i> Friese, 1900 – “Mosquito”	Mycosis in the mouth area
<i>Tetragonisca angustula</i> Latreille, 1811 – “Bee”	Cataracts, sinusitis, cough, flu, ophthalmological problems, sore throat, leucoma
<i>Trigona mosquito</i> Lutz, 1931 – “Stingless bee”	Cough

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Trigona spinipes</i> (Fabricius, 1793) – “Stingless bee”	Asthma, cough, flu, bronchitis, acne, diabetes, strokes, thrombosis, migraine, itching, sore throat, giddiness, weakness, scabies, nasal congestion, to induce abortion, whooping cough, irritation when milk teeth are erupting, earache, epilepsy, shortness of breath, late menstruation
Blattidae <i>Periplaneta americana</i> (Linnaeus, 1758) – “American cockroach”	Heartburn, asthma, stomach ache, intestinal colic, earache, alcoholism, epilepsy, vomit, boil, haemorrhage, bronchitis, diarrhea, gonorrhea, panaris, cancer, stroke, burns, menstrual cramps, wounds, to suck a splinter out of skin or flesh, detoxification (alcohol abuse)
Chrysomelidae <i>Coralimela brunnea</i> Thumberg, 1821 – “Fake cockroach”	Epilepsy
<i>Pachymerus</i> cf. <i>nucleorum</i> (Fabricius, 1792) – “Caterpillar”	Earache, stroke, swelling, wounds, seborrheic dermatitis, inflammation, thrombosis
Curculionidae <i>Rhynchophorus palmarum</i> Linnaeus, 1758 – “Pest of coconut palm”	Fever, headache, boils
<i>Rhinostomus barbirostris</i> Fabricius, 1775 – “Pest of coconut palm”	Fever, headache, boils
Formicidae <i>Atta cephalotes</i> (Linnaeus, 1758) - “Leaf-cutter ant”	Sore throat
<i>Atta serdens</i> (Linnaeus, 1758) – “Leaf-cutting”	Stomach ache, heart diseases, chest palpitations
<i>Dinoponera quadriceps</i> (Santschi, 1921) - “Bullet ant”	Asthma
<i>Solenopsis saevissima</i> (Smith, 1855) – “Ant”	Wart
Gryllidae <i>Acheta domesticus</i> (Linnaeus, 1758) - “House cricket”	Scabies, asthma, eczema, lithiasis, earache, oliguresis, rheumatism, urine retention, children that urinate in bed and speak with lateness, incontinence urinary, ophthalmological problems
<i>Paragryllus temulentus</i> Saussure 1878 - “Cricket”	Rheumatism
Meloidae <i>Palembus dermestoides</i> (Fairmaire, 1893) – “Peanut beetle”	Sexual impotence, ophthalmological problems, rheumatism, weakness
Muscidae <i>Musca domestica</i> (Linnaeus, 1758) - “House fly”	Boil, baldness, eyesore, external sebaceous lamps, stye, spots in the face, ophthalmological problems, dermatosis, cysties
Pediculidae <i>Pediculus humanus</i> Linnaeus, 1758 - “Body louse”, “Head louse”	Tootache

Family / Species / local name	Conditions to which remedies are prescribed
Psychidae	
<i>Eurycotis manni</i> Rehn, 1916 – “Beetle”	Headache
<i>Oiketicus kirbyi</i> Guilding, 1827 – “Case moth”	Asthma, earache, haemorrhage
Termitidae	
<i>Microcerotermes exignus</i> (Hagen, 1858), - “Termite”	Asthma, bronchitis, flu, whopping cough
Vespidae	
<i>Apoica pallens</i> (Oliv., 1791) – “Paper wasp”	Thrombosis, ashtma, giddiness, nasal haemorrhage, haemorrhage, stroke, disorders after parturition (to accelerate recovery after parturition), ophthalmological problems, mumps, late menstruation
<i>Brachygastra lecheguana</i> (Latreille, 1824) – “Dark paper wasp”	Cough, asthma
<i>Polistes canadensis</i> (Linnaeus, 1758) – “Wasp”	Cough, whooping cough
<i>Polybia sericea</i> (Olivier, 1791) - “Wasp”	Thrombosis
<i>Protopolybia exigua</i> (Saussure, 1854) – “Wasp”	Evil eye, tobaccoism, ophthalmological problems
<i>Synoeca surinama</i> (Linnaeus, 1767) – “Paper wasp”	Asthma, shortness of breath
ECHINODERMS	
Echinasteridae	
<i>Echinaster brasiliensis</i> Müller & Troschel, 1842 – “Starfish”	Asthma
<i>Echinaster echinophorus</i> Lamarck, 1816 – “Starfish”	Asthma
Echinometridae	
<i>Echinometra lucunter</i> (Linnaeus, 1758) – “Rock boring urchin”	Asthma
Luidiidae	
<i>Luidia senegalensis</i> Lamarck, 1916 - “Starfish”	Asthma, cough, metrorrhagia
Mellitidae	
<i>Mellita sexiesperforata</i> (Leske, 1778) – “Six holed keyhole urchin”	Asthma, cough
Oreasteridae	
<i>Oreaster reticulatus</i> (Linnaeus, 1758) – “Starfish”	Asthma
Toxopneustidae	
<i>Lytechinus variegatus</i> (Lamarck, 1816) – “Green sea urchin”	Snake bite
FISHES	
Auchenipteridae	
<i>Trachelyopterus galeatus</i> (Linnaeus, 1766) - “Driftwood Cat”	Umbilical hernia, asthma, sexual impotence
Anostomidae	
<i>Leporinus friderici</i> (Bloch, 1794) – “Frederici's leporinus”	Earache
<i>Leporinus piau</i> Fowler, 1941 “Black piau”	Rheumatism
<i>Schizodon knerii</i> (Steindachner, 1875) - “White piau”	Leucoma, edema
Ariidae	
<i>Bagre bagre</i> (Linnaeus, 1766) – “Coco sea catfish”	Injuries caused by itself
<i>Genidens barbatus</i> (Lacepède, 1803) – “White sea catfish”	Pain relief caused in injuries by the species’ sting
<i>Genidens genidens</i> (Cuvier, 1829) – “catfish”	Injuries caused by itself
<i>Sciadeichthys luniscutis</i> (Valenciennes, 1837) – “Catfish”	Pain relief caused in injuries by the species’ sting
Aspredinidae	

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Aspredo aspredo</i> (Linnaeus, 1758) – “Banjo, catfish”	Asthma
<i>Aspredinichthys tibicen</i> (Valenciennes, 1840) – “Tenbarbed banjo”	Asthma
Balistidae	
<i>Balistes capriscus</i> Gronow, 1854 – “Grey triggerfish”	Bronchitis
<i>Balistes vetula</i> (Linnaeus, 1758) ^{VU} – “Queen triggerfish”	Stroke, asthma, thrombosis, earache, pain relief caused in injuries by the species’ sting, haemorrhage, ascites, schistosomiasis, appendicitis, menstrual cramps, gastritis
Batrachoididae	
<i>Thalassophryne nattereri</i> (Steindachner, 1876) – “Venomous toadfish”	Pain relief caused in injuries by the species’ sting
Callichthyidae	
<i>Callichthys callichthys</i> (Linnaeus, 1758) – “Armoured catfish”	Asthma, umbilical hernia
Carcharhinidae	
<i>Carcharhinus limbatus</i> (Müller & Henle, 1839) ^{LR} – “Blackfin shark”	Osteoporosis
<i>Carcharhinus porosus</i> (Ranzani, 1840) – “Smalltail shark”	Asthma, rheumatism, wounds, inflammations, osteoporosis, anaemia
<i>Galeocerdo cuvier</i> (Péron & Lesueur, 1822) ^{LR} – “Tiger shark”	Osteoporosis
<i>Rhizoprionodon lalandii</i> (Müller & Henle, 1839) – “Brazilian sharpnose shark”	Rheumatism
<i>Rhizoprionodon porosus</i> (Poey, 1861) – “Sharpnose shark”	Rheumatism
<i>Sphyrna lewini</i> (Griffith & Smith, 1834) – “Scalloped hammerhead”	Asthma, wounds, rheumatism, inflammation
Salmonidae	
<i>Oncorhynchus mykiss</i> (Walbaum, 1792) – “redband trout”	Rheumatism, used with Borax to eliminate the bad smell of feet
Centropomidae	
<i>Centropomus parallelus</i> Poey, 1860 - “Smallscale fat snook”	Nephritis
<i>Centropomus undecimalis</i> (Bloch, 1792) – “Common snook”	Edema in the legs
Characidae	
<i>Astyanax bimaculatus</i> (Linnaeus, 1758) – “Twospot astyanax”	Alcoholism, leishmaniosis, skin burns, wounds, rheumatism
<i>Brycon nattereri</i> Günther, 1864 – “Pirapitinga”	Flu
<i>Colossoma macropomum</i> (Cuvier, 1818) – “Black-finned colossoma”	Paralysis of arms and legs
<i>Hydrolycus scomberoides</i> (Cuvier, 1816) – “Vampire characin”	Earache
Clupeidae	
<i>Opisthonema oglinum</i> (Lesueur, 1818) – “Atlantic thread herring”	Alcoholism
Dasyatidae	
<i>Dasyatis guttata</i> (Bloch & Schneider, 1801) – “Longnose stingray”	Asthma, pain relief caused in injuries by the species’ sting, burns
<i>Dasyatis marianae</i> (Gomes, Rosa & Gadig, 2000) – “Brazilian large-eyed stingray”	Asthma, pain relief caused in injuries by the species’ sting, burns
Doradidae	

Family / Species / local name	Conditions to which remedies are prescribed
<i>Franciscodoras marmoratus</i> (Reinhardt, 1874) – “Urutu”	Injuries caused by itself
<i>Lithodoras dorsalis</i> (Valenciennes, 1840) “Bacu Pedra”	Swelling
<i>Megalodoras uranoscopus</i> (Eigenmann & Eigenmann, 1888) – “Catfish”	Rheumatism
<i>Platydoras costatus</i> (Linnaeus, 1758) - “Catfish”	Rheumatism
<i>Pterodoras granulatus</i> (Valenciennes, 1821) - “Catfish”	Rheumatism
<i>Oxydoras niger</i> (Valenciennes, 1821) - “Catfish”	Rheumatism
Echeneidae	
<i>Echeneis naucrates</i> Linnaeus, 1758 - “Live sharksucker”	Asthma, bronchitis
Electrophoridae	
<i>Electrophorus electricus</i> (Linnaeus, 1766) – “Electric eel”	Sprains, bruises, insect bites, snake bite, asthma, flu, pain in general, muscle strain, rheumatism, osteoporosis, deafness, pneumonia, itching, tuberculosis, earache, toothache
Erythrinidae	
<i>Erythrinus erythrinus</i> (Bloch & Schneider, 1801) – “Red (hi-fin) Wolf fish”	Asthma
<i>Hoplias malabaricus</i> (Bloch, 1794) - “Trahira”	Ophthalmological problems, rheumatism, cataracts, wounds, snake bite, conjunctivitis, stroke, thrombosis, asthma, toothache, fever, earache, diarrhoea, deafness, boils, bleedings, alcoholism, tetanus, sore throat, itching, sprains, leucoma
<i>Hoplias lacerdae</i> Miranda Ribeiro, 1908 “Giant trahira”	Leucoma
Gadidae	
<i>Gadus morhua</i> Linnaeus, 1758 – “Atlantic cod”	Boils
Ginglymostomatidae	
<i>Ginglymostoma cirratum</i> (Bonnaterre, 1788) – “Nurse shark”	Rheumatism
Heptapteridae	
<i>Pimelodella brasiliensis</i> (Steindachner, 1876) – “Mandim”	Injuries caused by that fish species
<i>Rhamdia quelen</i> (Quoy & Gaimard, 1824) – “Catfish”	Tonic
Holocentridae	
<i>Holocentrus adscensionis</i> (Osbeck, 1765) – “Squirrelfish”	Wounds
Megalopidae	
<i>Megalops atlanticus</i> (Valenciennes, 1847) – “Tarpon”	Stroke, headache, asthma, shortness of breath, thrombosis, chest pain, injuries caused by bang
Muraenidae	
<i>Gymnothorax funebris</i> Ranzani, 1840 – “Green moray”	Bleeding (wounds)
<i>Gymnothorax moringa</i> (Cuvier, 1829) – “Spotted moray”	Bleeding (wounds)
<i>Gymnothorax vicinus</i> (Castelnau, 1855) – “Purplemouth moray”	Bleeding (wounds)
Myliobatidae	
<i>Aetobatus narinari</i> (Euphrasen, 1790) – “Spotted eagle ray”	Asthma, pain relief caused in injuries by the species’ sting, burns, haemorrhage
Narcinidae	
<i>Narcine brasiliensis</i> (Olfers, 1831) - “Brazilian electric Ray”	Toothache
Ogcocephalidae	
<i>Ogcocephalus vespertilio</i> (Linnaeus, 1758) – “Batfish”	Asthma, bronchitis
Osteoglossidae	
<i>Arapaima gigas</i> (Schinz, 1822) – “Giant arapaima”	Asthma, pneumonia
Pimelodidae	

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Phractocephalus hemiliopterus</i> (Bloch & Schneider, 1801) – “Redtail catfish”	Asthma, wounds, hernia, burns in the skin, rheumatism, flu, cough, pneumonia
<i>Pseudoplatystoma corruscans</i> (Spix & Agassiz, 1829) – “Spotted sorubim”	Flu
<i>Pseudoplatystoma fasciatum</i> (Lunnaeus, 1776) – “Tiger catfish”	Cold
<i>Sorubimichthys planiceps</i> (Spix & Agassiz, 1829) – “Sorubim”	Leishmaniosis, tuberculosis
<i>Zungaro zungaro</i> (Humboldt, 1821) – “Black manguruyu”	Asthma, toothache, earache, wounds, athlete’s foot, burns in the skin, rheumatism, flu
Potamotrygonidae	
<i>Paratrygon aiereba</i> (Müller & Henle, 1841) – Discus ray, “Arraia”	Asthma, hernia, flu, pneumonia, cough, earache, burns
<i>Potamotrygon hystrix</i> (Müller & Henle, 1834) - Porcupine river stingray arraia	Asthma, hernia, flu, pneumonia, cough, earache, burns
<i>Potamotrygon motoro</i> (Müller & Henle, 1841) - Ocellate river stingray arraia	Asthma, hernia, flu, pneumonia, cough, earache, burns
<i>Potamotrygon orbignyi</i> (Castelnau, 1855)	Pain relief caused in injuries by that species’ sting
<i>Plesiotrygon iwamae</i> Rosa, Castello & Thorson, 1987	Pain relief caused in injuries by the species’ sting, wounds, cracks in the sole of the feet
Pristidae	
<i>Pristis pectinata</i> Latham, 1794 – Smalltooth sawfish, “espadarte”, “peixe-serra”	Asthma, rheumatism, arthritis
<i>Pristis perotteti</i> Müller & Henle, 1841 – Largetooth sawfish, “espadarte”	Asthma, rheumatism and arthritis
Prochilodontidae	
<i>Prochilodus argenteus</i> Spix & Agassiz, 1829 – “curimatá-pacú”, “curimatá”	To avoid swelling of the breast feeding, mycosis
<i>Prochilodus nigricans</i> Spix & Agassiz, 1829 - Black prochilodus, “curimatá”	Chilblain, skin burns, wounds, rheumatism, eye pains
Rajidae	
<i>Atlantoraja cyclophora</i> Regan, 1903 - Eyespot skate	Haemorrhage after delivery
Serrasalmidae	
<i>Mylossoma duriventre</i> (Cuvier, 1818) – Pacupeba, “pacu-manteiga”	Venereal disease
<i>Serrasalmus brandtii</i> (Lütken, 1875) - White piranha, “pirambeba”	Inflammations, sexual impotence
Sciaenidae	
<i>Cynoscion acoupa</i> (Lacepède, 1801) - Acoupa weakfish, “pescada amarela”	Renal failure
<i>Cynoscion leiarchus</i> (Cuvier, 1830) - Smooth weakfish, “pescada branca”	Renal failure
<i>Micropogonias furnieri</i> (Desmarest, 1823) – Whitemouth croaker, “corvina”	Pain relief caused in injuries by the species’ sting, cough, asthma, bronchitis
<i>Pachyurus francisci</i> (Cuvier, 1830) - San Francisco croaker, “cruvina-de-bico”	Asthma, urinary incontinence, backache
<i>Plagioscion surinamensis</i> (Bleeker, 1873) – Bashaw, “pacora”, “Curvina”	Urinary disorders, haemorrhage, snake bites
<i>Plagioscion squamosissimus</i> (Heckel, 1840) - South american silver croaker, “curvina”	Urinary disorders, haemorrhage, snake bites
Sparidae	

Family / Species / local name	Conditions to which remedies are prescribed
<i>Calamus penna</i> (Valenciennes, 1830) - Sheepshead porgy, “peixe-pena”	Asthma
Synbranchidae	
<i>Synbranchus marmoratus</i> Bloch, 1795 - Marbled swamp eel, “muçum”	Bronchitis
Syngnathidae	
<i>Hippocampus erectus</i> Perry, 1810 – Horsefish, “cavalo-marinho”	Asthma
<i>Hippocampus reidi</i> (Ginsburg, 1933) -Longsnout seahorse, “cavalo-marinho”	Asthma, edema, bronchitis, haemorrhage, haemorrhage in women, disorders after parturition (to accelerate recovery after parturition), gastritis, tuberculosis, to prevent abortion
Tetraodontidae	
<i>Colomesus psittacus</i> (Bloch & Schneider, 1801) - Banded puffer, “baiacu”	Breast cancer, backache, warts
<i>Sphoeroides testudineus</i> (Linnaeus, 1758) - Checkered puffer, “baiacu”	Rheumatism
Trichiuridae	
<i>Trichiurus lepturus</i> Linnaeus, 1758 - Largehead hairtail	Asthma
Urolophidae	
<i>Urotrygon microphthalmum</i> (Delsman, 1941) - Smalleyed round stingray, “raia”	Asthma, pain relief caused in injuries by the species’ sting, burns
AMPHIBIANS	
Bufonidae	
<i>Chaunus schneideri</i> (Werner, 1894) – Cururu toad, “sapo cururu”	Urinary incontinence, dental caries, cancer, wounds, boils, erysipelas acne, to induce abortion
<i>Chaunus marinus</i> (Linnaeus, 1758) – Marine toad, “sapo-cururu”	Scorpion sting (antidote)
Leptodactylidae	
<i>Leptodactylus</i> cf. <i>labyrinthicus</i> (Spix, 1824) – South american pepper frog, “jia-de-peito”, “rã- pimenta”	Earache, rheumatism, joint pain, cancer, sore throat
REPTILES	
Gekkonidae	
<i>Hemidactylus mabouia</i> (Moreau de Jonnes, 1818) - Afro-American house gecko, “lagartixa”, “bribe”	Sore throat
Iguanidae	
<i>Iguana iguana</i> (Linnaeus, 1758) - Common iguana, “camaleão”	Earache, erysipelas, asthma, rheumatism, edema, abscesses, joint pain, wounds, acne, athlete’s foot, sore throat, swelling, burn, tumour, to suck a splinter out of skin or flesh, boil, injuries caused by the spines of the ‘arraia’ and others fishes, inflammation, hernia
Teiidae	
<i>Ameiva ameiva</i> (Linnaeus, 1758) – Lizard, “sardão grande”	Inflammation, dermatitis, venereal diseases, snake bites
<i>Cnemidophorus</i> gr. <i>ocellifer</i> (Spix, 1825) – Lizard, “sardão pequeno”	Inflammation, dermatitis, venereal diseases, snake bites
<i>Tupinambis merianae</i> (Duméril & Bibron, 1839) – Lizard, “tegu”, “tejuacu”	Earache, deafness, rheumatism, erysipelas, skin thorns and wounds, respiratory diseases, sore throat, snake bite, asthma, tumour, swelling, infection, bronchitis

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Tupinambis teguixin</i> (Linnaeus 1758) – Lizard, “tegu”, “tejuacuçu”	Sexual impotence, rheumatism, erysipelas, dermatitis, snake bites, asthma, tetanus, earache, thrombosis, wounds, panaris, swelling, herpes zoster, irritation when milk teeth are erupting, jaundice, inflammation, tumour, sore throat, infection, bronchitis, injuries caused by the spines of the ‘arraia’, pain relief in injuries caused by snake bites, toothache, suck a splinter out of skin or fresh, headache, cough, stroke, coarse throat
Tropiduridae	
<i>Tropidurus hispidus</i> (Spix, 1825) - Lizard, “lagartixa”, “catenga”	Alcoholism, dermatomycosis, warts, abscesses, boils, sore throat, erysipelas, healing of umbilical cord of newborn baby
<i>Tropidurus semitaeniatus</i> (Spix, 1825) – Lizard, “lagartixa-de-lajedo”	Measles, asthma, alcoholism, dermatomycosis, warts
<i>Tropidurus torquatus</i> (Wied, 1820) – Lizard, “lagartixa”	Chicken pox
<i>Uranoscodon superciliosus</i> (Linnaeus, 1758), “tamaquaré”	As a sedative
Boidae	
<i>Boa constrictor</i> (Linnaeus, 1758) - Boa, “jibóia”	Rheumatism, lung disease, thrombosis, boils, tuberculosis, stomach ache, edema, snake bite, cancer, ache, swelling, to prevent abort, pain in the body, inflammation, athlete’s foot, calluses, tumours, cracks in the sole of the feets, goitre, sore throat, arthrosis, insect sting, dog bite, erysipelas, thrombosis, asthma, neck strain, strain muscle, back ache
<i>Corallus caninus</i> (Linnaeus, 1758) - American emerald tree boa, “cobra papagaio”	Pain relief caused by sting of animals
<i>Corallus hortolanus</i> (Linnaeus, 1758) – Snake	To assist in removing spines or other sharp structures from the skin, rheumatism
<i>Eunectes murinus</i> (Linnaeus, 1758) - Anaconda, “sucurujú”, “sucuri”	Wounds, skin problems, bruises, sprains, arthrosis, rheumatism, boils, sexual impotence, headache, sore throat, thrombosis, swelling, tumour, asthma, muscle strain, numbness, syphilis, to reduce pain, luxation
<i>Epicrates cenchria</i> (Linnaeus, 1758) – Brazilian rainbow boa, “salamanta”	Rheumatism, pain in articulations, injuries caused by itself, sore throat
Colubridae	
<i>Leptophis ahetula</i> (Linnaeus, 1758) - Parrot snake, “cobra cipó”	Pain relief caused by sting of animals
<i>Mastigodryas bifossatus</i> (Raddi, 1820) – Rio tropical racer, “jaracuçu”	Snake bites
<i>Oxyrhopus trigeminus</i> Duméril, Bibron & Duméril, 1854 – “Coral falsa”	Rheumatism
<i>Spilotes pullatus</i> (Linnaeus, 1758) - Tiger snake	Pain relief in injuries caused by sting of insects and snake bite
<i>Tachymenis peruviana</i> Wiegmann, 1835	Pain in the bones, Pain in kidneys and to treat inflammations, toothache and scare
Crotalidae	
<i>Crotalus durissus</i> (Linnaeus, 1758) - Neotropical rattlesnake, “cascavel”	Asthma, snake bite, thrombosis, wounds, luxation, rheumatism, pain in the legs, erysipelas, deafness, epilepsy, skin diseases, tuberculosis, hanseniasis, backache, tumour, boil, headache, earache, osteoporosis, sore throat, toothache, pain relief in injuries caused by sting of insects and snake bite, irritation when milk teeth are erupting,

Family / Species / local name	Conditions to which remedies are prescribed
Elapidae <i>Micrurus ibiboboca</i> (Merrem, 1820) - “Cobra-coral”	Rheumatism, snake bite
Viperidae <i>Bothrops leucurus</i> Wagler, 1824 - Lance head, “jararaca”	Tumour, boils
<i>Lachesis muta</i> (Linnaeus, 1766) - Bushmaster, “surucucu pico-de-jaca”	Rheumatism, swelling, tumour, boil, pain relief in injuries caused by sting of insects and snake bite
Chelidae <i>Phrynops geoffroanus</i> (Schweigger, 1812) - Geoffroy’s side-necked turtle, “cágado”	Asthma, sore throat, swelling, earache, rheumatism, arthrosis, healing of umbilical cord of newborn baby, mumps
<i>Mesoclemmys tuberculata</i> (Luederwaldt, 1926) – Tuberculate toadhead turtle, “cágado”, “cágado-d’água”	Rheumatism, discharge, thrombosis, bronchitis, diarrhoea, haemorrhag, asthma, sore throat, hoarseness
Cheloniidae <i>Caretta caretta</i> (Linnaeus, 1758) - Loggerhead turtle, “tartaruga cabeçuda”	Injuries caused by bang, toothache, diabetes, headache, backache, wounds, cough, bronchitis, asthma, thrombosis, rheumatism, stroke, hoarseness, flu, backache, earache, sore throat, swelling
<i>Chelonia mydas</i> (Linnaeus, 1758) - Green sea turtle, “tartaruga verde”, “aruanã”	Injuries caused by bang, toothache, diabetes, headache, backache, wounds, cough, bronchitis, asthma, flu, thrombosis, rheumatism, toothache, stroke, hoarseness, earache, sore throat, swelling, whooping cough, arthritis, erysipelas, boil, wounds, arthrosis, inflammation
<i>Eretmochelys imbricata</i> (Linnaeus, 1766) - Atlantic hawksbill, “tartaruga de pente”	Injuries caused by bang, toothache, diabetes, headache, backache, wounds, cough, bronchitis, asthma, thrombosis, stroke, hoarseness, flu, rheumatism, earache, sore throat, swelling
<i>Lepidochelys olivacea</i> (Eschscholtz, 1829)	Injuries caused by bang, toothache, diabetes, headache, backache, wounds, cough, flu, bronchitis, asthma, thrombosis, rheumatism, stroke, hoarseness
Dermochelyidae <i>Dermochelys coriacea</i> (Vandelli, 1761) - Leatherback turtle, “tartaruga de couro”	Rheumatism, earache, sore throat, swelling
Geoemydidae <i>Rhinoclemmys punctularia</i> (Daudin, 1802) - Spot-legged turtle	Wounds, tumour, erysipelas, earache, rheumatism
Podocnemididae <i>Podocnemis expansa</i> (Schweiger, 1812) - Amazon river turtle, “tartaruga da amazônia”	Inflammation, acne, tumour, boil, rheumatism, pterygium, skin spots, backache, earache, arthrosis, arthritis, swelling, wrinkle
<i>Podocnemis unifilis</i> (Troschel, 1848) – Yellow-spotted river turtle, “tracajá”	Wounds, tumour, erysipelas, earache, rheumatism
<i>Podocnemis sextuberculata</i> Cornalia, 1849 - Six-tubercled Amazon River turtle	Blackhead; acne
<i>Peltocephalus dumeriliana</i> Schweigger 1812 – “Cabeçuda”	Blackhead; acne
Testudinidae <i>Geochelone carbonaria</i> (Spix, 1824) - Red-footed tortoise, “jabuti”	Catarrh, erysipelas, bronchitis, to stop the sensation to getting thirsty, asthma
<i>Geochelone denticulata</i> (Linnaeus, 1766) – Yellow-footed tortoise, “jabuti”	Sore throat, rheumatism, hernia, wounds, leishmaniosis, varicocele, earache, part of woman’s body
Alligatoridae	

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Caiman crocodilus</i> (Linnaeus, 1758) - Common cayman, “jacaré tinga”	Asthma, stroke, bronchitis, backache, earache, rheumatism, thrombosis, sexual impotence, snake bites (antidote), evil eye, irritation when milk teeth are erupting, discharge, swelling, scratch, athlete’s foot, ophthalmological problems, sore throat, amulet used as a protection against snake bite, hernia, prostate problems, infection, inflammation
<i>Caiman latirostris</i> (Daudin, 1801) – Cayman, “jacaré-do-papo-amarelo”	Asthma, sore throat, amulet used as a protection against snake bite, rheumatism, irritation when milk teeth are erupting, hernia, prostate problems
<i>Melanosuchus niger</i> (Spix, 1825) - Black cayman, “jacare açú”	Thrombosis, infection, swelling, asthma, amulet used as a protection against snake bite, injuries caused by spines of the ‘arraia’, pain relief in injuries caused by snake bites
<i>Paleosuchus palpebrosus</i> (Cuvier, 1807) - Cayman, “jacaré coroa”, “jacaré”, “jacaré-preto”, “crocodilo”	Snake bite, asthma, stroke, rheumatism, thrombosis, backache, sexual impotence, edema, mycosis, evil eye, irritation when milk teeth are erupting, discharge, sore throat, amulet used as a protection against snake bite, hernia, prostate problems
<i>Paleosuchus trigonatus</i> (Schneider, 1801) - , “Jacaré coroa”	Rheumatism
BIRDS	
Accipitridae	
<i>Geranoaetus melanoleucus</i> (Vieillot, 1819) - Black-chested Buzzard-Eagle	The feathers are used as inensing and to makemasks. The meat used to avoid the wrinkles.
Anatidae	
<i>Anser anser</i> (Linnaeus, 1758) – Greylag goose, “ganso”	Laryngitis, pharyngitis, tonsillitis
Anhimidae	
<i>Anhima cornuta</i> (Linnaeus, 1766) – Horned screamer, “anuhma”	Intoxication from poisonous animals
Ardeidae	
<i>Ardea cocoi</i> (Linnaeus, 1766) – White-necked Heron	Swelling, inflammation, injuries caused by the spines of the ‘arraia’ and others fishes, asthma, boil, tumour, rheumatism, earache
<i>Ardea alba</i> Linnaeus, 1758 – Galça	Bronquithis and pneumonia
Ardeidae	
<i>Tigrisoma lineatum</i> (Boddaert, 1783) – socó, Rufescent Tiger-Heron	Bronquithis and pneumonia
Caprimulgidae	
<i>Nyctidromus albicollis</i> (Gmelin, 1789) – Pauraque, “bacurau”	Amulets, snake bite
Cathartidae	
<i>Coragyps atratus</i> (Bechstein, 1793) - Black vulture, “urubu”, “urubu-preto”	Deafness, bronchitis, anaemia, alcoholism, asthma, flu (catarrh), earache, rheumatism
Cracidae	
<i>Penelope jacucaca</i> (Spix, 1825) – White-browed guan, “jacu”	Insomnia
<i>Penelope superciliaris</i> Temminck, 1815	Asthma
Phoenicopteridae	
<i>Phoenicopus andinus</i> Philippi, 1854	To alliviate labor pain, sprains and distend

Family / Species / local name	Conditions to which remedies are prescribed
<i>Phoenicopterus chilensis</i> Molina, 1782	To allviate labor pain, sprains and distend
<i>Phoenicopterus jamesi</i> Sclater, 1886	To allviate labor pain, sprains and distend
Ciconiidae	
<i>Vultur gryphus</i> Linnaeus, 1758	Not mentioned
<i>Ciconia maguari</i> (Gmelin, 1789) - Maguari stork	Injuries caused by the spines of the 'arraia' and others fishes, thrombosis
Columbidae	
<i>Leptotila rufaxilla</i> (Richard & Bernard, 1792) – Gray-fronted dove, 'jurití'	Thrombosis
<i>Columba livia</i> (Gmelin, 1789) – Rock pigeon, "pombo"	Asthma, laryngitis, pharyngitis, tonsilite
Corvidae	
<i>Cyanocorax cyanopogon</i> (Wied, 1821) – White-naped jay, "can-can"	Asthma, neurological problems
Cotingidae	
<i>Procnias nudicollis</i> (Vieillot, 1817) - araponga , Bare-throated Bellbird	Tuberculosis
Cuculidae	
<i>Crotophaga ani</i> Linnaeus, 1758 – Smooth-billed ani	Bronchitis, thrombosis, asthma, whooping cough, rheumatism
<i>Guira guira</i> (Gmelin, 1788) – Guira cuckoo, "anum branco"	Asthma
Charadriidae	
<i>Vanellus chilensis</i> (Molina, 1782) – Southern lapwing, "quero-quero"	To stay awake
Emberezidae	
<i>Coereba flaveola</i> (Linnaeus, 1758)– Banana quit, "caga-sebo"	Thrombosis
Falconidae	
<i>Herpetotheres cachinnans</i> (Linnaeus, 1758) - Laughing falcon, "acaúã"	Snake bite
<i>Caracara plancus</i> (Miller, 1777) - Southern caracara, "caracarã"	Snake bite
<i>Falco rufigularis</i> Daudin, 1800 - Bat falcon, "cauré"	Snake bite
Furnaridae	
<i>Furnarius rufus</i> (Gmelin, 1788)- Rufous hornero, "maria-barreira"	Mumps
Meleagrididae	
<i>Meleagris gallopavo</i> Linnaeus, 1758 – turkey, "peru"	Asthma
Phasianidae	
<i>Gallus gallus</i> (Linnaeus, 1758) - Domestic chicken, "galinha"	Catarrh, fever, warts, haemorrhage, bronchitis, nasal congestion, flu, skin thorns and wounds, asthma, sore throat, tumour, poor digestion, healing of umbilical cord of newborn baby, swelling, cough, tuberculosis, earache, tonsillitis, rheumatism, diarrhea, inflammation, pneumonia
Picidae	
<i>Dryocopus lineatus</i> (Linnaeus, 1766) - Lineated woodpecker, "pica-pau-de-banda-branca"	Sexual impotence
<i>Pavo cristatus</i> Linnaeus, 1758 - Indian peafowl	Thrombosis, epilepsy
Rallidae	

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Aramides cajanea</i> (Statius Muller, 1776) – Grey-necked wood-rail, “saracura”	Evil eye
Ramphastidae	
<i>Ramphastos tucanus</i> Linnaeus, 1758 - Red-billed Toucan, “tucano”	Thrombosis, Sexual impotence
<i>Ramphastos vitellinus</i> Lichtenstein, 1823 - Channel-billed toucan, “tucano-de-bico-preto”	Sexual impotence
<i>Pteroglossus aracari</i> (Linnaeus, 1758) - Black-necked aracari, “araçari-de-bico-branco”	Sexual impotence
<i>Pteroglossus inscriptus</i> - Swainson, 1822, Lettered aracari, “araçari-miudinho-de-bico-riscado”	Sexual impotence
Rheidae	
<i>Rhea americana</i> (Linnaeus, 1758) – Greater rhea, “ema”	General aches, rheumatism, thrombosis, strokes
<i>Pterocnemia pennata</i> (Orbigny, 1834)	Not mentioned
Tinamidae	
<i>Crypturellus noctivagus</i> (Wied, 1820) - Yellow-legged tinamou, “zabele”	Thrombosis, stroke, snake bites, tuberculosis, deafness
<i>Nothura boraquira</i> (Spix, 1825) – White-bellied nothura, ‘codorna”	Thrombosis, stroke, toothache
<i>Rhynchotus rufescens</i> (Temminck, 1815) – Red-winged tinamou, “perdiz”	Snake bite, thrombosis, tuberculosis
Trochilidae	
<i>Eupetomena macroura</i> (Gmelin, 1788) – Swallow-tailed hummingbird, “beijola”, “beija-flor”	Cardiopathies, asthma, flu, ache
Tyrannidae	
<i>Fluvicola nengeta</i> (Linnaeus, 1766) - Masked water-tyrant, “lavandeira”	Boils
<i>Pitangus sulphuratus</i> (Linnaeus, 1766)	Earache
MAMMALS	
Agoutidae	
<i>Agouti paca</i> (Linnaeus, 1766) – Spotted paca, “paca”	Wound in the breast caused by suckling, ophthalmological problems, stomach disorders, pterygium, to suck a splinter out of skin or flesh, injuries caused by the spines of ‘arraia’, control cholesterol level, thrombosis, General body pain, leishmaniasis, snake bite, rheumatism, heart pain, pain in bones, liver pain, urinary, fever, child birth, ant bite
Balaenopteridae	
<i>Balaenoptera acutorostrata</i> Lacépède, 1804 – Minke whale, “baleia minke”	Rheumatism, sore throat, wounds
Bovidae	
<i>Bos taurus</i> Linnaeus, 1758 – Cow, “vaca”	Thrombosis, evil eye, amulet used as a protection against snake bite, baldness, sexual impotence, measles, varicella, anaemia, whooping cough, alcoholism, rheumatism, inflammation, asthma, cough, sore throat, wounds, cracks in the sole of the feet, bronchitis, dizziness, anemia, bladder problems, chickenpox
<i>Bubalus bubalis</i> (Linnaeus, 1758) – Water buffalo (feral), “búfalo”	Rheumatism, osteoporosis, thrombosis

Family / Species / local name	Conditions to which remedies are prescribed
<i>Ovis aries</i> (Linnaeus, 1758) – Sheep, “carneiro”	Edema, fractures, erysipelas, herpes zoster, backache, swelling, to assist children who take longer than usual to start walking, arthritis, arthrosis, rheumatism, muscle strain, inflammation, luxation, cracks in the sole of the feet, joint pain
<i>Capra hircus</i> Linnaeus, 1758 – Domestic goat, “bode”	Evil eye, snake bite, muscle strain
Bradyrodidae	
<i>Bradypus variegatus</i> Shinz, 1825 – Brown-throated three-toed sloth, “Preguiça pequena”	Thrombosis
<i>Bradypus tridactylus</i> Linnaeus, 1758 – Pale-throated three-toed sloth, “Preguiça”	Thrombosis, insects bite, scorpions bite
Canidae	
<i>Lycalopex culpaeus</i> (Molina, 1782)	Scare
<i>Lycalopex gymnocercus</i> (G. Fischer, 1814)	Air loss, asthma, backache, disorders after parturition, pain in the bones, rheumatism, scare, sprains, ulcer.
<i>Canis lupus</i> (Linnaeus, 1758) – Domestic dog, “cachorro”	Chicken pox, mumps, smallpox, asthma, varicella, measles, menstrual cramps
<i>Cerdocyon thous</i> (Linnaeus, 1766) – Crab-eating fox, “raposa”	Rheumatism, flu, haemorrhoids, disorders after parturition (to accelerate recovery after parturition), diabetes, Thrombosis, backache
<i>Chrysocyon brachyurus</i> (Illiger, 1815) – Maned wolf, “lobo-guará”	Epilepsy
<i>Dusicyon thous</i> – Linnaeus, 1766 – Crab-eating fox, “raposa”	Alcoholism, thrombosis, rheumatism, ophthalmological problems, diabetes, urinary infection
<i>Speothos venaticus</i> (Lund, 1842) – Bush dog, “cachorro-do-mato”	Haemorrhoids
Caviidae	
<i>Cavia aperea</i> Erxleben, 1777 – “Preá”	Inflammation
<i>Kerodon rupestris</i> (Wied-Neuwied, 1820) – “Mocó”	Constipation
Cebidae	
<i>Alouatta belzebul</i> (Linnaeus, 1766) – Red-handed howler monkey, “guariba”, “macaco”	Whooping cough, sore throat, asthma
<i>Alouatta nigerrima</i> Lönnberg, 1941 -Amazon black howler	Whooping cough, inflammation
<i>Alouatta seniculus</i> (Linnaeus, 1766) - Red howler monkey, “guariba vermelho”	Whooping cough, inflammation, to accelerate parturition
<i>Ateles chamek</i> (Humboldt, 1812)	Fever, cough, cold shoulder pain, sleeping problems, Leishmaniasis, Spider bite, snake bites.
<i>Aotus azarai</i> (Humboldt, 1811)	To avoid the children to dribble
<i>Cebus apella</i> (Linnaeus, 1758) – Brow capuchin, “capuchin”, “macaco”, “macaco-prego”	Insect sting, Eye infection
Cervidae	
<i>Blastocerus dichotomus</i> (Illiger, 1815) – Marsh deer, “cervo-do-pantanal”	Diarrhoea, vomit
<i>Mazama americana</i> (Erxleben, 1777) – Red brocket, “veado gaedo”	Stroke, Cold
<i>Mazama simplicicornis</i> (Illinger, 1811)	Diarrhoea, verminosis, evil eye
<i>Mazama cf. gouazoupira</i> (G. Fischer, 1814) – Gray brocket, “veado-catingeiro”	Asthma, edema, rheumatism, snake bite, thrombosis, to assist children who take longer than usual to start walking, toothache, wounds, sprains
<i>Ozotocerus bezoarticus</i> (Linnaeus, 1758), veado campineiro	Diarrhoea, verminosis, evil eye
Dasyrodidae	
<i>Dasyypus novemcinctus</i> (Linnaeus, 1758) – Nine-banded armadillo, “tatu galinha”	Thrombosis, insects bite, scorpions bite, edema, asthma, deafness, earache, evil eye

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Euphractus sexcinctus</i> (Linnaeus, 1758) – Six-banded armadillo “tatu peba”	Wounds, earache, evil eye, asthma, sore throat, pneumonia, sinusitis, deafness, coarse throat
<i>Tolypeutes tricinctus</i> (Linnaeus, 1758) – Brazilian three-banded armadillo, “tatu-bola”	Thrombosis, rheumatism
<i>Priodontes maximus</i> (Kerr, 1792)	Embolism, ant bite, visions (hallucinations?), skin diseases
<i>Chaetophractus vellerosus</i> (Gray, 1865)	General diseases
Dasyproctidae	
<i>Dasyprocta prymnolopha</i> Wagler, 1831 – Black-rumped agouti, “Cutia”	Asthma, thrombosis
<i>Dasyprocta variegata</i> - Brown agouti	Childbirth, Afrodisiaco, Picadura de buna, Picadura de vibora
Delphinidae	
<i>Sotalia fluviatilis</i> Gervais & Deville, 1853 ^{DD/1} – Gray dolphin, gray river dolphin, “boto”	Asthma, headache, rheumatism, hernia, womb disorders, sore throat, injuries caused by the spines of the ‘arraia’, swelling, haemorrhoids inflammation, wounds, earache, erysipelas, athlete’s foot, tumour, cancer
<i>Sotalia guianensis</i> (P. J. Van Bénédén, 1864) – Guianan river dolphin, “boto”	Asthma, headache, rheumatism, hernia, womb disorders, sore throat, injuries caused by the spines of the ‘arraia’, swelling, haemorrhoids inflammation, wounds, earache, erysipelas, athlete’s foot, tumour, cancer
Didelphidae	
<i>Didelphis albiventris</i> (Lund, 1840) – Common opossum, “timbú”	Boils, rheumatism
<i>Didelphis marsupialis</i> (Linnaeus, 1758) – Southern opossum, “mucura”, “gambá”, “sarué”	Acne, wounds, bronchitis, joint pain, stomach ache, rheumatism, diarrhoea, inflammation, erysipelas, pain in gestation, asthma, headache, toothache, earache, sore throat, stomachache, flu, fever, body pain, fatigue
Megalonychidae	
<i>Choloepus hoffmanni</i> Peters, 1858	Visions, hallucination, cramps
Erethizontidae	
<i>Coendou bicolor</i> (Tschudi, 1844)	Hallucination, fever, ant bite, flu, whooping cough, scare, varicose veins
<i>Coendou prehensilis</i> (Linnaeus, 1758) –Brazilian porcupine, “coandú”, “porco espinho”	Bronchitis, thrombosis, epilepsy, stroke, abscesses, conjunctivitis, asthma
Equidae	
<i>Equus asinus</i> Linnaeus, 1758 – Asino, ass, “jumento”	Snake bite (antidote), whooping cough, asthma
<i>Equus caballus</i> (Linnaeus, 1758) – Horse, “cavalo”	Cough, deep cuts; dermatosis, wounds
Felidae	
<i>Felis silvestris</i> Schreber, 1775 – Domestic cat, “gato”	Asthma, snake bites
<i>Puma concolor</i> (Linnaeus, 1771) – Mountain lion, “onça”	Wounds, leishmaniosis, arthritis, pain in bones, rheumatism, distend, scare, sthomaschache, “evil eye”, fever, avoid acne
<i>Panthera onca</i> (Linnaeus, 1758) – Jaguar, ‘onça’	Wounds, leishmaniosis, Cough, fatigue, fever, pain in bones
<i>Leopardus jacobitus</i> (Cornalia, 1865)	Self encourage
<i>Leopardus colocolo</i> (Molina, 1782)	Self encourage
Octodontidae	
<i>Ctenomys opimus</i> Wagner, 1848	To make the child’s teeth stronger

Family / Species / local name	Conditions to which remedies are prescribed
Chinchillidae <i>Lagidium viscacia</i> (Molina, 1782)	Bad memory
Hydrochaeridae <i>Hydrochaeris hydrochaeris</i> (Linnaeus, 1766) – Capybara, “capibara”, “capivara”	Thrombosis, conjunctivitis, venereal disease, rheumatism, earache, strengthen bones, liver pain, bronchitis, asthma, wounds, erysipelas, cough
Iniidae <i>Inia geoffrensis</i> (Blainville, 1817) – Amazon river dolphin, “boto rosa”	Asthma, headache, rheumatism, hernia, womb disorders, sore throat, injuries caused by the spines of the ‘arraia’, swelling, haemorrhoids inflammation, wounds, earache, erysipelas, athlete’s foot, tumour, cancer
Leporidae <i>Sylvilagus brasiliensis</i> (Linnaeus, 1758) – Forest rabbit, tapeti, “coelho”, “coelho-do-mato”	Thrombosis, conjunctivitis, boils, burns, Ophthalmological problems, embolism, scare, fever, hallucinations
Mephitidae <i>Conepatus semistriatus</i> (Boddaert, 1785) – Striped hog- nosed skunk, “cangambá”, “gambambá”, tacaca <i>Conepatus chinga</i> (Molina, 1782) – Gambá, Molina's Hog-nosed Skunk	Rheumatism Thrombosis, Rheumatism, general diseases
Mustelidae <i>Lontra longicaudis</i> (Olfers, 1818) – “Lontra”	Thrombosis, Ampollas
Camelidae Lama glama (Linnaeus, 1758) Lama guanicoe (Müller, 1776) <i>Vicugna vicugna</i> (Molina, 1782)	Children “aicados” (a spiritual disease) Asthma, scare Not mentioned
Myrmecophagidae <i>Myrmecophaga tridactyla</i> Linnaeus, 1758 – Giant anteater, “tamanduá-bandeira” <i>Myrmecophaga tetradactyla</i> (Linnaeus, 1758) – Collared anteater, “tamanduá”	Thrombosis, stroke, General body pain, Snake bite, urinary problem, Heart pain, ant bite Edema, thrombosis, itching, ant bite
Procyonidae <i>Nasua nasua</i> (Linnaeus, 1766) – South American coati, “coati”, “quati” <i>Procyon cancrivorus</i> (G. [Baron] Cuvier, 1798) – Crab-eating raccoon, “guaxininim” <i>Potos flavus</i> (Schreber, 1774) - Kinkajou	Sexual impotence, wounds, skin burns, snake bites, backache, Cold, cough, leg pain, Wounded foot, Earache, neck strain, to help become pregnant, whooping cough Rheumatism, epilepsy, thrombosis, snake bite Earache, snake bite, ant bite
Physeteridae <i>Physeter catodon</i> Linnaeus, 1758 – Sperm whale, cachelot, “cachalote”	Asthma, backache, rheumatism, sore throat, wounds
Suidae <i>Sus scrofa</i> (Linnaeus, 1758) – Wild boar, “porco”	Acne, boils, tumours, asthma, Athlete’s foot, warble, wounds,
Tapiridae <i>Tapirus terrestris</i> (Linnaeus, 1758) – Brazilian tapir, “anta”	Rheumatism, arthrosis, osteoporosis, bursitis, muscular pain, asthma, tonsillitis, cough, General body pain
Tayassuidae <i>Pecari tajacu</i> Linnaeus 1758 – Collared peccary, “porco-do-mato”, “caititu”	Thrombosis, bronchitis, stroke

Table 1. (Continued)

Family / Species / local name	Conditions to which remedies are prescribed
<i>Tayassu pecari</i> (Link, 1795) – White-lipped peccary “porco-do-mato”, “queixada” Trichechidae	Thrombosis, stroke, Cold
<i>Trichechus inunguis</i> (Natterer, 1883) – Amazonian manatee, “peixe-boi”	Sprains, vaginal discharge, injuries caused by bang, burns, asthma, menstrual cramps, rheumatism, sore throat, wounds, muscle strain, suck a splinter out of skin or fresh, tumour, backache, hernia, arthrosis, luxation, menstrual cramps, insects bite
<i>Trichechus manatus</i> (Linnaeus, 1758) – Manatee, “peixe-boi”	Arthrosis, luxation, menstrual cramps, insects bites, sprains, vaginal discharge, injuries caused by bang burns, asthma, rheumatism, sore throat, wounds, muscle strain

The high taxonomic diversity of animal species used in traditional medicine is not surprising, as numerous workers have pointed out that animals are among the resources frequently used in folk medicine worldwide. However, considering the relatively small number of published studies on the subject in many countries of South America, we presume that the true number of medicinal animal species used is greater than that recorded here.

Some widespread species are used in different countries, such as *Tupinambis* spp. (in Argentina and Brazil), and *Tapirus terrestris* (in Brazil and Bolivia) (35,70). A given animal often has multiple medicinal uses and can be employed to treat more than one ailment, while different species can likewise be used to treat the same illnesses. Products derived from *Tupinambis merianae* and *T. teguixin*, for instance, were indicated for treating 14 and 29 conditions, respectively, in Brazil; in Bolivia, products derived from the *Agouti paca* (Linnaeus, 1766) have been documented as remedies for general body pain, leishmaniasis, snakebite, rheumatism, heart pain, pain in bones, liver pain, fever, and pain during childbirth (35).

Animals were used for treating 249 diseases, asthma, rheumatism, wounds, thrombosis and bronchitis being the most usual ones. Most animals (n=181, 56.21%) were prescribed for treating different diseases.

For geographically widespread species, similar uses were found in different countries. Some examples are: *H. reidi* and *C. durissus* for treating asthma and *Apis mellifera* (Linnaeus, 1758) (Apidae)

and *Mellita sexiesperforata* (Leske, 1778) for treating flu and cough (16-18,24,25,28,31,40,58,63,68).

Despite their importance, the use of animals and their body parts in medicine have been neglected, when compared to plants (24). Traditional drugs and traditional medicine in general represent a still poorly explored field of research in terms of therapeutic potential or clinical evaluation. There is a current preoccupation about this, since it is well-established that all sorts of vegetable, animal and mineral remedies used in a traditional setting are capable of producing serious adverse reactions. It is essential, however, that traditional drug therapies be submitted to an appropriate benefit/risk analysis. Numerous infectious diseases can be transmitted from animals to humans (i.e. zoonoses). In this context, the possibility of transmitting infections or ailments from animal preparations to the patient should be seriously considered (71). Several organs and tissues including bones and bile can be a source of *Salmonella* infection causing chronic diarrhoea and endotoxic shock. The possibility of transmission of other serious and widespread zoonoses such as tuberculosis or rabies should be considered whenever animal tissues from unknown sources are handled and used as remedies (72). The possibility of toxic or allergic reactions to animal products should also be considered (73).

As pointed out by Pieroni et al (74), the chemical constituents and pharmacological actions of some animal products are already known to some extent and ethnopharmacological studies focused on animal remedies could be very important in order to clarify the eventual therapeutic usefulness of this class of biological remedies.

Traditional medicine still makes use of animals and products derived from animal organs such in rural areas as in many urban and semi-urban localities. For instance, biological remedies are openly commercialized in essentially all of the towns and cities in Brazil, principally in public markets. It is common to find specific places in these markets where plants and animals are sold for medicinal purposes - locations that serve to unite, maintain, and diffuse empirical knowledge from different regions and of different origins (5,28,30-32,43,63,75-79). This reflect the widespread usage of animal-based remedies, and the resilience of zootherapeutic practices, which have come to co-exist with allopathic medicine in urban and semi-urban environments (31). As pointed by Athais (80) and Sanchez (81), even in many Indigenous communities, traditional medicine is still practiced, with a link to allopathic medicine use (80). In addition to the use of traditional healers, known as Shamans (more formally Opygua, Pai, and other denominations), many families have their own knowledge and access to medicinal plants and animals for use in emergencies.

Besides their role in healing, natural products often have magical-religious significance, reflecting the different views of health and disease that exist within different cultures. In this context, animal parts are used to prepare clinical remedies as well as to make amulets or charms used in magical/religious diagnoses. Popular beliefs usually affect the way species are used in zootherapy (24). One form of spiritual treatment involves the use of amulets containing animal parts to protect the user from the "evil-eye" or from diseases [30]. An example is caiman teeth (*C. latirostris*, *M. niger*, and *P. palpebrosus*) used as protection against snake bites (5).

In addition to the belief systems, the socioeconomics aspects also influence the zootherapeutic practices (5). Latin America has one of the greatest disparities in income distribution in the world. Overall, the health profile of the Latin American population can be classified as undergoing a slow epidemiological transition. At one extreme of the spectrum there is a high incidence of (and mortality from) chronic noninfectious diseases such as cardiovascular problems and cancer, which predominate in large metropolitan areas. On the other

hand, infectious diseases still impose a heavy burden on the poverty-stricken parts of the population. The reasons for this dichotomy are two-fold: uneven socioeconomic development within countries and the extreme diversity of regional environments (82). Brazil, for example, is a highly heterogeneous socially and regionally marked by profound internal inequalities in distribution of income (83). For the majority of population, access medical-hospital care is available within the public sector and the organization of health care system reflects the schisms within Brazilian society. High technology private care is available to the rich and inadequate public care to the poor (84,85). Studies suggest that Indigenous peoples of Latin America still have inadequate access to mainstream health services, and health prevention and promotion programmes, and that services that do exist are often culturally inappropriate (80,81). Some of the barriers to health care access are structural and economic factors (distance and location of health care facilities, isolation of Indigenous communities, scarcity of health insurance or funds to pay for services, or time factors) and poor cultural sensitivity and appropriateness of health care systems (disregard of health personnel towards Indigenous peoples or their culture, disrespect for traditional healing practices, language and religious barriers, or uncomfortable and impersonal environment of hospitals and clinics) (86-89). Hence, resorting to the use of medicinal animals and plants, which were easily accessible and relatively cheap is an important component to health care. Nevertheless, it has been documented that people sometimes resort to traditional home remedies as a means of resisting urban modern medicine (90) and of asserting their traditional culture (91). It is important to note that behind the perceived efficacy by users, the popularity of animal-based remedies is influenced by cultural aspects, the relations between humans and biodiversity in the form of zootherapeutic practices are conditioned by the social and economic relations between humans themselves (24).

The traditional medicine is widely available and affordable, yet in remote areas, and generally accessible to most people. In many developing countries, a large part of the population, especially in rural areas, depends mainly on traditional medicine for their primary health care, because it is cheaper and

more accessible than orthodox medicine (5,92-94). Traditional medicine is also more acceptable because it blends readily into the peoples' socio-cultural life (95). Nazarea et al (96) highlight that social, economic and cultural factors play a large role in determining how individuals and communities use natural resources.

The use of medicinal animals and plants is a fundamental component within traditional health systems and medical practice in South America. Recently, concern about the ethics of exploiting indigenous knowledge and resources from tropical countries, without sharing the benefits with those who are the traditional custodians of the knowledge and land, has gained attention through the convention on biological diversity (CBD), which requires that such knowledge be protected, respected and preserved [97]. Traditional knowledge related to traditional medicine may be protected and conserved through the development of intellectual property rights (IPRs) and/or through benefit sharing (98,99). Intellectual property rights are rights over intangible information that provides incentives for future innovations (98). The compensation of indigenous people can validate their knowledge of the biodiversity they manage and also provide them with an equitable reward for sharing it, thereby compensating biological stewardship and encouraging conservation (98,100). In fact, as pointed out by Smith et al (101), the explanations for difficulties in access to essential drugs in the poor countries relate not only to the population precarious socio-economic conditions, but also to lack of organization health services, inadequate supply system management and irrational prescription.

Many countries (including Argentina, Bolivia, Venezuela, Colombia, Ecuador, Mexico, Nicaragua, and Paraguay) have revised their Constitutions to legally recognize the rights of Indigenous people to maintain and promote their specific cultural, linguistic, and territorial integrity. In 2003, the Unit of Indigenous Communities and Community Development analysed the constitutions and legislation of 21 Latin American countries according to eight variables of best legislative practice.

In several countries, the importance of plants (and animals) and medication systems has led to the creation of national bodies to protect them. The main

threat to such natural resources in Latin America is the rapid destruction of ecosystems, and the loss of biodiversity, both exacerbated by climate change. Between 1975 and 1988, nearly 500 000 km² of tropical rainforest was deforested in Amazonia, 10·1% of the total surface (102,103). In the present review, we verified that is common the medicinal use of threatened species as remedies. From the perspective both of the faunistic resources and of traditional knowledge holders, habitat loss and landscape alterations are potential treats to the survival of many potential valuable medicinal animals and the cultural aspects associated to them. As discussed by Anyinam (104), environmental degradation also affects users of traditional medicine, both by limiting their access to the resources traditionally used and by extirpating from their community the knowledge base upon which traditional medicine is constructed.

If the need for conservation is to be accepted by people who make their livelihoods from wildlife or use wildlife as food and/or medicine, then care should be taken to avoid approaches with little or no social resonance (i.e., that may be perceived as ideological or culturally imperialistic) (25). Sustainability of harvesting of medicinal animals is challenged by many factors, from both social and ecological perspectives. It is important to respect differing views of the value of wildlife, while, at the same time, conserving biodiversity.

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Submitted: October 15, 2008.

Revised: December 20, 2008.

Accepted: December 25, 2008.

Rationality and irrationality in ryke geerd hamer's system for treatment of metastatic cancer revisited

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Abstract

The aim of this paper is to take into consideration the critique that met our first paper on Ryke Geerd Hamer's work. In that paper we examined the "five medical laws" found by the German physician Ryke Geerd Hamer and found that the first two were substantiated by contemporary holistic medical theory, while the last three were not substantiated. In the present paper we take into consideration the arguments presented against our analysis from Hamer and others. We conclude that our first analysis, in spite of being based on an incomplete reading of the sources, as most of them were in German, still seems to be accurate. We have met no arguments that can justify a shift in our position, either in the direction of giving more support to Hamer than admitting him two of five principles likely to be true, or in the direction of annulations of the given acknowledgment of the two first and most central principles of Hamer's medical system. We thus still expect Hamer's system to be efficient to some extent in helping patients with metastatic cancer to enter the state of existential healing called salutogenesis (possibly leading to survival and even "spontaneous remission" of cancer), but clinical testing of Hamer's approach is needed to take this exploration further.

Keywords: Quality of Life, QOL, human development, holistic medicine, cancer, spontaneous remission, alternative medicine, complementary medicine, holistic medicine, salutogenesis, consciousness-based medicine, Denmark.

Introduction

The aim of the first Hamer-paper (Ventegodt S, Andersen NJ, Merrick J. Rationality and irrationality in Ryke Geerd Hamer's system for holistic treatment of metastatic cancer. *ScientificWorldJournal* 2005;5:93-102) was to review from a theoretical perspective the Hamer system of cancer medicine (1-4), which he called "the new medicine" with the

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purpose to guide both the physician and the patient in the very difficult area of holistic treatment of cancer. We all want the best for our patients and we believe the solution is a wise combination of conventional and holistic therapies - in medicine in general and also in the treatment of cancer. We were not aware of the work by Ryke Geerd Hamer until his work was discussed at the First International Conference on Holistic Healthcare in Copenhagen, November 2004 in connection with the presentation of the first papers from our own holistic cancer healing project (5,6).

This presentation is a critical review of the arguments that met the first paper on Hamer. Our aim is to examine if the presented arguments have power to change our view on the medical principles found by Hamer. In the first paper we found that only the first two of what Hamer called his "medical laws" were substantiated by contemporary holistic medical theory.

It is no secret that our own research in clinical holistic medicine (5-62) the last decade has come to a modern synthesis that in many ways share similarities with the Hamer's systems of cancer healing (comp. 1-4 with 5, 6) in spite of it developing completely separated from Hamer's person or work. It might well be that we are to some extent positively biased towards Hamer's work from this fact. But we still find ourselves to be sober and conscious scientists only looking for the truth in the service of our patients.

A critical review of the work of hamer

As it seems that Hamer has found something of meaning for many patients we found it of importance to understand how his problems with the academic society and "medical establishment" came about, since it seemed as if he was successful in many cases, highly loved and appreciated by thousands of his patients. Unfortunately, a Medline search (www.pubmed.gov) made before we wrote the first Hamer Paper showed a complete lack of clinical trials testing his method.

The Hamer "iron law of cancer"

Law number 1

Hamer claimed that all cancer forms arise from an emotional and "biological" shock (1, page 12), causing the patient to retract from the world with a destructive resignation regarding his fundamental wishes. He stresses that this shock must go so deep that it influences the whole biology of the patient's organism and it must go deeper into existence than just the mind. Interestingly, this law is consistent with both Antonovsky's work on coherence (7-12) and on our own life mission theory (14-21), which explains development of non-genetic and non-traumatic disease in general and in the same way. Unfortunately Hamer insists that there is no genetic causes of cancer and that no drug can cause cancer either (1, page 49-54). In his radical insistence on an all-psychological approach Hamer intimidates a generation of physicians doing research in genetics and the toxicological dangers of smoking. Nevertheless, his "Iron law of cancer" stating the psychosomatic element seems to be basically in accordance with the works of Aaron Antonovsky (1923-1994), Viktor Frankl (1905-1997) and our own work in holistic medicine. From a theoretical perspective we therefore conclude that Hamer's first law of cancer is substantiated.

Interestingly, the process of healing according to Hamer, includes a period called the "epileptoform crises" (analogous to an epileptic attack with muscle spasms), where the patient spontaneously regresses to the trauma to integrate this crisis (22). Only after this incident of healing the patient will improve (1, page 20). It is most noteworthy that Hamer observed, that the crisis must be sufficiently strong, for the patient to heal (1, page 21). What Hamer describe here is exactly the same process of healing as described in most work with holistic healing of the patient's whole existence, improving health, quality of life and ability in general, as explained by the Antonovsky's concept of salutogenesis and the holistic process theory of healing (7-12,22,23).

The fundamental understanding of the psychosomatic cause of cancer and the ability to win the patient's trust and take them into the process of holistic healing of life and existence might very well

explain, why Hamer's clinical work has been successful for his patients. Claiming that traumas can produce cancer, we can also with our present knowledge comprehend, but also understand why he was not well understood and received 20 years ago. As a hypothesis for further research we would like to see this simple and somewhat provocative statement of Hamer expressed in a little more complex and deeper rooted way to embrace a better understanding of human consciousness (24-31). Only after decades of theoretical work and only after we recently have been able to induce similar healing processes with cancer patients in our own research clinic, have we been able to accept and understand the controversial first law of Hamer.

Law number 2: Every disease has a pathogenetic and salutogenetic phase

Unfortunately Hamer did not know about the work of Aaron Antonovsky (7-12), who at the same time did his clinical work and constructed his theory of salutogenesis. Antonovsky simply explained what Hamer observed, making the process of healing the reverse process of the process of pathogenesis (getting sick). His understanding of pain seems also to be in accordance with the contemporary understanding of pain, physically, emotionally and existentially, as a necessary part of the process of healing (1, page 56). Most importantly, Hamer stressed the importance of solving existential problems in real life, not only in the psyche (1, page 20). Understanding the process of healing and being able to take the patient into the process is really what makes a good holistic physician. From the success of Hamer with his patients, it seems he was able to do this.

Law number 3: Cancer development follows a simple system of symbolic transformation from psyche to brain and the organs of the body

Many holistic physicians and some of the very popular health prophets of our time, like Louise Hay (32), have claimed the existence of such simple systems, which can be used to read the mental and spiritual cause of a physical disease. Unfortunately we

have not yet seen such a system. Quite on the contrary it seems from our research that repressed emotional problems can be moved around in the body and resettle wherever it is most convenient for the organism. The chronic state of whiplash associated disorder is an example of this (33).

So law number 3, which Hamer gives phylogenetic and ontogenetic arguments for, seems from our present state of knowledge to be less accurate. Still there might be a considerable symbolic element in the disease making the patients able to "listen to the body", but not as schematic as Hamer believed, although we must admit that there could actually be such a symbolic psychosomatic system working in our organism, only with a more complex and not yet discovered set of rules. This is also an important hypothesis for further research.

Law number 4: Bacteria and virus are controlled by the body and helps the body in the process of healing

This law seems in complete contradiction with our present knowledge of immunology, so it is not likely to be true in our opinion. The reason for this understanding seems to be the benefit for the patient of going deeply into the salutogenic crisis, which often takes so many resources from the patient, that (s)he will get an opportunistic infection.

Law number 5: All diseases are rational and for the benefit of the patients

Hamer argues thus from an evolutionary and possibly teleological perspective. We have not found contemporary knowledge to support this law.

Critique on our first paper on Hamer

Hamer gave critique on the ScientificWorld Journalblog on our first Hamer-paper and other people were also active in this regard. Hamer presented several arguments (posted on the blog 30 May 2007), which we will go through:

Argument A: "... German New Medicine [or GNM, the name of Hamer's system] has three further biological natural laws [besides the two that we have acknowledged in the first paper as likely to be true] that logically derive from the first two natural laws."

RE argument A: We did not find argument A valid, as we cannot see how law 3-5 can possibly follow from law 1 and 2. The principles are not related.

Argument B: "Any competent radiologist with CT equipment can establish within a few minutes what is a Hamer focus in conflict activity and what is an artefact (they too exist, after all). All he would need to do is to shift the patient's head 5 cm from the center line of the apparatus. An artefact always stays in the middle line of the apparatus and shows through all layers. The Hamer focus on the other hand always remains at the specific brain location where it biologically belongs."

RE argument B: If Hamer is correct in his observation he might be right. We found this most unlikely. However this can be tested empirically, which is fine. We do not believe that geometrically perfect round circles are present in nature, and thus they must be artefacts.

Argument C: "...that something is wrong with the figure of 6,000 survivors (of 6,500 patients) that had passed through the Burgau Centre. In the meantime, I have been fortunate to obtain copies of all patients' records from the Office of the District Attorney of Vienna Neustadt. It is absolutely correct that more than 90% of the desperately ill patients survived 4-5 years. By myself I surely could never have verified this."

RE: Argument C: This is very interesting data; normally patients with metastatic cancer do not survive for so many years; mean survival time is for most metastatic cancers less than two years and often only a few month. But the diagnosis and prognosis for patients not having been through the Hamer cure should be compared for control. Hamer is not doing that systematically, so even if the data were accurate we still miss the compelling data that could prove his cure to actually work. However if the case records exist this can be tested empirically. We request Hamer to publish a more detailed analysis of these interesting data.

Argument D: "Aaron Antonovsky published already in 1985 (four years after Hamer's first presentation of his ideas and one year after the book "Cancer. Disease of the soul", 1984) his Pathogenesis and Salutogenesis - and that this should be considered contemporary with Hamer."

RE *Argument D.* We believe that Aaron Antonovsky presented the basic core of his idea of salutogenesis already in the 1960s and early 1970s (63,64). So it seems to us that Hamer might have caught some of his ideas from Antonovsky, most likely in an indirect way, as it seems that he has been unaware of the principles of holistic healing already being discovered by other researchers. It is quite normal that scientific principles are discovered many places in the same time, because the time is "ripe" for these discoveries. All pioneers often believe themselves to have invented the general principles.

Argument E: "It is also an indecency trying to indiscriminately throw German New Medicine into the same pot with so-called holistic or complementary medicine, using the rationale: "... it has so many aspects [of it] in accordance with established knowledge of holistic and complementary medicine". You simply cannot mix these, doing this is in fact very dangerous for the patients! "German New Medicine" has existed for the past 26 years and so far it has been officially and publicly verified 30 times. It is a coherent and logical system that comprises not a single hypothesis and it is, for all intents and purposes, in itself complete. One should really no longer doubt that German New Medicine is scientifically accurate."

RE *argument E.* We did not in Medline or PubMed find any of these verifications, so we cannot acknowledge these as they are seemingly not published in accredited, peer-reviewed journals. There might be valid studies in German, but we cannot read them and Hamer is not providing us with sources. Why Hamer is denying that his system is rooted in holistic thought is a mystery for us.

Summary: We have not found any compelling reason for changing our views presented in our first Hamer paper in the above arguments presented by Ryke Geerd Hamer.

Some general remarks

We still believe that Hamer's contribution to our knowledge on holistic treatment of cancer might be important, and we are anxious to see Hamer's documentation, which we hope that he will present soon. We have tried our best to assume a neutral, objective and scientific position, just evaluating Hamer's work according to known theory and experience in the field of complementary and holistic medicine. We are happy to see that Hamer wrote: "I am neither racist nor anti-Semitic. I cannot be bribed. I am only the tribune of all patients - Jews and non-Jews alike." Because this is what medicine is about: helping our patients, not discrimination anybody for political, financial or other reasons.

We do in contrast to Hamer believe that it is a fact that cancer often spreads to other organs (metastize); but things are really not simple in medical science as every type of cancer has its own individual pattern of spreading to other organs. Why is this so? Till this day nobody seems to be able to explain that strange fact. So Hamer could be right to speculate, and he has his right to make an alternative hypothesis, even if it seems strange, controversial and hard to understand. What would science be without creativity and free thoughts unbound by rigid and traditional views?

Until we know for sure what is going on in the body and how it manage its biological information, it seems a little arrogant just to neglect even the strangest of hypotheses. And please remember that in science we often see that the strangest theory becomes truth in the end – just think of how Niels Bohr and Albert Einstein's strange ideas were received in the world of physicists in the last century.

It has been criticized that we used a book in Norwegian as basis for our first paper on Hamer. But the book was by Hamer on his medical principles; it is a collection of interviews made in a very smart, sober, scientific, and convincing way. It is short, crisp, and businesslike, and therefore good for scientific discussion and critique. It also seemed to us that there was at least some hard evidence that Hamer actually did help a certain (low) percentage of the cancer patients that came to him with metastatic cancer and no hope of cure. That finally convinced us to write the paper on Hamer.

As we are not perfect in the German language, we cannot do the extensive review of the Hamer-material that is needed to make a fair scientific evaluation of his scientific and clinical work. And maybe that is not our job either.

As the issue of complementary treatment of cancer seems really to interest and concern many people, we do hope that a competent person or group of people with an intimate understanding of both complementary and holistic medicine and the German language, will take the next step into shedding light into this complicated issue.

A historical remark

Until about 1900 organic chemistry had not been sufficiently developed to give us all the drugs we have today; the biochemical revolution during the 20th century gave us penicillin and receptor-specific designer drugs, and these drugs dramatically empowered the physician to significantly impact the state of health of the patient. So around 1950 most physicians came to believe that the psychological and social dimensions of medicine were of much less importance than biochemistry, when treating a patient. This caused a major shift in the focus of medical science, and medicine turned from being "holistic medicine" - looking at the person as a whole - into "biomedicine", treating with drugs. So from 1950 the medical faculties of the universities of the world almost abandoned psychosocial strategies and biomedicine was given all the prestige and money for research.

The priority of the money for research meant a slow scientific development of issues relevant for holistic medicine and holistic health awareness like psychosocial medicine, quality of life, and sense of coherence. Only around 1990-2000 we saw enough evidence gathered to document that lifestyle, health attitudes, happiness, and philosophy of life might be extremely important for a person's health. In this period the use of complementary and psychosocial medicine - now becoming "alternative" - simply exploded. Today there are more consultations with complementary medicine than biomedicine in the USA, and this development is also happening in Europe now.

But strong financial interests and a strong lobby have been allowing industry and industry-friendly people to impact the policymaking of many European governments. Recent laws have made many types of complementary medicine illegal - comp. the fight around homeopathy used today by more than 10% of the physicians of the planet. Its medical practitioners have in some cases been sent to jail, or have lost their license, or their jobs. One recent way that complementary medicine has been repressed is by demanding that treatment results must be documented in the same way as the pharmaceutical companies are documenting their results - that is controlling against placebo.

But as a psychosocial intervention mostly is sheer placebo - the positive effect of a shift in patient's consciousness towards being positive, constructive and present - this design is robbing the holistic medicine of its fruits. Testing homeopathy the way penicillin is tested is going to kill this old and noble art, as the developing a person's character - the essence of homeopathy in our understanding - is sheer placebo. But nevertheless it seems to be highly effective medicine and has been so since Hippocrates and his students introduced the scientific character-medicine 2,300 years ago. Most interestingly, the science of holistic medicine is now beginning to understand why this is so healthy to step into character as a person.

A note on scientific documentation of the effect of holistic medicine

To solve the problem of documenting the effect of holistic medicine our group has turned an old design for documenting the effect of a medical treatment - going back to Hahnemann and further back to Hippocrates - into science. We have called this method the "Square curve paradigm". The idea is that you measure the state of physical and mental health of a chronic patient - as this is experienced by the patient - before and after the treatment, and if there is a significant and positive difference i.e. a treatment effect, you measure the patient's state aging after one year or so. If the effect is still there - if the patient feels cured by your treatment - and if you agree as a doctor - you can say that you have helped

the patient. A temporary improvement is of little value, and an improvement that you appreciate as a doctor that is not appreciated much by the patient is of little value. We would personally like all kinds of medicine - biomedicine, holistic medicine, and complementary medicine - to be tested this way, using the patient's own experience of being cured as the key to documenting success of treatment. We really like the concept of evidence-based medicine very much - especially because we are working with holistic medicine, where every therapist seem to think that there own method is superior, while it often is not - because only by scientific investigation can we approach the truth in a useful manner.

A careful reader should notice that we disagree with Dr. Hamar on this important issue. We do take a critical position towards Dr. Hamer's work, but as we find so many aspects of it in accordance with established knowledge of holistic and complementary medicine, we do believe that his complementary system might actually be able to help some of his patients - which represents very important progress as most of his patients are metastatic cancer patients judged to be hopelessly sick by biomedicine. If that is the case - if he can cure some of these, even just a small fraction - we most definitely should acknowledge Dr. Hamer for this important step forward. It is so easy to give critique of a colleague trying out a new path, and we also do believe Dr. Hamar to be completely wrong in several of his assumptions. But without such pioneers as Dr. Hamar daring to learn from observing the unexpected and taking it to radical new thinking and further into models and new ways of treatment, the whole development of medical science would most certainly stop. Please read our paper again carefully, and let us know if there are some points where we go along with Dr. Hamar, where we should not have. We are eager to learn about any mistakes we might have made, and we do not believe that our paper on Dr. Hamer's work will be the final word.

The authors are in no way supporting any philosophically nor politically direction or fraction. But, it is important to differentiate between a man's scientific contribution and his political attitudes; if we only accepted scientific contributions from people who shared our view of the world, science could soon be a dull enterprise. Dr. Hamer has made an important

contribution to holistic medicine, because he seemingly has shown the world that even very sick cancer patients can sometimes be cured. We know of spontaneous remissions of cancer - many cases actually from Dr. Úlrik Dige's research in Denmark - but we do not yet know how to induce such remissions (please see 5,6). Dr. Hamer's work seems to point in this direction. When it comes to Dr. Hamer's merits, our paper on his work presents what we found of documentation for the efficiency of his cures. This was actually sufficiently convincing for us to bring it to a wider attention through our article. Our interpretation of the documented material is not quite as positive as Dr. Hamer's own view. Please go through the material yourself and see if you can find errors in our presentation of the data. We will be most happy to correct any errors or misunderstandings on our side.

Discussion

We have seen many arguments from both opponents and supporters of Hamer's work on the TSW-Hamer blog, but none of the arguments presented have made us change our position on Hamer. The arguments of Hamer himself need scientific support to be convincing; just stating the superiority of his system is not convincing by itself. There might actually be some convincing data in the case records referred to by Hamer, but we need a sober scientist, preferably a non-supporter and non-opponent of Hamer, to go through the material, if it is in fact available at all.

From a scientific point of view, Hamer's life and work is interesting and important for the development of scientific holistic medicine. Most of the problems of Hamer's work (seen from the written texts on his work only) has seemingly arisen from the way Hamer has structured his understanding into an idiosyncratic system of holistic healing with five fundamental "medical laws", intending to address the healing of the patient as a whole person, while healing spirit, mind and body at the same time. Some of these "medical laws" are in agreement with the theories acknowledged by modern holistic medicine, like the theory of coherence by Aaron Antonovsky (1923-1994) explaining that health comes from re-establishing coherence (63-70). This is related to the

work and ideas of Abraham Harold Maslow (1908-1970) and Viktor Emil Frankl (1905-1997) and the most progressive resilience literature, as well as our own work, theory of the purpose of life and the life mission theory, explaining the cause of much suffering and disease from resignation of the purpose of life (13-21). The simple explanation is that we repress our deep wishes and needs - our self - to adapt to our early environment and our parents; when we do so to radically we accumulate vulnerability, which become an important co-factor in a later development of diseases like cancer. Other of medical principles Hamer identified and called "medical laws" unfortunately lacks the content and structure that is normally expected from medical science, as they do not acknowledge and incorporate the established knowledge of immunology, toxicology, and other medical fields.

While reading his book, it appears that Hamer was a truly holistic physician: "The most important of everything is that the patient...have obtained new understanding, deep trust in the physician and a real insight in what is going on" (1, page 45). Hamer has in his work used the well-known efficiency and healing power of first winning the trust of his patients and then letting the patient do the work of healing himself. From our perspective, built on many such meaningful statements, his widespread reputation and popularity among patients, Hamer was a great clinical physician. From our review of his writings it seems that he was not such so great on theory. The lack of an academically acceptable explanation for his work is really very sad. Had Hamer only known more of Hippocrates, the holistic medical history of Hinduism, Buddhism and Islam, he would have been much better off referring to these traditions instead of insisting on finding out everything for himself and making his own new system.

On the other hand, we need the wheel of medicine to be reinvented again and again to keep it fresh and useful for the patients of our time and in the actual cultural setting. Hamer has done this with great effort and with the intent to benefit his patients. Many of his patients have apparently rejected the help they could have gotten from conventional physicians, like chemotherapy and radiation therapy, and turned to Hamer, but that made him open for criticism by other physicians, who saw him as responsible for harming

these patients. What is stated by Hamer in his book (1) might very well be understood as a warning to the patients towards his biomedical colleagues and thus he might actually be responsible for inspiring some patients to choose not to accept a documented cure and thus, if not cured by Hamer, dying in spite of the existence of a cure.

We believe that an adult patient must be respected for his autonomy and integrity, but at the same time a physician must do whatever he can to convince the patient to accept the most rational treatment. When it comes to metastatic cancer, the problem is that there often is very little to do, which has a documented clinical significant effect, the NNT (numbers needed to treat) to obtain an effect going up to between 10 to 20 (6,13). Patient autonomy must therefore from a medical ethical perspective be stressed more and the paternalistic position of the physician stressed less. Still, if we as physicians can understand the Hamer system and give advise to the patients about this system, we will be able to form a good dialogue with the autonomous and often desperate cancer patient.

We have in the present work no intention of testing the Hamer system clinically, but only to analyse it from a theoretical point of view. We wanted to compare the Hamer system with contemporary theoretical holistic medicine, to see what in his system must be acknowledged as true and valuable insight into the mechanism of holistic health and healing and what must be seen as not true (from our present state of knowledge).

A deeper theoretical understanding of holistic medicine in the future might show that this analysis is unjust to Hamer's system. To make it simple we have chosen to build this paper on a small book based on interviews with Hamer called "Cancer. The riddle that does not exist" (1), instead of on the very comprehensive and complex presentations (2-4) of his work. We believe that an analysis of the five principles or "medical laws" presented as the fundamentals of his holistic system of healing is sufficient for establishing the theoretical value of the Hamer system. In this paper we use our own wordings of Hamer's last four "medical laws", not to confuse the subject with the many idiosyncratic concepts of Hamer.

Ryke Geerd Hamer wanted his peers to acknowledge his discoveries as hard science. He therefore used the CT-scanner to make images of the brain and found that circular patterns (well-known as artefacts from the CT-scanner) carry vital information on the process of disease and healing. After studying the patterns for years, he claimed that visual pattern, which he then called the "Hamer Herd" or "Hamer focus" (the German word "herd" means "hearth", the central place of fire in the house) was always present in the CT scan of a cancer patient's brain in the pathogenic phase, revealing the path to healing for this patient. The Hamer focus looks like concentric circles around the part of the brain that in Hamer's interpretation represented the sick organ.

There is a slight possibility that the Hamer focus is actually a great new scientific discovery. It is though much more likely to be an artefact, which Hamer in lack of other hard evidence of his theory (which he desperately needed to get his position back in the medical society) gave too much importance. Unfortunately we do not have the resources necessary to test this part of Hamer's work. The concentric circles in the Hamer focus, shown on the front page of his book (1), looks like an artefact and very little as a biological phenomena, which in humans are almost never seen as concentric circles. If the centre of the phenomena actually is placed in the brain according to the system Hamer's described, this must be given further analysis.

The way we recommend holistic medicine to be practiced and understood (5-52), the use of CT scans and other high tech tools are not necessary, as the direct communication and emotional contact with the patient gives all the necessary information for the anamnesis and treatment. One of Hamer's mistakes, in our opinion, might have been to connect what seems to be an important re-discovery of the Hippocratic tradition of holistic treatment used on cancer patients, with the CT-scan picture, which made it very easy for his peers to ridicule his "spiritistic readings" of the CT-images.

The most problematic consequence of this attachment to his third law and the CT scans was his belief that cancers were not able to metastasise (1, page 47). He believed that metastases were new cancers developed by the new shocks patients received, when they encountered biomedicine. This

conviction made him highly unpopular with many biomedically-oriented oncologists (cancer physicians), because it made many of his believers avoid the conventional physicians. Our own position is the opposite and we believe that the modern holistic medicine should acknowledge the well-documented and sad fact that cancers do metastasise, often with the death of the patient as a consequence.

It seems to us that Hamer was too little rooted in the science of biology to make sufficient theories of the highly dynamic picture of cancer he experienced in his clinical practice. On the other hand biology definitely needs an upgrade to embrace this dynamics (53,62), as already stressed by big thinkers like Nobel laureate (in 1933) Erwin Schrödinger (1887-1961)(63). Our review of the work of Hamer came to the same conclusion as the Swiss Study Group for Complementary and Alternative Methods in Cancer (SCAC) (64), who found no evidence that most of his assertions were correct, no case of a cure has been published, and an investigation by Der Spiegel through the German authorities identified 50 cancer patients that had been in the care of Hamer and only seven survived (56). Still we find that when treated only with psychosocial intervention a success rate of 15% with this group of mortally ill metastatic cancer patients is remarkable and encouraging for further research.

Conclusions

Ryke Geerd Hamer has for decades been a controversial figure with the claim that cancer was a simple thing to heal with holistic medicine. He gave his peers grey hair, because of his reference to his five “medical laws”, most of which were not substantiated, and some of which were in direct conflict with existing medical theory and knowledge. It is pretty clear from our analysis, though, that the two most fundamental principles of Hamer’s work, the principle of psychosomatically caused vulnerability (“The Iron law of cancer”, Hamer’s first “law”), and the principle of salutogenesis as the reverse of pathogenesis (Hamer’s “second law”), are established principles of holistic medicine, worded nicely by the Jewish thinker Aaron Antonovsky, but in reality going all the way back to the father of medicine Hippocrates (71).

Hamer’s understanding of symbols in medicine, on virus and bacteria and on the evolutionary process itself differs a great deal from traditional science and we cannot in contemporary holistic medical theory find support for his last three principles or “medical laws”. As Hamer’s understanding of cancer metastasis was built on these failing principles, we suggest that this aspect of Hamer’s thinking is also not substantiated.

Altogether it seems that Hamer is in accordance with contemporary holistic medical theory. Regarding the most fundamental postulate that cancer patients can be healed by his system of holistic medicine, we believe this could actually be the case for some of the motivated patients. This must however be tested scientifically, before being accepted. If proven, we must recommend a rehabilitation of the name and work of Ryke Geerd Hamer. Clinical testing of a cure for cancer based on Hamer’s system must be considered worth the effort; it must be done with physicians trained by Hamer if at all possible.

At the Research Clinic for Holistic Medicine in Copenhagen we do clinical research to understand how to use the first two established “laws of cancer”, namely that we are often damaged by emotionally painful life-events making us vulnerable also to the development of cancer and that we can heal by reversing the pathogenetic process into a salutogenic process and regaining biological order. It is of utmost importance that we test and document the effect of such experimental treatments, and we have therefore developed a simple, easy-to-use, and low-cost strategy for documenting holistic healing (66). We invite the scientific medical community to cooperate in this important new field of evidence based holistic medicine growing from an emerging scientific understanding of the connections between health, quality of life, and consciousness (72). We encourage governments and research foundations to give funding for research in this promising area of holistic cancer treatment. The chance of succeeding with the development of a scientific holistic cure for cancer seems fair from a theoretical perspective and Hamer’s work has pointed out a direction to follow, even if we do not want to use his particular system.

Acknowledgments

The Danish Quality of Life Survey and the Quality of Life Research Center has been supported by grants from the 1991 Pharmacy Foundation, the Goodwill-fonden, the JL-Foundation, E Danielsen and Wife's Foundation, Emmerick Meyer's Trust, the Frimodt-Heineken Foundation, the Hede Nielsen Family Foundation, Petrus Andersens Fond, Wholesaler CP Frederiksens Study Trust, Else and Mogens Wedell-Wedellsborg's Foundation and IMK Almene Fond. The research was approved by the Copenhagen Scientific Ethical Committee under numbers (KF)V. 100.1762-90, (KF)V. 100.2123/91, (KF)V. 01-502/93, (KF)V. 01-026/97, (KF)V. 01-162/97, (KF)V. 01-198/97 and further correspondence.

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Submitted: November 15, 2008.

Revised: December 31, 2008.

Accepted: January 11, 2009.

The therapeutic value of antipsychotic drugs: A critical analysis of cochrane meta-analyses of the therapeutic value of anti-psychotic drugs used in Denmark

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Abstract

A rough estimate of the therapeutic value of a drug can be established from the ratio "Number Needed to Treat to Harm/Number Needed to Treat to Benefit" (NNH/NNtB or NNtH/NNtB). The ratio illuminate the degree to which the treatment with the drug respects the ethical rule of "first do no harm"; if the ratio is >1 the drug helps more than it harms and is thus primarily beneficial. We need to compare the upper confidence limit of the NNtB with the lower confidence limit of the NNtH to assure that a drug helps and does not harm the patient.

Methods: We compare NNH/NNtB ratio from the Cochrane meta-analyses of the commonly used antipsychotic drugs in Denmark.

Results: All antipsychotic drugs used in Denmark had a $NNH/NNtB < 1$, and often $1/5$ and $1/10$, meaning that the drugs are likely to harm many more patients than they help. Antipsychotic drugs are known to have not only physical adverse effects, but also mental, existential, social and sexual side effects that are seldom included in the studies, giving a strong bias in favor of the drugs. Important factors that are often ignored in the studies were: suicides from drug-induced depression, suicide attempts and their consequences, spontaneous drug-induced death, drug-induced self-molestation, damage to learning and working ability, sexual function, social function, self-esteem and self-confidence, and cognitive factors.

Conclusions: Antipsychotic drugs on the Danish market today have a very low therapeutic value and seems to be primarily harmful to the patients. From an ethical perspective antipsychotic drugs can therefore not be used as a standard treatment for any mental illness. Further scientific investigation into the significance of this finding is urgently needed. Antipsychotic drugs might still be justified in the treatment of specific subgroups of patients like violent and sexually aggressive, acute psychotic, schizophrenic patients.

Keywords: Therapeutic value, psychiatry, psychotherapy, antipsychotic medicine, adverse effects, Cochrane meta-analysis, ethics, evidence-based medicine, suicide, global quality of life.

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Introduction

From the days of Hippocrates in 300 BCE medical ethics has stressed the importance of avoiding harm to your patient: “primum non nocere” – first do no harm. To serve the patient’s best interest a physician must be certain that the drugs are helping and not causing harm to the patient. Most patients will accept mild adverse effects, and serious adverse effects can be tolerated if they are rare and the drug is useful, but it is unethical to give drugs that severely harm a substantial fraction of the patients, and it becomes a really serious ethical problem if a drug harms more patients than it helps.

In medical science today we use the concept “Number Needed to Treat to Benefit” (NNT or NNtB) about the number of patients that must be treated for one to be helped, and the Number Needed to Treat to Harm (NNtH or NNH) to tell the number of patients that must be treated for one to be harmed. NNtB and NNtH are measured with an uncertainty (CI means confidence interval at $p=.05$), so there are always a highest and a lowest value for each NNT measure. To be sure that a drug really helps and does not harm we need to compare the lowest empirically supported value (i.e., the upper confidence limit, or pessimistic harms assessment) with the highest empirically supported value of the Number Needed to Treat to Benefit (NNtB), i.e. a pessimist’s assessment of benefits. In principle the NNtH/NNtB ratio can be calculated better, if all positive and negative effects were added up to one number; the importance of each treatment effect factor should be multiplied with its likelihood before taken into the addition, and a negative effect should be given negative value. The problem with such a “smart” strategy is that the result will be totally dependent on the number of included factors – what makes it less smart than it appears at first glance.

Methods

We have compared the Cochrane meta-analyses of the commonly used antipsychotic drugs in Denmark (1-27) (see table 1). Surprisingly we found that almost all the drugs were harming more patients than they were helping, and often five or even 10 times more.

We typically found NNtB to be 5-20 and NNtH 2-5. Just using a drug, which needs 10 patients treated for one to be helped, seems highly unethical, if a large fraction of the patients are harmed. Another serious problem is that the placebo effect is included in the results, making many drugs look active, when they are only slightly more effective than placebo.

Discussion

A serious problem with the data is that they are provided by the industry, which has an interest in marketing their products. We found that most of the trials reviewed of the pharmaceuticals were designed to be very kind to the drugs. Only a small improvement of psychotic symptoms is often taken as help for the patient, in spite of the sad fact that these drugs rarely cure any patient for any disease. On the other hand the industry-imposed design has looked mostly at short-term physical adverse effects and often many extremely serious mental (28), social, existential, sexual, financial and other adverse effects and side effects were not included in the studies. Among some of the important factors often ignored in the studies were: suicides from drug-induced depression (28,39), suicide attempts and their consequences or spontaneous drug-induced death (4,30), drug-induced self-molestation (cutting etc), damage to learning and working ability, sexual function, social function, self-esteem, self-confidence and quality of life (4), notably including some adverse phenomena which physicians, and even psychiatric investigators, rarely have been trained to probe into. Other important biases have also been found (31). All this makes the NNtH likely to be systematically much too large and the NNtB likely to be systematically much too small, giving a very severe bias in favor of the drugs in the pharmaceutical studies, and most unfortunately also to the Cochrane meta-analyses re-using these data most often without any chance of mounting the appropriate critique. We definitely need to collect this information for the drugs being used to day. It has been argued that the positive effects are qualitatively more important than the negative effects of the drugs, but we have analyzed this and found that both positive and negative changes were registered, when they were clinically noticeable.

Table 1. NNH/NNB ratios for the antipsychotic drugs used in Denmark (1-23) are when calculated as described below always smaller than one, often 1/5 and sometimes less than 1/10, implying that many more patients are harmed than benefited by the antipsychotic drugs, making them unethical to use. NNH/NNT is calculated here according to the principles of securing a positive effect for the patient, see text; if calculated without this principle the NNtH/NNtB ratio will still often be less than one. The list of drugs is found in (31)

<p><i>“Atypical” antipsychotics</i></p> <p>Sertindole (N05AE03) [1] NNtB: 'very much improved' as compared to those taking placebo NNT 7.9, CI 4.3 to 41.1 NNtH: almost as haloperidol. Akathisia - 8mg: 1 study, n=245, RR 0.2, CI 0.1 to 0.5, NNH 6.0, CI 4.1 to 11.2; 16mg: 1 study, n=252, RR 0.1, CI 0.0 to 0.3, NNH 5.4, CI 3.9- 9.0; 20mg: 1 study, n=253, RR 0.3, CI 0.2 to 0.7, NNH 7.3, CI 4.6 to 17.9; 24mg: 2 studies, n=524, RR 0.5, CI 0.3 to 0.7, NNH 8.6, CI 5.6 to 18.3. Tremor - 8mg: 1 study, n=245, RR 0.3, CI 0.1 to 0.7, NNH 8.5, CI 5.2 to 24.0; 16mg: 1 study, n=252, RR 0.2, CI 0.1 to 0.5, NNH 7.3, 4.8 to 15.6; 20mg: 1 study, n=253, RR 0.2, CI 0.1 to 0.6, NNH 7.8, CI 4.9 to 18.1; 24mg: 2 studies, n=524, RR 0.4, CI 0.2 to 0.6, NNH 8.2, CI 5.6 to 15.3. For Hypertonic - 24mg: 2 studies, n=524, RR 0.5, CI 0.3 to 0.8, NNH 12.4, CI 7.5 to 35.0. NNtH/NNtB=4/41.1= 0.097</p> <p>Ziprasidone (N05AE04) [2] NNtB: As haloperidol. NNtH: Not calculated; almost as haloperidol.</p> <p>Clozapin (N05AH02), No Cochrane study found</p> <p>Olanzapine (N05AH03) [3] NNtB: 'no important clinical response' NNT 8 CI 5 to 27 NNtH: weight gain NNH 5 CI 4 to 7). Insufficient data. NNtH/NNtB=4/27= 0.15</p> <p>Quetiapine (N05AH04) [4] NNtB 11 CI 7 to 55. NNtH: Movement disorders NNH 4 CI 4 to 5. Dry mouth NNH 17 CI 7 to 65. Sleepiness NNH 18 CI 8 to 181. NNtH/NNtB=7/55= 0.13. No summarized data of spontaneous patient death (4 of 728 died in one RCT, 2 of 618 died in an other RCT).</p> <p>Amisulpride (N05AL05) [5] NNtB not specified: NNT 3 CI 3 to 7. NNtH: Need for antiparkinson drugs: NNH 4 CI 3 to 6. Agitation NNH 11 CI 6 to 50. NNtH/NNtB=3/7= 0.43 (Chlorpromazine used as reference').</p> <p>Risperidone (N05AX08)[6,7] NNtB: As Olanzapine. NNtH: sexual dysfunction abnormal ejaculation NNH 20 CI 6 to 176. Impotence RR 2.43 CI 0.24 to 24.07. One third of people given either drug experienced some extrapyramidal symptoms (n=893, 3 RCTs, RR 1.18 CI 0.75 to 1.88) but 25% of people using risperidone require medication to alleviate extrapyramidal adverse effects (n=419, 2 RCTs, RR 1.76 CI 1.25 to 2.48, NNH 8 CI 4 to 25). Weight gain: NNH 7 CI 6 to 10). NNtH/NNtB=4/27= 0.15</p> <p>Aripiprazole (N05AX12) [8] NNtB: NNT 5 CI 4 to 8. NNtH: Need for antiparkinson drugs NNtH 4 CI 3 to 5. (Previous study included NNtH: Insomnia NNH 4 CI 3 to 9.) NNtH/NNtB=3/8= 0.37</p>
<p><i>High-dose typical antipsychotics</i></p> <p>Chlorpromazine (N05AA01) [9] NNtB: Prevents relapse, longer term data: NNT 4 CI 3 to 5. Improves symptoms and functioning NNT 6 CI 5 to 8. NNtH: Sedation: NNH 5 CI 4 to 8. Acute movement disorder NNH 32 CI 11 to 154. Need for antiparkinson drugs NNH 14 CI 9 to 28. Lowering of blood pressure with accompanying dizziness NNH 11 CI 7 to 21. Considerable weight gain NNH 2 CI 2 to 3. NNtH/NNtB=2/5= 0.15</p> <p>Levomepromazine (N05AA02). No Cochrane study found</p> <p>Promazine (N05AA03). No Cochrane study found</p> <p>Thioridazine (N05AC02)[10] NNtB: “global state outcomes” NNT of 2 CI 2 to 3; NNtH: Sedation NNH 4 CI 2 to 74. Cardiac adverse effects NNH 3 CI 2 to 5. NNtH/NNtB=2/3= 0.67</p> <p>Melperone (N05AD03), No Cochrane study found</p> <p>Pipamperone (N05AD05) No Cochrane study found</p> <p>Chlorprothixene (N05AF03)No Cochrane study found</p>
<p><i>Middle-dose typical antipsychotics</i></p> <p>Perphenazine (N05AB03) [11]NNtB: 2 CI 1 to 20. NNtH: invalid data.</p> <p>Depot perphenazine decanoate[12]: NNtB as clopenthixol decanoate and other antipsychotic drugs. Need for anticholinergic drugs (one RTC NNtH 4 and another NNtH 10), movement disorders (RR 1.36, CI 1.1 to 1.8</p>

Table 1. (Continued)

<p>NNT 5). NNtH/NNtB = 4/8 = 0.50 (Chlorpromazine used as reference).</p> <p>Zuclopenthixol (N05AF05) [13] NNtB: Patient not unchanged or worse: NNT 10 CI 6 to 131. NNtH: Extraparamyodal symptoms NNH 2 CI 2 to 31. Need for antiparkinson drugs NNH 3 CI 3 to 17. NNtH/NNtB=3/131= 0.023</p> <p>Zuclopenthixol decanoate [14] NNtB: Prevented or postponed relapses NNT 8, CI 5-53. NNtH: Adverse effects NNH 5, CI 3-31. NNtH/NNtB=3/53= 0.057</p>
<i>Low-dose typical antipsychotics</i>
<p>Fluphenazine (N05AB02) [15] NNtB: NNT= placebo (not effective). NNtH: Experiencing extrapyramidal effects such as akathisia NNH 13 CI 4 to 128. NNtH/NNtB=4/Infinite= 0.00</p> <p>Haloperidol (N05AD01) [16] NNtB: NNT 3 CI 2 to 5/Global improvement NNT 3 CI 2.5 to 5. NNtH: Acute dystonia NNH 5 CI 3 to 9. Need for antiparkinson drugs NNH 3 CI 2 to 5. NNtH/NNtB=2/5= 0.40</p> <p>Flupentixol (N05AF01) [17] NNtH/NNtB: as other depot antipsychotics.</p> <p>Pimozide (N05AG02) [18] NNtB: Prevents relapse NNT 4 CI 3 to 22. NNtH: Tremor NNH 6 CI 3 to 44- Need for antiparkinson drugs NNH 3 CI 2 to 5. NNtH/NNtB=2/22= 0.091</p> <p>Penfluridole (N05AG03) [19] NNtB: 'improvement in global state' NNT 3 CI 2 to 10 – as chlorpromazine, fluphenazine, trifluoperazine, thioridazine, or thiothixene. NNtH as chlorpromazine, fluphenazine, trifluoperazine, thioridazine, or thiothixene. NNtH/NNtB=4/10= 0.40</p> <p>Sulpiride (N05AL01) [20] NNtH/NNtB: evidence is limited and data relating to claims for its value against negative symptoms is not trial-based.</p> <p>New generation antipsychotics[21]: NNtH: Of the new generation drugs, only clozapine was associated with significantly fewer extrapyramidal side-effects (EPS) (RD=-0.15, 95% CI -0.26 to -0.4, p=0.008) and higher efficacy than low-potency conventional drugs. These findings might have been biased by the use of the high-potency antipsychotic haloperidol as a comparator in most of the trials. First episode schizophrenia[22]: NNH 3 CI 2 to 6 The results of this review are inconclusive.</p> <p>Antipsychotics in treatment of childhood onset psychoses[23]: NNtH/NNtB: There are few relevant trials and, presently, there is little conclusive evidence regarding the effects of antipsychotic medication for those with early onset schizophrenia. Some benefits were identified in using the atypical antipsychotic clozapine compared with haloperidol but the benefits were offset by an increased risk of serious adverse effects. Early intervention for psychosis[24]: NNtB: Six month follow up: less likely to develop psychosis at a six month follow up NNT 4 CI 2 to 20, 12 month follow up: Not significant! NNtH: Weight gain etc., insufficient data</p>
<i>Other drugs sometimes used against psychosis</i>
<p>prochlorperazine (N05AB04), No antipsychotic Cochrane study found</p> <p>periciazine (N05AC01), No Cochrane study found</p> <p>tetrabenazine (N05AK01) No antipsychotic Cochrane study found</p> <p>Litium (N05AN01) [25] NNTB: as placebo (not efficient). NNtH: Insufficient data. NNtH/NNtB=something/infinite<<1</p> <p>Benzodiazepines [26] NNTB: NNT 3 CI 2 to 17. NNtH: Maybe worse than placebo. NNtH/NNtB= 100/17? Probably >1</p> <p>Valproate [27] NNTB: Insufficient data. NNtH: Insufficient data</p> <p>acepromazine (N05AA04), No Cochrane study found</p>

It therefore seems likely that NNtB and NNtH numbers build on equality noticeable phenomena, and therefore comparable. The fact that the antipsychotic drugs have highly unfavorable NNH/NNT ratios cannot be dismissed by the argument the positive effects of the drugs (i.e. the anti-hallucinating effect) are more important than the negative side effects (i.e. severe obesity). We found that there is not one single, antipsychotic, psychopharmacological drug that can be used without harming the patients more than benefiting them; NNH/NNT were always <1 (see table 1).

During the last 10 years the many Cochrane units all over the world have provided us with highly valuable meta-analyses. Because of this unique source of scientifically established high-level knowledge, we now in our opinion know that the ethical treatment of many psychiatric disorders is still psychotherapy, which on one hand in many studies has been documented to help and on the other never has been documented to harm the patients (see 32-34).

To compare NNtH and NNtB will always to some extent be comparing apples and pears; this problem can only be solved by measuring one integrated endpoint of both positive and negative effect like *global quality of life* (which can be measured with a simple questionnaire like the QOL1 with one questions on self-assessed global quality of life (35)), self-assessed physical and mental health, or self-assessed ability of functioning in a number of relevant domains (work, social life, family, sexuality). We recommend the use of a wise and balanced combination of self-assessed mental and physical health, global quality of life, and ability in general as the endpoints for any medical treatment. The low ratio NNH/NNT is the likely reason that the pharmaceutical industry systematically has avoided the use of such endpoint that illuminates the effect of the drugs on the whole person. It has also avoided long-term documentation of adverse effects, in spite of many physicians and patients have been asking for these data for years.

We suggest that we call the inverse number NNH/NNT for "the ethical treatment value of the drug". The way it is calculated is in a way "double pessimistic"; we estimate that a drug with NNH/NNT >10 has a 99% chance to be a primarily beneficial (valuable) drug, and a NNH/NNT

value $<1/10$ signifies a 99% risk of being a primarily harmful drug. We suggest that the NNH/NNT value of "penicillin in the treatment of syphilis" (about 100) can be a benchmark for a highly valuable drug.

If effects and side effects are mechanistically related, like the better mobility after curing a femoral fracture leading to an increased future fracture rate, the above-mentioned "smart" formula must be used. The last important thing is that most symptoms and side effects are reversible, but brain damage, suicide and dead are not. Suicide is a negative effect that is much more difficult to tolerate than all other adverse effects and every study must therefore include a long-term survey of increased or diminished suicide rate.

The last thing to consider is that placebo often has a NNT=3; the difference between the antipsychotic drugs and placebo are therefore only marginal; an alternative explanation to a therapeutic effect is the fact that you can feel the drug in your brain, destroying the blindness of the study and creating an "active placebo" effect. If this is the case, we are actually only using placebo to treat, but with high risk of causing side effects and serious harm to the patients. This has never been investigated for the antipsychotic drugs neither by the pharmaceutical companies nor by neutral researchers, and this must urgently be done.

Conclusions

In conclusion, the NNH/NNT ratio might be the needed guideline for evaluating the therapeutic effect of drugs; when this analysis is carried out on the antipsychotic drug using the upper confidence limit of NNT and the lower confidence limit of NNH for the comparison, we find that all antipsychotic drugs used in Denmark are more harmful than beneficial.

We presume that the antipsychotic drugs on the market today in Denmark are very much the same as in all other countries, as the same drugs are used almost everywhere. The analysis indicates that the antipsychotic drugs are likely not to improve health and thus to be without any net therapeutic value; they are likely to be primarily harmful to the patients. This does not mean that the drugs cannot be used for life-saving and other compelling reasons, like on extremely aggressive patients that urgently need to be calmed down, or on acute psychotic sexually

violent schizophrenic patients etc., but they can not be used ethically as a standard treatment for any kind of mental illness.

On the other hand recent research comparing psychotherapy with psychiatric treatment has documented psychotherapy to be helpful to many groups of patients (32-34), and also more helpful than the psychiatric standard treatment, without having the adverse effects of the anti-psychotic drugs.

We believe that the NNH/NNT ratio is the best indicator we have today of the total therapeutic value (benefit-vs.-harm) of a drug, but we must admit that it is a crude summary index of benefit-vs.-harm. For a better evaluation of a medical treatment we need to use a combined measure of *global quality of life* (like QOL1 and QOL5) (35), self-assesses health (36), and self-assessed ability (in a number of relevant domains) (36).

We need urgently - for the sake of all patients - to be able to estimate the total therapeutic value of a drug (or any other treatment) more accurate in the future, and recommend that all clinical trials in the future use *global QOL and self-assessed physical and mental health* as obligatory outcomes; long term studies including all relevant dimensions like *loss of working and studying ability, suicide, and spontaneous drug-induced death* are also absolutely necessary for an ethical evidence-based medicine in psychiatry.

Acknowledgments

This study was supported by grants from IMK Almene Fond.

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Submitted: September 15, 2008.

Revised: December 30, 2008.

Accepted: January 11, 2009.

The right of the patient to refuse medical care

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Abstract

When people's health is affected, their lives change radically. Suddenly they find themselves in a foreign environment speaking an unfamiliar language, replete with terms that are not used on a daily basis. They are forced to discuss the fate of their intimate body parts with total strangers, while in a state of physical and mental stress. Even the patients' prostrate position in bed, looking up at the physician standing above them, emphasizes their infirmity. For a time patients cease to be the ultimate authority concerning their body and life. In this review we have looked at the legal aspects and guidelines provided by the Ministry of Health and the Israeli Parliament (Knesset) for the right of the patient to refuse treatment, consent and situations where informed consent is not possible. The medical staff must respect the autonomy of the patient, the right for refusal to receive treatment and sometimes it may facilitate the assistance provided to patients. The autonomy of each individual emphasizes the existing uniqueness and diversity.

Keywords: Medical ethics, patient-physician relationship, medical care, legal aspects.

Introduction

Healthy people live in a social environment with clear rules of behavior. They are capable of working and they exercise personal choice. Their family and society surround and support them, although they spend a significant portion of their time at work. They have obligations (financial, social, familial) and rights in virtue of being human beings, citizens, employees. All this is true until they become ill. When people's health is affected, their lives change radically. Suddenly they find themselves in a foreign environment speaking an unfamiliar language, replete with terms that are not used on a daily basis. They are forced to discuss the fate of their intimate body parts with total strangers, while in a state of physical and

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mental stress. Even the patients' prostrate position in bed, looking up at the physician standing above them, emphasizes their infirmity. For a time patients cease to be the ultimate authority concerning their body and life.

Until the 1980s it was customary to use only technical terms to describe mutual relations between patients and medical staff. Patients sought medical treatment and the healthcare system provided the care necessary to promote their health. Patients were passive partners in the treatment process, and the fact that they are actually responsible for their body had no significance. In this approach no regulations defined patients' needs as human beings, aside from the technical aspects of preserving their health (Public Health Regulations of 1940 (1), valid today, are the basis of the secondary regulations and the instructions of the Director General of the Ministry of Health in Israel (2), which regulate the Ministry of Health in Israel).

The Western World has long understood the problematic aspects of a situation in which people, who have been equal members of society and transformed into patients, are now deprived of their rights. Civil rights movements in Israel and elsewhere have paved the way for increasing recognition of both patients and medical institutions in the medical system's need to focus on the patients for whom it exists.

Present-day patients have begun to recognize and insist on their rights. They seek to construct a system of communication between themselves and the clinicians in order to be included in decisions that concern their care. However until recently, they had no way of knowing their rights. Even medical experts, despite their good will, do not always know with which of the patients' demands they must comply under all circumstances and which depend on medical opinion. At the same time, the new generation of Israeli physicians is currently demanding a permanent legal definition of patients' rights.

Since its formulation in 1987, the "Patient bill of rights"(3), co-authored by a large number of Members of Knesset, underwent many changes in the Knesset and its committees until the law was finally approved by second and third reading on May 1 1996. The law is not perfect and there is still room for improvement. However its enactment is a milestone on the road to

new and uniform rules of behavior obligating everyone involved in patient care.

Israel's Patient's Rights Act supplements the National Health Insurance Act of 1994 (4) that bestows on all residents of the State of Israel the right to receive medical care and defines the obligation of the state to provide healthcare services to all its residents, with no discrimination. Both these laws perceive patients' physical and mental needs as inseparable (5).

Some historical aspects

The "Patient bill of rights" (3) was written in 1987. If we look at the history of bills proposed, Israel's legislation has no specific reference to patients' rights, which are mentioned only in court judgments. In 1986 the former district court president Hadassah Ben Ito proposed at a nurse convention that the State of Israel should enact a scroll of rights similar to that existing in most United States and elsewhere, which resulted in the "Patient bill of rights" being formulated. We shall focus on clause 5 of the bill, subtitled "Refusal", where it is stated that the patient is entitled to refuse to receive medical care offered, either partly or completely and the medical staff and the nursing staff will not bear any criminal or other responsibility for the consequences of the refusal.

In 1981 the 34th World Medical Assembly of the World Medical Association convened in Lisbon, capital of Portugal. This convention unanimously embraced what is today known as the "Declaration of Lisbon" (6). This declaration is based on the premise that physicians encountering practical, ethical or legal problems must always act according to their conscience and must always operate to the patients' benefit. The patient has the right to accept or to refuse treatment after receiving adequate information.

This international principle was also taken into account, when the Israel "Patient bill of rights" (3) was written and the Minister of Health at the time stated that "the patient's consent to medical care is essential today and is anchored in legislation. The required norm is informed consent, i.e., after the patient receives an explanation and comprehends the nature of the treatment and the dangers inherent in it". The requirement of consent to medical care was also

included in the public health regulations of 1987 (7). One of the stipulations of these regulations was a form in which treating physicians provide patients with detailed information of all the risks inherent in the proposed treatment. The form is signed by the physician and the patient. In the absence of patient consent, any medical treatment will be considered an assault in the criminal sense, so obviously patients are entitled to refuse medical care. This principle was again discussed in the Israel Knesset in 1990 and 1997 and accepted as fundamental.

The right to refuse from a legal perspective

The media in Israel often deals with issues related to the right to die with dignity, i.e., the right of the terminally ill to request not to receive medical care or pharmaceutical or other interventions intended to artificially lengthen their lives. The focus is on the distress of the patients and their families in the struggle against the medical-legal system, which does not make allowance for the patients' wishes. For example in the case of a woman (from Tiberias, the late Ruth Trabelsi), who refused amputation of her foot even at the expense of her life, a case that aroused particularly strong emotions. The patient preferred her foot over life, while her family was conflicted. Some were in favor of honoring the patient's will and some objected and even enlisted the support of rabbis and public figures. Since the woman was lucid and adamant, the court ruled that her will and request be honored. Eventually, the family convinced her to have her foot amputated, but she died a short while later nonetheless.

However even when cases reach the courts and even when patients are lucid, their wishes are not always taken into consideration. For example in the case of an 82-year-old woman from Beersheba, who was completely lucid and required an operation due to a tumor in her bladder. The tumor caused constant bleeding, requiring repeated blood transfusions. The woman refused to undergo surgery to remove the tumor. Her condition was not defined serious or dangerous, but there was need of surgical intervention to put an end to the blood transfusions. However the woman had a rare blood type. In light of the shortage

of this blood type in the blood bank, which might have led to aggravation of her condition, the court decided in a special night session, in the presence of the Attorney General, to approve the surgery and it was indeed performed a few hours later. It seems that patients' lucidity and legal competence are insufficient to ensure heeding their refusal of medical care. Sometimes the medical system's interests override patients' considerations. The judge's rationale was: "The basic law of human dignity and freedom recognizes the value of humankind and the sanctity of life and determines that human life is worthy of protection. In this case, the guardian is attempting to save a life, thus realizing the purpose of this basic law".

Patients' refusal of medical care, or their demand to cease ongoing medical treatment, puts physicians in a difficult situation. Physicians take an oath to provide medical care to those who require it. The law states explicitly that physicians must provide necessary medical care, with the patients' informed consent. The "Patient bill of rights" (3) discusses the issue of informed consent to medical care and emphasizes in clause 13(a): "No medical care shall be given unless and until the patient has given his informed consent to it". The manner of giving informed consent to medical care is described in clause 14 of the law: "Informed consent may be given verbally, in writing, or demonstrated by the patient's behavior". As a result, it is usually possible to provide patients with medical care.

The situation is different when patients are unable to give informed consent to medical care due to restricted capacity or medical emergency. The "Patient bill of rights" (3) details in clause 15 circumstances justifying provision of medical care to patients even lacking their consent:

- 1) The patient's physical or mental state does not permit obtaining his informed consent;
- 2) Should the patient be deemed to be in grave danger but rejects medical treatment, which must be provided under the circumstances as soon as possible, the clinician may perform the medical treatment against the patient's will, if an Ethics Committee has confirmed that all the following conditions obtain:

- a) The patient has received information as required to make an informed choice.
- b) The treatment is anticipated to significantly improve the patient's medical condition.
- c) There are reasonable grounds to suppose that after receiving treatment the patient will give his retroactive consent.

All three conditions must exist in order for the committee to give its consent. In emergencies, when the patient is unconscious, three physicians must approve treatment, when lacking the patient's informed and express consent, as stated in clause 15(3): "In a medical emergency, a clinician may give urgent medical treatment without the patient's informed consent, if it is not possible to obtain his informed consent due to the emergency circumstances, including the patient's physical or mental state".

Clause 16(a) allows the patient to appoint himself a representative authorized to consent to medical treatment in his place. Patients' representatives are usually their companions, and particularly close relatives.

Physician-patient relationship

The physician-patient relationship might be disrupted due to patients' refusal to receive, or continue receiving, medical care. The physician's attitude to the patient might be affected, whether the refusal stems from treatment that does not conform to patient demands concerning comfort, time or place, or from loss of confidence in the physician and the methods used. This antagonism might express itself in anger and animosity and even sanctions. Patients might find themselves denied all medical care, even if their refusal only refers to part of the treatment, and this must be prevented.

According to the law, patients' consent to medical care must be "informed consent". It must be given after all details relating to the treatment and its consequences have been explained. One of the details that should be given to patients in order to obtain their informed consent is stated in clause 13(b)(5): "Where

the treatment is innovatory, the patient shall be so informed".

Problems arise when a request is submitted to be included in the trial group of a medical experiment, or to receive experimental medical care. In these cases the type of treatment offered by the medical staff is usually clear, however its results are not always clear and there is a risk that the experimental treatment will not work as expected or will be detrimental to the patients.

Patients may find themselves in a sensitive position versus the medical staff. On the one hand they wish to maintain a good relationship, however they may be concerned that refusal to take part in a medical experiment or to receive unproven treatment might harm this relationship. The public health regulations on medical experiments with humans (8) determine with regard for the various aspects of research, that "a patient's refusal to take part in research must not affect the physician-patient relationship".

Artificially life extending medical care

Who decides whether artificially life-extending medical care benefits patients or whether they would be better off if allowed to die with no external interference? Physicians are convinced that they have a moral and professional obligation to compel patients to accept emergency life-saving treatment. The physician's oath, the fear of ethical deviation, physicians' conviction of their mission to save lives and cure the ill, repeatedly appear in legal debates on euthanasia. Physicians claim that they cannot disconnect a person from life-supporting instruments, as this is a betrayal of their mission. However in private many will admit that this ethical assertion is only a pretense concealing legal concerns. They are concerned of the possibility that as a result of their support for patients' wishes to end their life, the family of the deceased might sue them for punitive damages. This fear is not unfounded, as patients' relatives are guided by financial and other interests that might facilitate conflicts.

The "Patient bill of rights" (3) proposed a solution to this problem. Clause 5 of the bill stated: "The patient is entitled to refuse medical care offered

to him, partly or in its entirety. The medical staff, the nursing staff and the professional staff will not bear any criminal or other responsibility for the consequences of such refusal”.

Many mistakenly assume that the right to die with dignity is the major issue ensured by the right to refuse medical care. However, what about people who refuse to be vaccinated against infectious disease? What about patients who ask to avoid painful medical examinations? As stated, the provision of medical care is contingent on patients' informed and express consent, and lack of this consent can serve as grounds for charges of assault. However in practice we see quite a few cases of physicians, who tell patients that refusal to undergo examinations or treatments will lead to termination of care.

When non-consent to a specific medical treatment leads to threats of denying all medical care patients are in a quandary. For example: A patient hospitalized following a high fever requiring thorough examination underwent a series of comprehensive tests conforming to all scientific innovations. While the tests were being performed he began receiving appropriate medical care as stated in the protocol.

When the medical staff wished to perform a bone marrow test, which is quite painful, the patient refused, claiming that it is unnecessary and that he is already receiving treatment. In this case, is the physician entitled to deny the patient all medical care?

What would happen to a cardiac patient who refuses to have an abortion for religious reasons, if her right to receive treatment for her cardiac condition is denied? These are dilemmas encountered by physicians and clinicians.

The solutions can be found in the physician-patient relationship. If recalcitrant patients cannot be coerced, they must be convinced. If patients do not understand the significance of the proposed treatment or test, they must be convinced of their essentialness, and if they are not convinced despite all efforts, it is necessary to desist.

Refusal of non-life saving medical care

Refusal of non-life-saving medical care is usually recorded in the patient's medical file. However there

is also room to consider the possibility of taking a written declaration from patients, who refuse specific medical treatments, as this releases the physicians and the medical staff from their obligation to provide care. Thus the patients will not have future recourse to claims of lack of comprehension or improper explanation of the implications of treatment refusal.

In some cases patients request cessation of ongoing medical care: disconnection from a drug infusion or cessation of psychological counseling. Clinicians are wary of interrupting treatment, as it would not have been initiated to begin with, if it was not essential. When patients are legally competent and do not require guardians, their judgment obligates the medical staff to comply even if they do not agree and even if their attempts at convincing the patients to continue treatment are in vain.

Patients' right to cease receiving medical care at any time is binding even when contrary to the opinion of the medical staff. It is possible to retract informed consent to treatment at any time. Exceptions are mentally ill patients, who refuse medical care. These patients are not always aware of their true condition. Even if they are conscious of their problems, sometimes they may refuse medical care offered to them for their own reasons.

Thus it is important to stress that patients who are lucid adults capable of reaching decisions are always legally entitled to refuse medical care. The law identifies alternative solutions, through guardians or forced hospitalization, for the incapacitated.

As a result of massive immigration to Israel in recent years the country has absorbed people with infectious diseases, such as tuberculosis or AIDS, who did not receive medical care in their countries of origin. These immigrants come to Israel, underwent medical tests and required medical care for their own benefit and for the benefit of society. Some refused adamantly for social and cultural reasons and evaded the medical staff. The conviction that their disease originates from sin and the feeling of shame at telling their relatives of their condition caused them to refuse medical care, even at the price of exposing their close environment to the disease. The right of these patients to refuse medical care is not compatible with the right of others to good health. The healthcare system uses all means available to convince those requiring

medical care, however presently there is no legal way of forcing them to accept it.

There are religious sects all over the world, who object to blood transfusions or vaccinations. In the case of capable adults their wishes must be honored, as they cannot be compelled to receive treatment, contradicting patients' right to protect themselves from attack. When dealing with minors the situation is different. Although there is no Israeli law obliging parents to provide their children with routine care, the Penal Law determines in clauses 322-323 that people, who do not tend to their health – will be considered responsible for the consequences. Thus, if a blood transfusion may save the life of a minor and the parent refrains from providing this treatment on religious or philosophical grounds, this justifies sanctions. An inference is that anyone preventing vaccination against known diseases is also liable for these sanctions, although the accused may employ the defense that the vaccination itself poses a risk.

At such a time when the medical staff will be free of their concern from legal actions – express informed refusal, similar to express informed consent to medical care, will form part of the basic rules of medical ethics (5).

The health regulations of 1984 (9) were intended to prevent a situation, where patients are hospitalized and receive medical care without their express consent. Patients' consent must be obtained in order to perform any medical treatment of their body. Accordingly, patients should sign a form of consent to hospitalization upon admission to the hospital. In addition, they must sign a consent form prior to surgery or catheterization. Most patients admitted to the hospital do not read the form and do not ask for a copy. Therefore they themselves do not know what they have signed. They assume in good faith that their interests coincide with those of the medical staff and therefore that they will come to no harm. When patients sign a form of consent to medical care they cannot add any reservations such as: "I am interested in this treatment and not in that", or: "I am interested in treating part of my body and not another". The process is performed rapidly, usually by a clerk, who cannot provide explanations about the treatment given and its consequences. Obviously, consent given under such conditions is not informed consent.

While patients are in the hospital it is sometimes necessary to perform invasive procedures, such as catheterization or surgery. In such cases patients must sign another consent form. Such consent is partially informed, as the explanation is usually given at the last moment by the physician on call or by the clinicians, and patients are not always informed of all the risks and benefits of the proposed treatment or of alternative treatments.

The guideline of the Ministry of Health Director General (2) determines that any use of force, while providing medical care is grounds for a legal claim of "assault". Therefore it is necessary to receive patients' consent to treatment performed on them and this consent must be based on information provided. The nature of the information that should be provided:

- a) 13.(a). No medical care shall be given unless and until the patient has given his informed consent to it.
- b) In order to obtain informed consent, the clinician shall supply the patient with medical information to a reasonable extent such as to enable the patient to decide whether to agree to the proposed treatment; for this purpose "medical information" includes –
 - 1) The diagnosis and the prognosis of the patient's medical condition.
 - 2) A description of the essence, course, goal, anticipated benefit and likelihood of success of the proposed treatment;
 - 3) The risks entailed in the proposed treatment, including side effects, pain, and discomfort;
 - 4) The likelihood of success and the risks of alternative forms of treatment, and of non-treatment;
 - 5) Where the treatment is innovatory, the patient shall be so informed.
- c) The clinician shall furnish the patient with the medical information at the earliest possible stage and in a manner that maximizes the ability of the patient to understand the information and to make a free and independent choice".

In special circumstances the “Patient bill of rights” (3) (clause 15) permits clinicians to provide medical care to patients even without their consent. This depends on the following three stipulations: First, if patient informed consent cannot be obtained due to their physical or mental state. Second, if clinicians are not aware of any objection to the medical treatment on the part of the patients or their guardians. Third, if it is not possible to receive the consent of patients’ representatives or guardians, in the case of minors or the legally incapacitated.

Another situation, where it is permissible to provide medical care even against patients’ will, is if the hospital Ethics Committee approve the treatment with the conviction that certain conditions exist: If patients object to their treatment although their life is in grave danger, or in a situation of medical emergency, when it is not possible to receive patients’ informed consent due to their physical or mental state.

The guidelines of the Director General of the Ministry of Health (2) discuss the issue of patient consent to medical care and details in clauses 4 and 5 “the process of providing information in order to obtain consent for treatment”. Among other things it states:

“A) The first stage is to clarify to the patient his right to receive full information about the treatment in order to reach an independent decision or not to receive information and to leave the decision to the physician.

B) If the patient chooses to be involved in the decision he must receive full information in a clear manner and in language that he can understand, according to his needs and his level of comprehension, with the opportunity to present questions and receive honest answers.

The circular proceeds to detail the information that should be provided to the patient, similar to instructions mentioned in the “Patient bill of rights” (3). Informed consent is necessary also in the case of patients asked to participate in medical experiments. The regulations (8) list all the details entailed in medical experiments involving humans. They explicitly state that it is imperative to inform all research candidates of the goals, methods, and expected benefits of the experiment. In addition, they must be made aware of the risks involved and of possible consequent discomfort. They must be informed of their liberty to refuse to take part in the

study or to retract their consent at any time. It is recommended to obtain the informed consent of medical study participants in writing.

Informed consent

Clause 14(a) says: “Informed consent may be given verbally, in writing, or demonstrated by the patient’s behavior” (3). It is easy to understand the nature of verbal or written consent to medical care. However “consent as demonstrated by the patient’s behavior” is a new concept. Patients who extend their arm for infusion are considered to have given their consent to the infusion.

Patients who pull back their arm, when asked to extend it to perform a blood test – are considered refusing medical treatment.

This manner of informed consent is permissible in cases of medical treatment that do not require written consent, according to the Supplement to the “Patient bill of rights”. The second Supplement to the act defines which types of treatment are included in this list: “surgery, other than minor surgery, blood vessel catheterization, dialysis, radiotherapy, in vitro fertilization, chemotherapy for malignancies” (5).

Patient consent to medical care

The demand of consent to medical care is based on one of the fundamental values of medical ethics: the concept of patient autonomy. Respecting patient individual liberties as human beings requires obtaining their consent to proposed treatment, in recognition of their freedom of choice and their right to self-definition. One of the basic rights of all people is that they not be touched without their consent. Even if they are ill and it is necessary to touch them in order to effect a cure, this does not justify denial of their basic rights or legitimize acts involving such denial.

On the contrary, it is precisely, when people are vulnerable due to health problems that their autonomy requires the most protection. “A man’s will is his dignity” and our duty as clinicians is to demonstrate consideration of patients’ wishes in order to preserve their dignity. People’s right to their body and dignity

is anchored in the Basic Law of Human Dignity and Freedom. Intentional use of force of any type towards a person's body without his consent is legally considered an act of "assault", which is a personal injury and also a criminal offence.

According to the public health regulations (7), patient consent is required for hospitalization, surgery and catheterization, and also for specific operations such as: clinical experiments, in-vitro fertilization, and amniocentesis. There is also an express legal demand for written consent in order to perform an abortion. The demand for patients' consent as part of the appropriate process involved in reaching a decision to provide treatment has important consequences both for quality of care and for the atmosphere and patient satisfaction:

- Encouraging a maximally reliable and comprehensive decision-making process;
- Reducing the possibility of coercion, mistakes and negligence in the decision-making process surrounding each medical treatment;
- Encouraging self-criticism and examination of medical operations performed by others;
- Maintaining an equitable physician-patient relationship;
- Increasing patients' confidence in the medical system;
- Improving patient care – Patients tend to comply to treatment more often, their level of anxiety is reduced, they recover more rapidly and they demonstrate better ability to control dosage mistakes etc. as well as side-effects of the treatment;
- Reconciling patients' expectations with the treatment's limitations and the uncertainties involved.

Providing information

Receiving patients' consent for medical treatment is the final stage of the process of reaching a decision to perform the treatment. The process is enacted in a cooperation between the physician and the patient: The physician makes a recommendation of treatment based on his knowledge and professional experience

and the patient considers the matter in light of personal values and feelings. In order to realize the goal of consent it is necessary to hold an open, fair and efficient discussion, each side indicating relevant aspects of the issue, with the aim of reaching a joint decision. The information that should be provided to patients is as follows:

- The need that calls for the specific operation, i.e. explanation of diagnosis and prognosis;
- Explanation of the nature of the specific operation and its purpose;
- Anticipated results of the proposed treatment – its expected benefits and chances of success;
- Acceptable risks involved in the proposed treatment – including side-effects, pain and discomfort;
- Alternative treatments, including non-treatment and benefits and risks of non-treatment;

The obligation to provide patients with information on the risks involved in treatment arouses problems: On the one hand patients are entitled to know what they are getting into in order to make the correct choice whether to consent to the proposed treatment, but on the other hand full disclosure of all possible risks might scare them and negatively affect their condition or prevent their consent to possibly beneficial treatment. The position shaped in rulings of Israeli courts: The greater the risk, the greater the obligation of disclosure. It is not imperative to state very rare or limited risks.

Anglo-American law has recognized physicians' privilege to provide brief explanations and to spare patients information that might harm them, where there is a concern that providing all the information might have a negative effect on their mental or health state, whether due to the contents of this information or to the time required to explain it.

However this only refers to patients' conceivable reaction to the information or to the delay stemming from the process of consultation. The concern that patients will choose to refuse treatment due to information received and thus cause harm to their health does not eliminate the obligation to provide them with all the information.

In case of refusal

The rule is that it is forbidden to act in contradiction with the patient's wishes. Therefore, if the patient is capable of understanding the data required in order to make the decision, have sufficient judgment in order to form a decision on the matter at hand – the refusal should be honored and the patient should not be forced to receive treatment against their will.

When the treatment is essential and patients refuse treatment for untenable reasons, the clinicians must make every reasonable effort to convince patients to consent to treatment. This may be effected through relatives, psychologists, social workers, clergy, or any other influential factor.

If patients insist on refusing on unreasonable grounds, their competency should be reconfirmed. However the mere fact of refusal is not an indication of incapacity.

Medical ethics

Until recently the physician-patient relationship was based on the principle that physicians who have the knowledge and the will to help should determine patient care at their discretion. Patients who appeal to physicians for help express their full confidence in the medical profession. In the last few years there have been a number of developments:

- Patients have acquired medical knowledge and are at present more knowledgeable in all spheres of life.
- At the same time, many are now of the opinion that constant developments in the medical field question the value of treatment methods that only yesterday were considered completely safe and efficient.
- Today the prevalent view is that each person controls his destiny and has the right to decide for himself on all matters.

This explains the demand that physicians shall not perform any operation on their patients without receiving their prior consent. In order for the consent to be valid, patients must understand the meaning of the treatment, its risks and likeliness of success, and

be informed of other treatment options from which to choose. This is stated in the law, however rather than discussing the legal situation the committee was interested in discussing the conduct of physicians, who are required to include their patients in decisions reached, since patients are human beings entitled to their dignity and freedom.

The committee did not refer in particular to situations in which people are incapable of reaching a decision, where they cannot express their opinion, and such situations will require special discussion. The committee sought to determine rules regarding adults capable of making decisions. The major dilemmas that appeared during the discussions:

- The conflict between physicians' obligation to act to their patients' benefit as perceived by the physicians, and the physicians' obligation as human beings to respect their patients' freedom.
- Does physicians' obligation to provide explanations to their patients require them to present all possibilities, both common and rare? Will this not cause patients unnecessary anxiety by presenting the risks of every vaccination and medication?
- Should physicians provide information only to patients who require it or should they initiate the request for information? Should physicians determine independently which information is relevant?
- Is the definition of capable patients – patients who are capable of making any decision, or should the necessary capability be proportionate to the gravity of the decision and the anticipated risk?
- What is the relation between patients' right to refuse care and their right to receive a certain type of treatment?
- Are physicians entitled to cease treating a patient if this patient does not accept their opinion and rejects the treatment proposed?
- Is there a special Israeli reality stemming from Jewish Law and Israeli law?

The committee referred to the issue of people's right to decide what is done to them. According to Jewish law, physicians are obliged to take steps to

prevent people from reaching decisions that might endanger their life. The committee's recommendations were as follows:

- 1) Unrelated to the legal situation, the need to receive patients' informed consent is an ethical dictate.
- 2) The consent is ethically valid if it is based on a collaborative decision, with mutual respect, and not only a technical presentation of the diagnosis and treatment details.
- 3) The need for informed consent should not depend on patients' education, culture, or consciousness. This should be the rule and not a luxury intended for a privileged elite. This rule should be implemented in a flexible manner ensuring patients' maximal comprehension and ability to decide.
- 4) Patients' decision to accept or reject a medical operation depends on personal values and on their life goals. Patients' choice is limited in the following cases:
 - Physicians are not obliged to consent to patients' demands to perform operations that contradict reasonable behavior or religious belief or moral conviction
 - or that contradict the physicians' professional conviction
 - If it has been proven that the patient is incompetent, and all citizens are considered competent as long as not proven otherwise, the fact that patients are prisoners or restricted for any other reason shall not preclude their right to decide what is done to them.
- 5) Patients shall not be refused information unless:
 - They themselves requests so, directly or indirectly.
 - If the disclosure itself might cause the patients harm.
- 6) Patients should be able to receive information about the course of their disease not only at the time of treatment. They should be encouraged to realize this right.
- 7) The medical school should be approached and requested to teach its faculty and students to carry out these functions.
- 8) The goal should be maximal cooperation with patients' families, barring patient objection.
- 9) In cases when patients cannot decide for themselves, medical operations must be performed in the same manner that they would have chosen if able to do so.
- 10) Cooperation between patient families and medical professionals should be the goal, as implemented by operating Ethics Committees comprised of professionals and other representatives.
- 11) Legal appeals should be made only if these elements are unable to reach an agreement. The courts and the legislator should be extremely wary of their willingness to intervene in such cases, due to the uncertainty and sensitivity of the issue.

Conclusions

The professional literature indicates that clinicians and their critics realize patients' rights to refuse treatment (10,11). This is true even when patients refusing treatment become their own enemy and even when the decision to refuse is completely contrary to medical opinion (10,11).

In the general approach concerning patients' responsibility for their health, physicians and medical staff recognize patients' right to refuse care, however this requires the system to provide patients with full and comprehensive information, including various alternatives, and to equip patients with the tools necessary to be active partners in the treatment process. Thus if they decide to refuse care this decision will be well-founded and informed. Therefore, the medical staff must support the patients at all times unrelated to their decision regarding consent or refusal of care, even when the refusal is contrary to medical opinion.

In any case, patients' rights and dignity must be honored. It is always necessary to remember that the patients' goals are important and should be honored even when they contradict those of the clinicians. The question is how the staff copes with situations of refusal, are they obligated to try and convince the patients and if so, what is the limit?

What type of information should be provided to the patients and how much? Are patients in a given health state capable of choosing between alternatives (12)? Are the staff's goals congruent with those of the patients? In other words, who knows better what is best for the patients? These existential questions appear daily in the staff's work, together with their full schedule and the need to supervise and care for a large number of patients, conditions that make it difficult to cope with these basic patient needs.

The medical profession, despite its ideal of professional autonomy, is still mutually dependent on other professions. There is also a conflict of interest between the medical discipline's obligation to the system and its obligation to the patients. The struggle to separate the obligation to the patients from the obligation to the system – the institution, the physician - might even portray the medical staff as double agents.

Our goal in this review was to perceive how the medical staff reacts, when patients refuse care and to try and form a written procedure that will help the staff cope with situations of refusal. In an era of increasing patients' autonomy and increasingly complex treatments, it is essential to maintain patients' rights on the one hand and those of clinicians on the other. Obtaining informed consent before providing medical or nursing care and understanding the staff's legal situation in each event will enable their integration. At present, perception of the medical discipline and its workers has undergone a transition. Today the customers, the patients, have become service purchasers and active partners in everything done to them. Accordingly, if previously the prevalent model had consisted of active clinicians and passive patients, today we can definitely speak of an active-active model in which patients and clinicians interact, causing increased mutual obligations. These obligations concern the rights and duties of the other

party, however it must be clear that customers possess an autonomy which they are entitled to realize at all times. The medical staff must respect this autonomy and sometimes it may facilitate the assistance provided to patients. The autonomy of each individual emphasizes the existing uniqueness and diversity.

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Submitted: November 01, 2008.

Revised: December 30, 2008.

Accepted: January 11, 2009.

Improving homeopathic practice using bayes' theorem and likelihood ratio

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Abstract

Homeopathic medicines should be handled individually, the doctor must often choose between a large number of medicines for the same condition. The medicine should fit the 'type' of person, according to specific symptoms and characteristics. Homeopathic doctors use symptoms and characteristics seen in cases responding well to a specific medicine to select the same medicine in a new patient. Such data are recorded in the homeopathic repertory, the most well-known is Kent's repertory. Until recently, little attention was paid to the influence of chance in such data. Data collection was insufficiently systematic and the theoretical background was weak. This could become a threat to the reliability of our most important instrument, especially now repertories are easily updated by the use of computers. Bayes' theorem provides a theoretical basis for translating experience into knowledge. The knowledge of homeopathic doctors is built upon implicit comparisons of the prevalence of a symptom in a population-subgroup responding well to a specific homeopathic medicine (medicine population) and the prevalence of the same symptom in the remainder of the population.

Ten Dutch homeopathic doctors recorded prospectively all cases during more than three years and checked the presence of six homeopathic symptoms in every new patient. They also recorded the results of each prescribed medicine. In the end 4,094 patients entered the study and we evaluated 4,072 prescriptions.

Comparing the prevalence of a symptom in a population that responds well to a specific medicine with the prevalence of the symptom in the remainder of the population renders the Likelihood Ratio (LR) of this symptom. If $LR > 1$ the symptom indicates the corresponding medicine. Our findings confirm the most well-known – and accepted - entries of Kent's repertory, but are different in more than half of the other entries.

Keywords: Complementary and alternative medicine, integrative medicine, homeopathic medicine.

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Introduction

Quite a lot of research has already been done to prove the efficacy of homeopathy, but research to improve homeopathy as a method has been scarce so far. Frei et al (1) showed that results of Randomised Controlled trials (RTC) can be improved by investigating the efficacy of the symptoms that indicate the choice of homeopathic medicines and subsequently asking better questions. Regarding the history and the structure of homeopathic knowledge it is easy to understand that there is much room for improvement. Homeopathic medicines cannot be prescribed on medical diagnosis only. The medicine should fit the 'type' of person. The description of the type of person that responds well to a specific homeopathic medicine comes from different sources. One of them is practice experience; cases that respond well are retrospectively analysed as to their characteristics and symptoms. Over two centuries thousands of cases have been reported and the homeopathic database has grown correspondingly. The data were recorded in the homeopathic materia medica and in the index to this materia medica, the homeopathic repertory. As the database grew we lost sight and grip on the prerequisites for entering information into the materia medica and the repertory. As a general rule a symptom or characteristic is entered in the materia medica if it is seen in a patient responding well to a specific medicine, and the medicine is entered in the corresponding repertory-rubric. Therefore, the entries are based on absolute occurrence. Some medicines are used frequently, others seldom. If a medicine is frequently used any symptom will come up eventually in a patient responding well to that medicine, especially if the symptom is also frequently occurring. This is due to mere chance. Suppose that a symptom has a prevalence of 5% in, say, the Sulphur population (the population responding well to Sulphur). If each doctor has one 'best' Sulphur case, due to chance one out of 20 doctors has seen this symptom in his Sulphur case. For this doctor the symptom will be an important indication for Sulphur, while it is not for the other doctors.

One of the well-known problems of the homeopathic repertory is that especially larger rubrics are unreliable and that especially frequently used

medicines are over-represented. As said, this is due to chance. In this respect the computer becomes a mayor threat to the reliability of the homeopathic repertory and materia medica. Updating these sources has become very easy and all manufacturers of homeopathic programs for repertories and materia medica advertise with completeness and the vast number of data they comprise. As yet there are no generally accepted rules for ascertaining the reliability of our data. Such rules should be clear, unambiguous and reproducible. First we need a sound theoretical ground and then a methodology based on this ground. The most elegant and widely used theory is Bayes' theorem.

Bayes theorem

Reverend Thomas Bayes (1702-1761) based his theorem on the law of conditional probability and it is explicitly or implicitly used to update prior beliefs in a particular hypothesis after observations or experiments (2). The founder of homeopathy, Christian Friedrich Samuel Hahnemann (1755-1843), already based his use of the homeopathic medicine *Rhus toxicodendron* on his observation that 'Amelioration from motion' was a symptom that occurred more frequently in patients responding well to that medicine than in other patients. Based on this experience homeopathic physicians will prefer *Rhus toxicodendron* (and other medicines related to the same symptom) if the complaints are better from motion. We refer to patients who respond well to a specific medicine as 'medicine population', the patients that respond well to *Rhus toxicodendron* constitute the '*Rhus toxicodendron* population'.

The addition 'more than in other patients' is a crucial element in finding ways to select reliable entries for the homeopathic materia medica and repertory. This can be translated into Bayes theorem. This theorem has several expressions, one of them is:

$$P(M_i | S) = \frac{P(S \cap M)}{P(S)} = \frac{P(S | M_i) * P(M_i)}{\sum_{\text{all hypotheses}} P(S | M_i) * P(M_i)}$$

Bayes' theorem is not only applicable in increasing or decreasing belief in one particular

hypothesis, it can also be used in differential diagnosis. In his textbook on bayesian biostatistics Woodworth describes the application of the above formula in the famous OJ Simpson judicial trial (3). Blood with DNA matching OJ's was found on the crime-scene. In classic (frequentists) statistics only the chance that this DNA came from someone else was calculated, in bayesian statistics a differential diagnosis with the possibility that the DNA was planted on the crime-scene was possible. The denominator of Bayes' formula is complete only if each possible hypothesis is included. Of course, this is a subjective criterion, it is impossible to know all possible hypotheses. Another subjective element in bayesian calculations is the use of the prior chance which is often estimated by experts in the field and then updated with the new evidence. In general bayesian statistics are more subjective and (therefore?) stronger related to daily practice. For our attempt to constitute an algorithm for homeopathy we use another expression of Bayes' formula:

$$\text{Posterior odds} = \text{LR} * \text{prior odds}$$

LR = Likelihood Ratio = prevalence in target population / prevalence in remainder of the population.

Odds = chance / (1-chance); chance = odds / (1+odds)

The Likelihood Ratio (LR) is always larger than zero. If LR>1 the posterior odds increases; if LR<1 (>0) the posterior odds decreases.

Algorithm for homeopathy

Bayes' theorem enables us to formulate an algorithm for homeopathy; experience from the past tells us what to do in new cases, people who respond well on a specific homeopathic medicine have specific symptoms that distinguish them from other homeopathic medicines. In other words: the prevalence of certain symptoms in the 'medicine population' is larger than in the remainder of the population.

To assess the LR of a homeopathic symptom we use the model of diagnostic tests with specification as in table 2.

Table 1. 2x2 contingency table for assessing relation between symptom and effect

	Medicine worked	Remainder of population	
Symptom positive	a= True Positives (TP)	b= False Positives (FP)	a+b
Symptom negative	c= False Negative (FN)	d= True Negatives (TN)	b+d
	a+c	b+d	a+b+c+d

Table 2. sequential updating of chance of effect regarding 3 medicines, starting from different indications/ symptoms. LRA = Likelihood Ratio for the symptom considering medicines A. Same for LRB and LRC

Information	LRA	Posterior chance medicine A	LRB	Posterior chance medicine B	LRC	Posterior chance medicine C
Joint pain	3	13.6%	1	5%	2	9.52%
Desire for cold milk	5	44%	2	9.52%	2	17.3%
Vertigo turning in bed	0.8	38.5%	6	38.6%	1	17.3%
Wet weather aggravates	3	65.2%	2	55.6%	5	51.1%
Restlessness	3	84.8%	4	83.3%	2	67.6%

The reference standard in our research is a good response to the medicine. The control group is the remainder of the research population, this will be explained later. The homeopathic 'diagnosis' is the best medicine for this particular patient.

One of the basic concepts of bayesian reasoning is updating of beliefs. This is best shown in the odds formula. Suppose the chance that the homeopathic medicine Rhus toxicodendron will work is 5%, the odds being 5/95, if we know nothing about the

patient. Then suppose that amelioration of pain is known to occur ten times as frequently in the population responding well to Rhus toxicodendron then in the remainder of the population, the LR being 10. Then, if the patient has amelioration from motion the odds that the patient responds well to Rhus toxicodendron becomes $10 * 5/95 = 50/95 = 0.53$, and the chance $0.53/1.53 = 0.35$.

The real situation in daily practice is much more complicated. Table 2 shows a hypothetical outcome of a consultation with an indication and four additive symptoms. We assume that the chance that any medicine will work is 5% if no other information is known (first prior chance). After each symptom the chance that a medicine will work is updated to the posterior chance. This posterior chance becomes the prior chance before the next symptom. If the symptoms were considered consecutively the chances that medicine A, B or C could work increase stepwise, but all medicines should be considered. Medicine B could be indicated, *even if medicine B has no relation to joint pain (LR=1)*. Symptoms could even contra-indicate certain medicines, like 'vertigo on turning in bed' contra-indicates medicine A. There is a fair chance that the doctor will choose medicine B, because of other information that the patient had not yet revealed or was until then not noticed. This situation is common in homeopathic practice; nearly always there are symptoms pleading for and symptoms pleading against specific medicines. The homeopathic decision process appears to be even more complex than we can describe here.

In practice a limited number of symptoms is selected to get some indication about possible medicines. This indication should be interpreted as a weather-forecast: there are many other variables that influence your decision what to do next, but you like the forecast to be correct. Likewise, the doctor will consider many other variables to come to his final choice of prescription.

One of the decisions to make in LR assessment is the choice of the control group, the patients that did not respond to the medicine. There are two extreme choices:

- the patients that used the medicine without result;

- the patients that used the medicine without result, + the patients that received other medicines.

This fundamental difference can be shown in relation to one of the versions of Bayes' formula:

$$P(M_i | S) = \frac{P(S \cap M)}{P(S)} = \frac{P(S | M_i) * P(M_i)}{\sum_{\text{all hypotheses}} P(S | M_i) * P(M_i)}$$

For $P(M_i|S)$ we can read: the chance that medicine M_i will work given the symptom S (herpes lips). The denominator of the formula can be interpreted in many ways, with two extremes:

- the chance that the symptom will occur in patients responding to the medicine, plus the chance that it will occur in patients not responding to the medicine;
- the chance that the symptom will occur in patients responding to the medicine, plus the chance that it will occur in patients not responding to the medicine, plus the chance that it will occur in all other patients responding to other medicines

Bayes formula is very versatile, it can be used for all kinds of differential diagnoses. One of them is the construction of a so-called credible interval, analogous to the credibility interval. For this purpose the posterior chance of all hypothetical possibilities given the observed data. One could also compare the DNA of thousand suspects with DNA on a crime scene and calculate the probability of each suspect to be the owner of the crime scene DNA. Likewise we can calculate the probability of each homeopathic medicine given a specific symptom.

The denominator of Bayes' formula is the complete chance of S and the question is in fact when S is complete. In conventional medicine the control group always consists of patients that did not respond to the medicine and this point reflects the core of the difference between homeopathy and conventional medicine. In conventional medicine the complaint or medical diagnosis (condition) is the starting point which limits all following considerations. There are medicines for this condition and there are other

medicines for other conditions. The population with the condition is not divided into sub-populations for different medicines; there is no differential diagnosis regarding medicines, see figure 1. From this point of view it is correct to compare the patients that responded well to the patients that did not respond.

The symptom S is confined to the condition once the condition is chosen. In this case we don't really need the bayesian formula shown above to calculate sensitivity, specificity or LR because we disregard the possibility of other medicines.

Conventional medicine

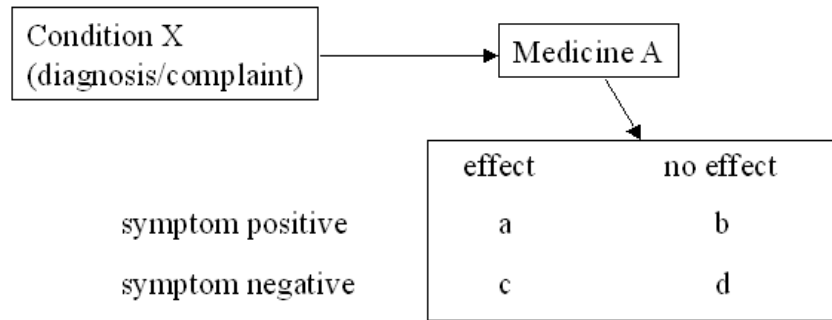


Figure 1. serial process; the choice of the medicine is highly restricted by the condition.

Homeopathy

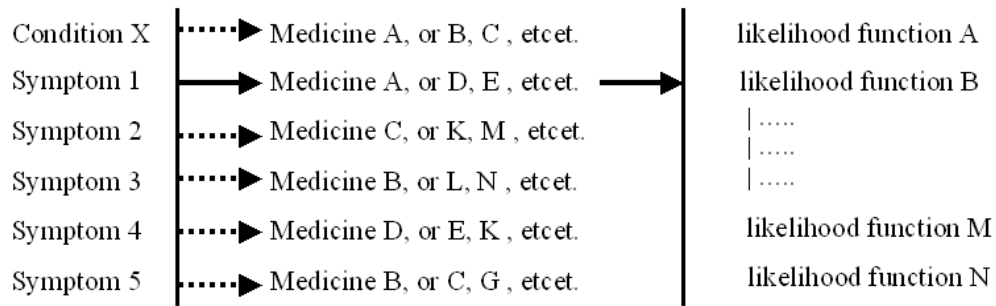


Figure 2. Parallel process; the choice of medicine is not restricted by the condition or a single symptom.

In homeopathy the condition is not defining the rest of the choices and the relation between medicine and diagnosis or complaint is weak. Consequently the relation between symptom and condition is weak. The population with a certain condition is divided into a rather large number of sub-populations responding to different medicines. Each sub-population has its own prevalence of the symptom, this is called the 'likelihood function'. The choice of medicine is made after parallel gathering of both condition and

symptoms/characteristics, see figure 2. If we consider the position of one symptom/ characteristic or the presented condition in our database we see a large number of medicines linked to that item via the likelihood function, but all in different degrees. The bayesian method allows us to differentiate the relation between medicine and symptom/characteristic/ condition and that is what the practitioner is interested in.

Methods

Study design and setting

In 2002 a pilot study was performed to test feasibility and methods for data collection. Based on this experience we defined, implemented and tested existing database programs. From June 2004 until December 2007 we conducted an observational study including all consecutive new patients older than two years. Observers were 10 experienced Dutch homeopathic doctors, working as consultants especially for chronic cases. There were no limitations as to disease, the only limitations were the use of single homeopathic medicines and the possibility to evaluate effect. Practices were divided over the Netherlands. Candidates were selected among participants in our materia medica validation project and received a questionnaire in advance. In the first consensus meeting with the participants the symptoms were defined. See figure 3 for the flow chart of the whole project.

Variables

Six symptoms were assessed: 1. 'Diarrhoea from anticipation', 2. 'Fear of death', 3. 'Grinding teeth during sleep', 4 'Recurrent herpes lips', 5. 'Sensitive to injustice' and 6. 'Loquacity'. These six symptoms were checked in all patients.

We used two cut-off values for each symptom, one for the stronger form (grade 2) and one for the mild form of the symptom (grade 1). Grade 2 should be used when the symptom was strong enough to make the doctor consider corresponding medicines. Grade 1 should be used when a medicine related to the symptom was considered to verify possible absence of the symptom. So, grade 2 to include the medicine into the considerations, grade 1 to exclude the medicine. Beforehand, the participating doctors specified the symptom in a consensus meeting using the Delphi method. For grade 2 the following definitions were used: Diarrhoea from anticipation was defined as 'Diarrhoea from anticipating all kinds of events'. Fear of death as 'Definite fear, occurring more than once a week'. Grinding teeth as 'Grinding teeth during sleep, more than once a week'. Herpes

lips as 'Herpes lips more than 5 times a year'. Sensitivity to injustice was defined as 'Sensitivity to injustice done towards others, resulting in subsequent behaviour like turning off the television, writing letters, protesting etceteras'. Loquacity as 'Loquacity apparent during consultation or mentioned as an important character trait'. But for all symptoms clinical judgement prevails because age, profession and circumstances can be relevant. A paper about handling vagueness of symptoms was used to prepare participants for this meeting (4). We wanted to get an impression of the role of vagueness in this kind of research and therefore assessed symptoms with different degrees of vagueness from 'herpes lips' to 'sensitivity to injustice'. For two symptoms, 'grinding teeth during sleep' (bruxism) and 'herpes lips' data about prevalence were available (5-14). The prevalence of frequent grinding teeth varied from 3.7% to 8.5%; frequent herpes lips from 4% to 5.4%. The general idea communicated to the participating doctors was that symptoms should be treated as in their daily practice, but now they should be checked in every new patient. Participants were also trained in the idea of bayesian reasoning; if a symptom is very common, say occurring in half of the population, the symptom is worthless.

Data recording

Symptoms were recorded in database programs used in daily practice for billing, correspondence about patients etceteras, in order to minimise the effort to record data. The programs were based on FilemakerPro® and Access®. In a pilot study we experimented with gathering data in a spreadsheet or on paper; this turned out to be not feasible. The database-programs were adjusted for our purpose. These programs were already suited to record prescribed medicines and effects of the medicines. One program had to be used with special instructions because it recorded incidence of prescriptions; this could not be corrected within the available budget. Observers were instructed to fill in just one result for each medicine in each patient.

Results were recorded for each prescribed medicine, after evaluation according to the Glasgow Homeopathic Hospital Outcome Scale (GHHOS). The

use of the GHHOS scale was already trained in the consensus meeting mentioned above and in other activities of our group. The GHHOS scale is not explicit about causal relation between medicine and effect.

The importance of causal relation between effect and medicine was well discussed; success without causal relation is not relevant for assessing symptoms. Consensus was also reached about required follow-up before entering results in the database.

Result GHHOS 2 or higher indicates that there other effects than just improving of the presented complaint, like general well-being, energy or body functions. Therefore result GHHOS 2 or higher can be seen as an indication for a causal relation. Result GHHOS 2 was entered after at least one month after prescription, result GHHOS 3 or 4 after at least 6 months.

Default value for result was a blank, zero or negative results were recorded after at least two

months follow-up. Blanks (no follow-up or causal relation unclear) were not used for calculating results.

Monitoring bias

The observers were familiar with assessing results after former consensus meetings. Data were send to the co-ordinator and analysed every 6-8 months. Differences between observers concerning assessment of symptoms and results of treatment were monitored. Feedback was given in a newsletter every 1-3 months. Differences between observers were discussed in consensus meetings twice a year and definitions of symptoms and criteria for assessing results were adjusted if necessary. Results were monitored over time to check for consistency. Confirmation bias was detected by comparing data at the beginning and at the end.

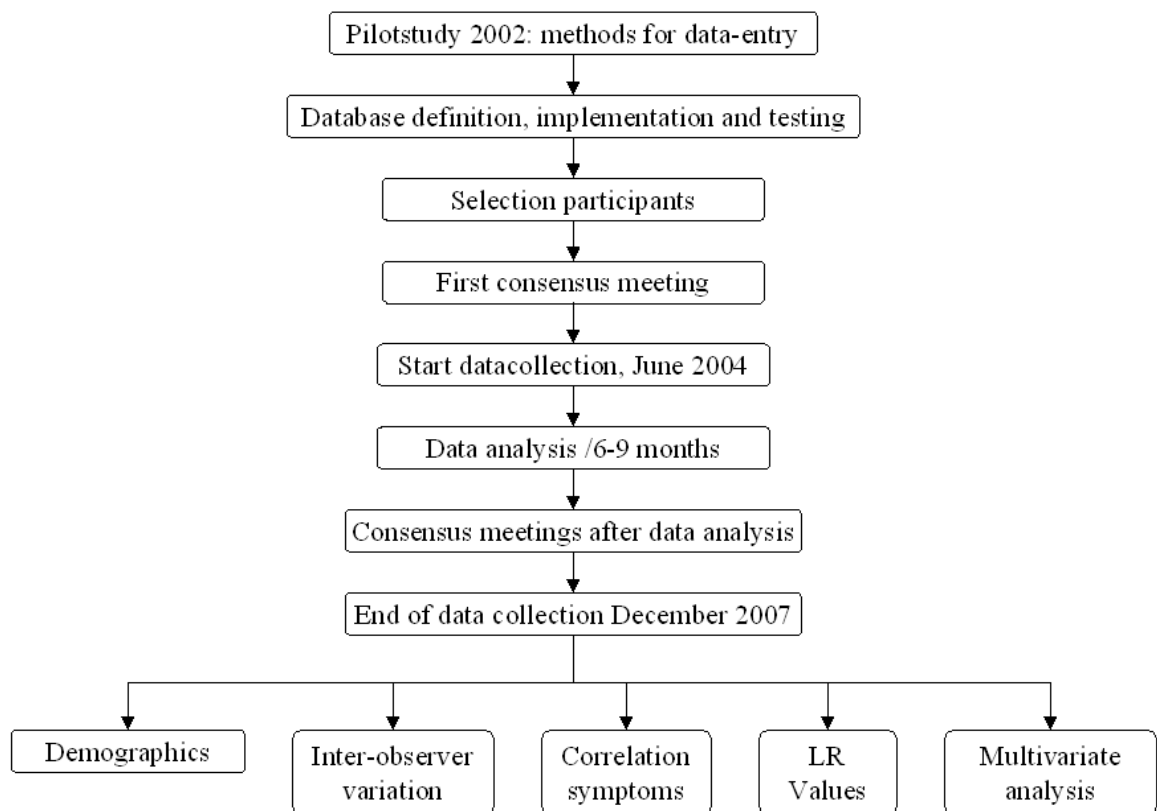


Figure 3. Flow chart of the project.

Analysis

The co-ordinator (AR) used Excel® spreadsheets, the statistical programs Epi-info® and SPSS® , Confidence Interval Analyser (BMJ) for confidence intervals of LRs (log method) and the VassarStats website to evaluate other results.

LR values for a particular medicine were calculated using the prescriptions of that medicine with result GHHOS 2-4 as target population and the remainder of the population as control, see 'Which control group?'.

Results

In the end 4,094 patients were included; 1,314 (32.1%) male, 2,752 (67.2%) female, 28 (0.7%) missing values. Mean age was 39.62, standard deviation 20.952, range 3 to 95. All doctors had more than 10 years of experience in homeopathy. The number of evaluated prescriptions was 4072. Table 3 shows the distribution of numbers of patients, the number of evaluated prescriptions and the number of different medicines per doctor.

Table 3. Patients and prescriptions of all observers

Doctor	Nr. of patients	Percent patients	Nr. of prescriptions	Percent prescriptions	Prescriptions per patient	Nr. of different medicines
1	243	5.9	67	1,6	0.276	35
2	537	13.1	884	21,7	1.646	148
3	503	12.3	160	3,9	0.318	75
4	268	6.5	950	23,3	3.545	295
5	268	6.5	266	6,5	0.993	86
6	878	21.4	626	15,4	0.713	123
7	353	8.6	263	6,5	0.745	71
8	306	7.5	208	5,1	0.680	71
9	309	7.5	115	2,8	0.372	41
10	429	10.5	533	13,1	1.242	144
Total	4094		4072		0.995	421

There were considerable differences between doctors regarding numbers of patients and numbers of evaluated prescriptions per patient. This difference could be caused by:

- number of prescriptions per patient, some doctors change medicine more often;
- loss to follow-up;
- incomplete data; one doctor (3) lost part of the evaluation data, two (1, 9) also used other therapies for a number of patients.

Despite the consensus meeting to define symptoms and feedback on differences between doctors, differences in prevalence of symptoms remained. These differences were most pronounced for the vaguest symptoms, sensitive to injustice and loquacity. The prevalence of all symptoms except 'sensitive to injustice' was much alike. However, the

corresponding repertory-rubrics are very different regarding size. The smallest rubric, 'diarrhoea from anticipation', contains three medicines in the original repertory; the largest rubric, 'fear of death' contains 103 medicines in the original repertory.

The prevalence of the symptoms 'grinding teeth during sleep' and 'herpes lips' was not different from the values with the same specifications that we obtained from literature. The differences between observers for the symptoms in the stronger degree are specified in table 4. When we order the symptoms according to mean prevalence we see that the cut-off value of symptoms varies among observers, but also among the symptoms for each observer. This is also shown in figure 4. The variance between doctors was significant for all symptoms (Kruskal Wallis test), but the least for the symptoms 'Fear of death', 'Herpes lips' and 'Grinding teeth'.

Table 4. Prevalence of symptoms in 10 practices

Doctor symptom	1	2	3	4	5	6	7	8	9	10	mean
Fear	1,23%	2,79%	2,78%	4,85%	4,48%	5,13%	5,10%	2,29%	2,91%	5,13%	3,86%
Diarrhoea	5,35%	2,61%	2,39%	5,22%	4,85%	7,40%	1,70%	1,96%	0,65%	8,39%	4,42%
Herpes lip	5,35%	2,79%	2,58%	7,46%	3,73%	6,26%	4,25%	4,90%	2,27%	9,79%	5,01%
Grinding teeth	7,82%	3,54%	3,98%	6,34%	7,09%	5,81%	5,67%	6,21%	1,62%	6,99%	5,35%
Loquacity	8,64%	6,15%	2,58%	6,72%	11,19%	9,00%	2,83%	7,84%	2,27%	7,46%	6,52%
Injustice	15,64%	6,33%	4,57%	2,24%	17,54%	12,98%	4,82%	1,63%	2,91%	20,05%	9,26%
Mean	7,3%	4,0%	3,1%	5,5%	8,1%	7,8%	4,1%	4,1%	2,1%	9,6%	5,7%

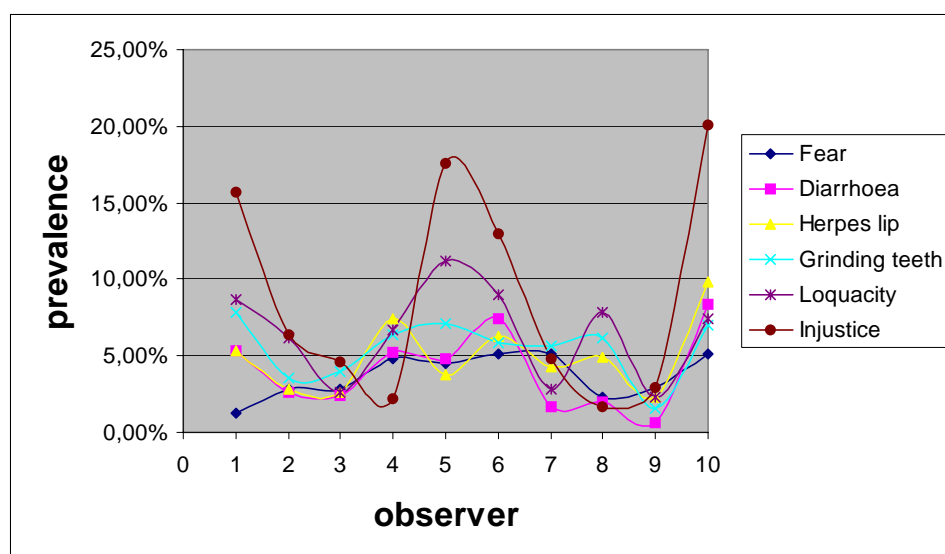


Figure 4. Inter-observer variation of prevalence of symptoms.

There were also differences between observers in estimating effect according to the GHHOS scale. These differences are partly explained by the fact that some doctors thought that results lower than GHHOS 2 should not be recorded, because they were irrelevant for another project of our group. This problem was detected halfway the project. In the beginning negative results after one month were recorded. Later we decided to record negative results after more than two months to avoid the recording of initial aggravations which are common in homeopathy and will often reverse into positive result, which is not noticed in case of loss to follow-up.

All together, 421 different medicines were prescribed, but in different frequencies. The 10 most

prescribed medicines were responsible for 38% of the successful prescriptions; the 20 most prescribed medicines rendered 53% of the successes. The mean success rate of all prescriptions was 51%. There was no clear difference in success rate between frequently and seldom prescribed medicines.

Correlations between pairs of symptoms in the whole population were calculated by correlation matrix. No correlations were found, the highest being $r=0.063$ between loquacity and sensitivity to injustice.

Multiple correlations were analysed by Principal Component Analysis. There were no indications for correlation between groups of symptoms, variance explained was not much different for all 6 Principal Components, see table 5.

Table 5. Variance explained by six components. Extraction method: Principal component analysis

Component	Initial Eigenvalues	
	Total	% of Variance
1	1,155	19,245
2	1,021	17,011
3	1,011	16,844
4	,971	16,179
5	,942	15,694
6	,902	15,027

Table 6. LR values. a= symptom present in patients responding well to the medicine; b= symptom present in remainder of the population; c= symptom absent in patients responding well to the medicine and d= symptom absent in remainder of the population

		a	c	b	d	LR+	95% CI
Diarrhoea	N=182						
	arg-n	12	14	170	3909	11.1	7.13 to 17.2
	cimic	2	5	180	3918	6.5	2.00 to 21.17
	elaps	2	6	180	3917	5.69	1.70 to 19.06
	gels	8	5	174	3918	14.5	9.19 to 22.78
	ph-ac	7	16	175	3907	7.1	3.76 to 13.39
	pic-ac	1	2	181	3921	7.55	1.52 to 37.67
Fear	N=159						
	acon	4	6	155	3940	10.6	4.87 to 22.93
	am-c	2	7	157	3939	5.8	1.69 to 19.87
	anac	5	7	154	3939	11.1	5.57 to 22.02
	ars	6	21	153	3925	5.92	2.88 to 12.2
	carc	4	39	155	3907	2.44	0.95 to 6.28
	cench	1	3	158	3943	6.49	1.18 to 35.67
	lac-c	2	6	157	3940	6.52	1.95 to 21.88
	lach	4	38	155	3908	2.5	0.97 to 6.42
	naja	1	3	158	3943	6.49	1.18 to 35.67
	tab	1	2	158	3944	8.65	1.73 to 43.19
	verat	2	4	157	3942	8.7	2.78 to 27.27
	zinc	1	3	158	3943	6.49	1.18 to 35.67
Grinding teeth	N=219						
	am-m	2	3	217	3883	7.56	2.56 to 22.28
	bell	6	15	213	3871	5.48	2.75 to 10.90
	calc-m	2	9	217	3877	3.43	0.97 to 12.10
	calc-p	4	24	215	3862	2.71	1.08 to 6.77
	carc	7	36	212	3850	3.12	1.56 to 6.22
	car-c-c	2	7	217	3879	4.19	1.23 to 14.34
	cench	2	2	217	3884	9.45	3.52 to 25.39
	cocc	3	10	216	3876	4.37	1.61 to 11.90
	ign	4	29	215	3857	2.3	0.91 to 5.81
	merc	7	47	212	3839	2.48	1.23 to 5.01
Herpes lips	N=205						
	aloe	2	3	203	3897	8.08	2.74 to 23.83

	a	c	b	d	LR+	95% CI	
Injustice N=380	caust	6	40	199	3860	2.66	1.27 to 5.68
	nat-m	24	132	181	3768	3.36	2.26 to 4.98
	sep	10	83	195	3817	2.21	1.21 to 4.04
	staph	5	27	200	3873	3.18	1.41 to 7.20
	stram	2	7	203	3893	4.48	1.31 to 15.33
	am-m	2	3	378	3722	4.34	1.48 to 12.75
	anac	6	6	374	3719	5.47	3.08 to 9.72
	bor	2	3	378	3722	4.34	1.48 to 12.75
	carc	9	34	371	3691	2.29	1.27 to 4.13
	car-c-c	4	5	376	3720	4.84	2.32 to 10.12
	caust	18	28	362	3697	4.39	3.02 to 6.38
	cocc	5	8	375	3717	4.2	2.10 to 8.40
	ign	6	27	374	3698	1.98	0.95 to 4.11
	med	5	19	375	3706	2.27	1.03 to 4.98
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Loquacity	N=267						
ambr	3	5	264	3833	5.82	2.36 to 14.35	
bell	4	17	263	3821	2.96	1.22 to 7.20	
cimic	2	5	265	3833	4.42	1.36 to 14.34	
dig	2	1	265	3837	10.3	4.60 to 23.16	
hyos	5	10	262	3828	5.2	2.52 to 10.75	
lach	14	28	253	3810	5.35	3.43 to 8.35	
saccha	2	5	265	3833	4.42	1.36 to 14.34	
stram	2	7	265	3831	3.43	1.01 to 11.73	
tarent	2	6	265	3832	3.87	1.16 to 12.91	
verat	3	3	264	3835	7.76	3.46 to 17.43	

Lr values

Calculating LR rendered 50 (nearly) significant values for LR+ regarding the symptoms in strong degree, see table 6.

Which control group?

The fundamental methodological issue as shown above is indication-centred or patient-centred approach. In conventional medicine a medicine works or does not work for a certain indication and medicines for that indication are usually much alike. In our assessment the patients with recurrent herpes lips received 93 different medicines, most of them were not related to the symptom herpes lips according to the repertory-rubric 'recurrent herpes lips' (containing 34 medicines). Out of the 34 medicines in

the rubric 12 were not used, so the doctors used 71 medicines not included in the rubric. This confirms that the choice of the medicine is only partly determined by one symptom.

The choice of the control group is analogue to the constitution of the denominator in Bayes' formula, or $P(S)$: does a symptom delimit the number of possible medicines? In other words: do we have the total prevalence of symptom S if we consider a population responding to a limited set of medicines? Follow-up of patients can show us which medicines work after a specific medicine failed; these medicines should anyway be considered in the differential diagnosis.

We reconstructed what happened in actual practice in our research after the most prescribed medicine, Natrium muriaticum (Nat-m). We recorded 248 prescriptions of Nat-m, 156 (63%) with good result. This result was above average (51% good result). We traced all prescriptions after the 92 Nat-m prescriptions that failed, altogether 153 medicines.

The follow-up prescriptions were less successful than the first Nat-m prescriptions, 51 (33.3%) had good result, 102 (66.6%) had no result. Among the 51 successful follow-up prescriptions there were 16 medicines that were not indicated by herpes lips. The choice of the follow-up medicine not only depends on the symptom herpes lips, but also on a very large variety of possible other symptoms. Another research group assessing the same symptom could come up with a very different set of successful follow-up medicines because the number of possible combinations with other symptoms is endless.

Suppose we were to choose a set of medicines after the symptom herpes lips comes up as a first symptom. Based on our research, including the LR data and the data considering the follow-up after Nat-m, the doctor could fill in Bayes formula shown before for each possible medicine; part of the possible medicines is shown in the table. Here we assumed that the prior-chance that any of these medicines could work is 0.05. The medicines in the table are based on the list of medicines that worked after Nat-m failed and the list of medicines that are indicated by herpes lips. But other colleagues might have experience with other medicines that worked well after Nat-m failed, so the list is probably very incomplete.

The differential diagnosis of table 7 does not reflect clinical practice. Our best option would be Stramonium (stram), because it has the highest posterior chance, but the posterior-chance is still only 7.4%. Medicines like Alumen (alumn) and Ambra (ambr), which were actually effective in clinical practice, would not stand any chance if we were to base our next prescription on only this symptom. It is impossible to say which medicines should be taken into account for the denominator in bayesian formula because the choice is hardly limited by the presented complaint or diagnosis. The outcome of the posterior chance heavily depends on the choice of the medicine you consider in the differential diagnosis. If you include only medicines with high prevalence of the symptom herpes lips posterior chance is lower. If you include more medicines with low prevalence of herpes lips posterior chance becomes higher. Intuitively this is easier to understand: if you consider only 'herpes lips medicines' there is hardly any distinction between these medicines in prevalence of

this symptom. The other medicines to consider depend on other symptoms that will come up during the consultation and that is totally unpredictable. Therefore, we cannot know which medicines without a relation to herpes lips we should consider.

The homeopathic diagnostic process is not sequential. In reality homeopathic doctors do not make a differential diagnosis after one symptom. Any medicine is still possible, depending on the other symptoms of the patient. They gather as much characteristic symptoms as possible about the patient, make a hierarchy of these symptoms and then make a differential diagnosis.

We conclude that things become complicated when we limit the list of possible medicines after one symptom, especially when we choose patients that used the medicine without result as control group. In this case the numbers of the control group are low and the symptom has little influence on the choice of medicines. If we fill in all other medicines in Bayes' formula comparing with Nat-m we get the following result (table 8).

We could make the same calculations for any other medicine, like Baryta carbonica (bar-c) (table 9). This way the posterior chance will be 15% for Nat-m and 16.1% for Bar-c. The result is the same as using the simple and intuitive formula Posterior odds = LR * prior odds. Another advantage of representing the indications for medicines with LR is that it corresponds with the existing homeopathic repertory. In the repertory medicine entries are presented as if they were independent of other symptoms. It is the responsibility of the homeopathic physician to correct intuitively for possible interactions with other symptoms. In the end of the parallel diagnostic process of symptom gathering the doctor makes a differential diagnosis like in table 10.

The ordering of symptoms in this repertorisation does not reflect the importance of the symptoms. In this scheme the possibility of interaction between symptoms is disregarded, but intuitively the practitioner is well aware of that. He will choose a variety of characteristics and symptoms that are not likely to be inter-related. Furthermore, from experience and expert knowledge of others he might know that symptoms can be related for certain medicines.

Table 7. Differential diagnosis calculated by Bayes' formula for a limited number of medicines

medicine	prior	likelihood	$S \cap M$	posterior
alumn	0.05	0.000	0.000	0.000
ambr	0.05	0.000	0.000	0.000
aur	0.05	0.000	0.000	0.000
calc-p	0.05	0.000	0.000	0.000
carb-v	0.05	0.000	0.000	0.000
ign	0.05	0.000	0.000	0.000
graph	0.05	0.037	0.002	0.012
calc	0.05	0.040	0.002	0.013
ph-ac	0.05	0.043	0.002	0.014
merc	0.05	0.056	0.003	0.018
tub	0.05	0.063	0.003	0.021
staph	0.05	0.080	0.004	0.027
Lyc	0.05	0.093	0.005	0.031
acon	0.05	0.100	0.005	0.033
sep	0.05	0.108	0.005	0.036
arn	0.05	0.125	0.006	0.042
ferr-m	0.05	0.143	0.007	0.048
bry	0.05	0.154	0.008	0.051
nat-m	0.05	0.154	0.008	0.051
staph	0.05	0.156	0.008	0.052
bar-c	0.05	0.182	0.009	0.060
stram	0.05	0.222	0.011	0.074
ruta	0.05	0.200	0.010	0.067
gels	0.05	0.154	0.008	0.051
chin	0.05	0.143	0.007	0.048
caust	0.05	0.130	0.007	0.043
rhus-t	0.05	0.105	0.005	0.035
lach	0.05	0.095	0.005	0.032
thuj	0.05	0.083	0.004	0.028
nat-c	0.05	0.080	0.004	0.027
sulph	0.05	0.068	0.003	0.023
hyos	0.05	0.067	0.003	0.022
carc	0.05	0.047	0.002	0.015
med	0.05	0.042	0.002	0.014
ars	0.05	0.037	0.002	0.012
iris	0.05	0.000	0.000	0.000
mag-m	0.05	0.000	0.000	0.000
nat-s	0.05	0.000	0.000	0.000
nit-ac	0.05	0.000	0.000	0.000
P(S)			0.150	1.000

Table 8. LR for 'Herpes lips' regarding Natrium muriaticum with the remainder of the population as control group: the possible number of medicines is not limited

Medicine	prior	Likelihood	$S \cap M$	Posterior
nat-m	0.05	0.154	0.008	0.150
other	0.95	0.046	0.044	0.850
P(S)			0.051	1.000

Table 9. LR for 'Herpes lips' regarding Baryta carbonica with the remainder of the population as control group

Medicine	prior	Likelihood	$S \cap M$	Posterior
bar-c	0.05	0.182	0.009	0.161
Other	0.95	0.050	0.047	0.839
P(S)			0.056	1.000

Table 10. Hypothetical differential diagnosis for five medicines with LR values of each symptom for different medicines

Information	Medicine A	Medicine B	Medicine C	Medicine D	Medicine E
Joint pain	3	1	2	1.5	2
Herpes lips	2	1.5	1	0.8	3
Desire for cold milk	5	2	2	1	0.9
Vertigo turning in bed	0.8	6	1	1	2
Wet weather aggravates	3	2	5	3	1.5
Restlessness	3	4	2	2	1

The combination of joint pain and desire for cold milk is known as an indication for the homeopathic medicine Rhus toxicodendron, stronger than expected from the single symptoms. As said before, the repertorisation should be interpreted as a weather-forecast: there are many other variables that influence your decision what to do next, but you like the forecast to be correct.

Discussion

As far as we know this was the first prospective assessment of homeopathic symptoms. Bayes' theorem could provide criteria to indicate relations between symptoms and effectiveness of medicines. Our starting point was clinical practice and this opens a number of methodological pitfalls. Vagueness cannot be avoided in clinical practice and especially in homeopathy. Confirmation bias is present, even if we are aware of it. Inter-observer variation is considerable.

One of the biggest issues is the choice of the control group for our LR calculations, which has the largest effect on results and reflects the essence of holistic medicine. The most striking difference between homeopathy and conventional medicine is the weak relation between condition (complaint or diagnosis) and medicine. The choice of a medicine is only made after obtaining the whole picture and

subsequent parallel comparison of a large number of medicines, related to several symptoms and characteristics as well as the presented condition. We think that the population where the medicine did not work is not the right choice and that the strength of bayesian approach is the comparison of likelihood functions related to each medicine. The differential diagnosis of eligible medicines cannot be restricted by the condition or one symptom. Another complaint or symptom could open up a very different set of eligible medicines; this is where holistic medicine stands for. Even after parallel comparing of all symptoms the resulting set of medicines has no more predictive value than a weather forecast has on our activities for the next day. The number of variables is too large to make a definite choice on the mechanistic process of repertorisation.

The reference (gold) standard for our assessment - good response to the medicine according to a specified GHHOS scale - is not perfect, but it is as yet uncertain how this influences our results.[16] The general idea of bayesian analysis is improvement: we select half of our prescriptions that we regard as best prescriptions and analyse their relations with symptoms and characteristics. This way our results should move in the direction of our best prescriptions.

This research shows the subjectivity involved in clinical practice. Even after repeated consensus meetings considerable differences between observers remained, in assessing symptoms as well as assessing

results of treatment. Apparently, practitioners have their own references based on a complex system of knowledge and experience. Within this system the materia medica and the repertory function as a useable guide. We must be careful not to overestimate numbers and formulas. Confidence intervals could misguide us; they show the influence of chance, not of bias. Nevertheless, we cannot avoid to be more accurate in adding new knowledge to our materia medica and repertory. Background information should be as complete as possible, symptoms should be better defined. The influence of chance is so far totally neglected. The prevalence of the symptom and the spread of this prevalence in the research population should be mentioned, so that every user of this information can estimate the accuracy of the information and compare it with his own particular situation.

Subjectivity is an inherent part of bayesian statistics. Prior chances are often elicited from expert opinion. The subjectivity of bayesian statistics is often criticised, but it performs well in all kinds of real-world systems. Former projects of our group showed that estimations about prevalence of symptoms in the whole population and in various medicine populations are close to prevalences we assessed in the LR project.

Because of the vagueness and possible bias the absolute LR values should be considered carefully. We cannot predict accurately what the posterior chance will become when a symptom is present. Not only because we don't know the prior chance that a medicine will work before we have any symptom and because of the uncertainty in the LR value, but also because of the uncertain role of other symptoms. Another symptom might be more indicative because it fits better in the whole picture of the patient. Interaction between symptoms cannot be predicted from the LR values. Bayes theorem can express the difference between common and peculiar symptoms, but the LR values of different symptoms cannot fully be compared. Each symptom has its own definition and cut-off values, differences are both qualitative and quantitative.

We performed this research to discard statistically incorrect entries from the repertory, but we don't know which statistical certainty we need for homeopathic practice. The usual 95% certainty (2-

tailed) for scientific research is meant to obtain proof for our hypotheses, but that is not our goal here. We want to know if a specific symptom is an indication for a certain medicine and is 70% certainty (1-tailed) useless? Should we discard existing entries if the certainty from our research that $LR > 1.5$ is 40% or lower?

To start up the discussion about these matters we propose a cut-off value of $p < 0.40$ that $LR > 1.5$ for discarding existing entries and $p > 0.70$ that $LR > 1.5$ for entering new medicines in a rubric.[17] Based on these cut-off values we can make some proposals for changes in the existing repertory rubrics based on our research.

If we compare our results regarding five symptoms ('Sensitive to injustice' is not in the original repertory) with the symptom-rubrics in the original repertory half of our results are different. If we follow our results the larger rubrics become smaller, the smaller rubrics larger. This is as expected; the prevalence of the five symptoms in the repertory is about the same and we should therefore expect small differences between sizes of the rubrics. As expected, frequently used medicines are unjustly entered in the repertory, but we cannot make a general rule out of this. A frequently used medicine like *Lycopodium* could be added to the rubric 'Recurrent herpes lips' if we consider $p = 0.70$ as a sensible cut-off value for new entries, $LR = 1.89$ ($p = 0.805$). A somewhat less used medicine like *Staphisagria* should be added.

In this first project of this kind we decided to monitor data closely and to adjust procedures if necessary. We adjusted the criteria for entering zero result in the database; after one year we no longer entered blanks for result after one month but after three months. Some observers did not enter results below 2 during the first year. These facts and the monitoring could have influenced results.

Future possibilities of symptom assessment

Assessment of homeopathic symptoms becomes a necessity if we want to apply Bayes' theorem in homeopathy, but there are limitations as to feasibility. The essence is that we use the prevalence of symptoms instead of absolute occurrence. There are

several ways to estimate this prevalence; there are retrospective methods like consensus meetings and analysis of practice registrations, but prospective assessment is generally considered to be the best method. The prospective assessment requires discipline, adequate software, sufficient doctors following roughly the same method, prepared to discuss their personal opinions and committed to sustain the effort for a period of three years.

Not all symptoms are eligible for prospective research. The prevalence in the research population should be enough to acquire sufficient numbers. This depends on the inflow of new patients. A prevalence above 2% seems appropriate. Symptoms with higher prevalence should have priority for this kind of assessment; they constitute the larger repertory rubrics that are most polluted by 'mere chance entries'. On the other hand, symptoms with prevalence above 25% are not interesting for homeopathy because LR cannot be higher than 4, even if all patients of the corresponding medicine-population have that symptom.

The most eligible symptoms to assess are the so-called keynotes of the materia medica; these are symptoms characteristic for the medicine with higher prevalence. These are the symptoms we use everyday to detect or confirm our medicines. We counted about 600 keynote symptoms in Clarke's materia medica. A beginning research group can assess five symptoms, after experience with one assessment this group might handle eight symptoms at a time.

Acknowledgments

The doctors participating in this research were Rob Barthels, Hetty Buitelaar, Paul Fruijtier, Gerard Jansen, Jean Pierre Jansen, Stan Jesmiatka, Christien Klein, Roland Lugten, René van der Reijden, Lex Rutten, Erik Stolper, Janny Verhey and Mechtild Wijdeveld. The research was sponsored by KVHN (Royal Dutch patient's organisation for homeopathy), the Louise van Eeghen foundation, SFWOH (foundation for homeopathic research), the Blackie Foundation Trust and VHAN (Dutch homeopathic doctor's association). I especially thank Christien Klein, my colleagues from the Committee for

Methods and Validation, my wife and my daughter Martine for their help.

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- Submitted:** October 01, 2008.
Revised: December 07, 2008.
Accepted: December 24, 2008.

Clinical holistic medicine: A case of induced spontaneous remission in a patient with non-hodgkin *b-lymphoma*

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Abstract

This case is part of our research project with clinical holistic medicine (CHM) patients, who are treated with a modern version of the old Hippocratic character medicine in order to improve quality of life and health by rehabilitating the patient's character, life mission, and sense of coherence. A male 45 years old patient with non-Hodgkin B-Lymphoma diagnosed at the pathological institute of the University Hospital was cured within three months and 14 sessions of CHM and 250 hours of existential exercise. His ultrasound and CT-scans showed retroperitoneal tumours and his needle biopsy showed highly pathological cells of malignant lymphoma. The treatment with CHM was done, while the patient waited for the final diagnosis and biochemical cancer treatment. When he started he was in a very poor condition clinically; he was unable to work, unable to sleep due to constant fear, his self-assessed quality of life was low (measured by QOL1 and QOL5), his self-assessed mental health was low, and he had severe problems with his partner, including sexual problems. He was completely caught in the dark side of life and was tormented by the most evil obsessive fantasies of a violent character. Every relation he has to other people seemed negative and he had big problems relating to self and to the surrounding world. He was most definitely low in his sense of coherence. As his existential issues were solved in therapy his quality of life improved and his cancer disappeared.

Keywords: Quality of Life, QOL, philosophy of life, human development, clinical holistic medicine (CHM), salutogenesis, sense of coherence, spontaneous remission, cancer, alternative and complementary medicine (CAM), Denmark.

Introduction

The common definition of spontaneous remission is "a complete or partial, temporary or permanent

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disappearance of all or at least some relevant parameters of a soundly diagnosed malignant disease without any medical treatment or with treatment that is considered inadequate to produce the resulting regression (1). A search for “spontaneous remission and cancer” on Medline (www.pubmed.gov) December 20, 2008 gave 8,489 records, while in April 2004 the same search gave only 5,458 hits (2) documenting the intensity of the research in this area. Some remarkable examples are seen in several publications (3-42).

The incidence of spontaneous remission of cancer has been disputed. Some researchers found the phenomenon to be extraordinary rare, like 1-50 in 100.000 (43,44), while other researches believed the incidence to be 1:10.000 or even higher, as they without much effort found over 40 cases documented, but most of them not reported in the scientific literature (45). A massive under-reporting of the spontaneous remissions seems to happen due to the unwillingness of the physicians to recognise, appreciate, and investigate the phenomenon. Dige (45) found that about 2/3 of the patients had experienced some kind of spiritual awakening increasing the sense of coherence, before the remission took place, indicating that the patient himself played a central role in the process of healing.

The purpose of our intervention in the holistic clinic is strongly inspired by the work of David Spiegel et al (46), who helped women diagnosed with terminal cancer to improve their QOL in the remaining part of their life. After 12 months Spiegel and his co-workers demonstrated a significant improvement by various psychological tests: reduced pain, milder depression and less anxiety, so we believe that QOL can be improved for this group. Most importantly the intervention on quality of life seemed to improve survival time, and several patients had seemingly spontaneous remission of their cancer, surviving more than 10 years. David Spiegel showed one of the authors (SV) how he worked with these patients and how he supported the women in finding their internal and external resources for their struggle to improve the quality of life.

The concept used for the intervention in the Research Clinic for Holistic Medicine in Copenhagen (2,47) is close to the original concept of “natural healing” acknowledged and used by Hippocrates and

his students (48) and since that time by European doctors for over two millennia. The physician’s intent was to improve the patient’s quality of life, health and ability in general by the induction of existential healing (what Aaron Antonovsky (1923-1994) later called “salutogenesis” (49,50)). This was done by the combined recovery of human character (48,51), life mission, or purpose of life (51-57) and sense of coherence (49,50,58-63).

The focus of the original Hippocratic medicine seems to have been on the emotional and spiritual experience of what we today call the sense of coherence (48), as a recent analysis has indicated that the rehabilitation of emotions and sexuality (ESOC) (63) are core factors in the rehabilitation of sense of coherence and quality of life. The Hippocratic tradition of “character medicine” has as its core intent the rehabilitation of the patient’s character, including sexual character, so we feel safe to say that we practise holistic medicine in a manner very close to the original Hippocratic medicine, at least when it comes to the intent of inducing existential healing through the rehabilitation of character.

Regarding the mechanism of spontaneous healing it seems that the cancer cells are disappearing by apoptosis (for every cell, there is a time to live and to die and there are two ways in which cells die, either killed by injurious agents or they are induced to commit suicide. Programmed cell death is also called apoptosis), so a holistic cure for cancer is most likely to be successful if apoptosis can be induced (2). It might be a surprise for many researches, who follow the typical biochemical way of thinking, that induction of apoptosis seems quite possible and quite natural from a holistic medical perspective, as we believe that we are dealing with the same formative forces – the overall information system of the body (64-74) - in the body that induced apoptosis in embryonic life. If we radically can increase the coherence of the organism (49,50) and remove the disturbances that give the cells problems with their communication, the level of information in the tissues can be radically improved due to holistic healing (75) and the apoptosis thus induced, as apoptosis presumably happens as a function of the cells realising that it is not a natural and sound part of the body any more.

After having developed our research protocol for treatment of cancer patients with CHM (2,47), we have learned that other holistic therapists before us have tried and seemingly succeeded to induce spontaneous remission of cancer using similar, holistic principles (76).

Clinical holistic medicine

Clinical holistic medicine (CHM), or “quality of life as medicine” is a research program initiated by the late pediatric professor Bengt Zachau-Christiansen at the University Hospital (Rigshospitalet), Unit for Prospective Paediatrics, in 1990 (77). In 1997 it was clear that what we tried to do was re-vitalize the old tradition of Hippocratic holistic medicine, and a comprehensive protocol for complementary intervention on 1,000 somatically and mentally ill patients with a number of mild and severe health conditions (78), including cancer (2,47) and schizophrenia (79), were implemented. The Scientific Ethical Committee originally accepted the project in 1990 including intervention on mentally ill patients and children. We have reviewed the history of clinical holistic medicine (80) and our work lead us to use quality of life as medicine (78,81-84). For an overview of tools used in the CHM-therapy, please see (85,86). For the principles of healing taken into use, see (48,75). For the results from CHM-treatment on mental, somatic, sexual, and existential problems, see (87-91). Since 2000 the Nordic School of Holistic Medicine in Copenhagen has used this experience to train therapists and physicians in clinical holistic medicine.

What can be achieved with a patient with metastasized cancer?

The first and most important thing is to cooperate with the patient, helping the patient to achieve what is possible in every single case. This is extremely difficult, because the resources of the patient are often small, but if the will to live is strong, then there might be extraordinary resources in the patient. Therefore the assessment of the patient’s resources and direction is the first thing to do and everything depends upon

this judgment. The second thing is to understand the patient’s individual process of learning and transformation and especially what the patient is willing to give up in this process. If you want a new life, the price is your old life. So if you will not let go of your old way, values, perspectives and habits not much can be done for you in consciousness-based, holistic medicine. This willingness is in part related to the level of personal resources and in part related to the will to survive.

A general thing to learn from your cancer is that you can come closer to life (49,50). You can change, you can move into life, you can conquer the meaning of life, understanding its purpose and step into character more fully, being yourself more. This strange process of “becoming yourself” is what holistic medicine is all about, because you are this wholeness and healing is to become your true, whole self. So dependent of the resources, the will to live and the willingness to “let go of the ego and surrender” and take learning and thus transform into a more true and whole person, there is very little or very much that a holistic physician can do for his patient. The case in this paper is about a male patient with small resources, a strong will to live and with an impressive willingness to take learning and to transform.

A case story

The patient was a 45-year-old male Caucasian. He started in clinical holistic therapy [according to the research protocol (2,47)] the very same day he was diagnosed with non-Hodgkin B-Lymphoma at the pathological institute THG Århus University Hospital. His ultrasound and CT-scans showed retro peritoneal tumours and his needle biopsy showed highly pathological cells (T06002 (marrow from crista) M96003 (malignant lymphoma), M96103 (B-Lymphoma), P30990 (needle biopsy) P3A070 (enzyme histochemical examination) P3B000 (immune histochemical examination)).

He was in a very poor condition clinically, unable to work, unable to sleep due to constant fever, his self-assessed quality of life was low, his self-assessed mental health was low, and he had severe problems with his partner including sexual problems

(standard questionnaire administered at in-take). He was completely caught in the dark side of life and tormented by the most evil obsessive fantasies about cutting a woman into pieces with a sharp knife. Every relation he has to other people seemed to be negative, and he had big problems relating to self and to the surrounding world. He was most definitely low in his sense of coherence.

The therapy focused on helping him back into contact with his self and others also. It took three months of intensive therapy to make this happen. He entered into a huge personal crisis, where he mentally returned to childhood, cried constantly for a period of time as he re-experienced how he as child was treated badly by both his father and mother; during the therapy he confronted his childhood reality and learned how he then took all his parents problems in (called “introjections” in the therapy) and since then lived from that crippled existential position, spoiling his life for so many years. This process is called “spontaneous regression” in clinical holistic medicine, and it happens when a patient who intends to heal finally gets the resources necessary for the healing process (75). After the healing crisis (metamorphosis) he felt much better indeed. He actually did not feel sick anymore and started quite suddenly to work again.

In the meantime the hospital physicians had established his exact diagnosis and allocated the chemotherapeutic treatment. He therefore needed a final check-up at the hospital to establish the tumour burden and exact health status before initiating the treatment. But the scan now showed no sign whatsoever of the patient being ill. The patient told us that the hospital physician made a big cry out of surprise and used rather bad language. He just could not believe that the patient’s cancer had suddenly disappeared. The PET scan showed normal conditions and no area suspect for cancer. The CT-scan radiologist concluded: “Compared with the earlier CT scan (three months earlier) there are significant remission of earlier seen pathologically enlarged retro-peritoneal lymphatic glands” and in conclusion: “No sign of changes due to malignancy. The CT-scan shows complete remission of the retro-peritoneal tumours found earlier”.

The patient continued to go to control at the hospital for six months, but the cancer did not

reappear. Most interestingly the patient told the holistic therapist (SV) at that point that he now had got a completely new life – “as if he was part of a completely new movie”. Now he was able to love and be close and intimate to other people. He was happy with his girlfriend – whom he hated before and wanted to separate from. He felt good about himself and at home in the world.

During the process of healing his self-rated quality of life (QOL5) (92) went up from 3.2 (under neither good nor bad) to 2.2 (good), and his self-rated physical health went from 4 (bad) to 2 (good) on a five point Likert scale from QOL5. This was a large improvement of his quality of life, and a very large and radical improvement of his self-rated health, documenting the shift in his subjective experience of life and health. His self-rated quality of life (QOL) improved from 3 to 2 on the Likert scale as measured by QOL1 (92). He had a total of 14 sessions of CHM-treatment, and 250 hours (estimated) of exercise at home between sessions.

Discussion

Improving the quality of life can be done in a few days or weeks by the recovery of character, purpose of life and will to live. We believe from working with over 500 patients with clinical holistic medicine (CHM) that the gains on quality of life, health and ability in general are permanent. We have seen no significant side effects to the CHM-treatment, but patients often have temporary, developmental crises, when they overcome old trauma and enter into a new kind of life and experience (93).

Hippocratic medicine, in the modern form of CHM, have now been clinically tested on various samples of patients with physical illness and chronic pain, mental illnesses, sexual and existential problems, and we have found it surprisingly efficient. Often even severe health problems have been solved in only 20 sessions and one year of therapy.

We believe that all physicians are ethically obliged to take medical science a step further and develop new treatments, where the old ones have failed or are insufficient. We believe that holistic medicine can also help cancer patients subjectively to improve their quality of life; as we have already seen

happen in patients with a wide range of diseases. We are still developing the CHM-method, but we feel it is safe to conclude that the reason holistic medicine has been on the market for over 2000 years is that it is extremely efficient. The possibility that CHM actually can induce spontaneous remission of cancer indicates that Hippocrates' holistic medicine might be the most efficient medicine ever invented by man; it definitely seems to be the least harmful treatment for cancer we have if it works.

It is impossible to say if the spontaneous remission reported in this paper was actually induced by the CHM-therapy, but as it happened according to holistic medical theory, and as the subjective sense of coherence was recovered immediately before the remission of the cancer, we find it likely to be the case.

Holistic medicine aims at improving the patients QOL, and is thus compatible with any other treatment, biomedical or complementary. What is of great importance in the actual case is the extreme speed of the full recovery happening within only three months. For the many cancers known to grow slowly, it might therefore be considered to try a CHM-treatment just after the diagnosis and before engaging in the much more demanding chemotherapeutic treatment, that often has serious side effects. In this actual case, the treatment with CHM went so fast that the physicians at the hospital did not even establish the diagnosis and thus the rational biochemical cure, before the cancer was gone, probably due to the treatment with clinical, holistic medicine (CHM). This way of complementing a biomedical examination and treatment can only be considered as completely ethical and totally without any other problems, as it cures the patient without colliding with or postponing a chemotherapeutic treatment.

The recovery of human character, purpose of life, coherence, and will to live, with consciousness-based, holistic medicine (CHM) seems both fast and efficient in improving the QOL and health at least in some patients with cancer. We find it important that the holistic treatment for the patient highly motivated for personal development can be done with a limited number of hours of holistic therapy during a few days or weeks. From a holistic perspective cancer can be understood as a simple disturbance of the cells, arising from the tissue holding on to a trauma with

strong emotional content, in what we call "a blockage", allocating the function of the cells from their original function in the tissue to a function of holding emotions. Improving QOL and helping the patient to process and integrate these traumas might help the patients to survive longer or in some cases heal completely.

We believe that the consciousness-based/holistic medical toolbox has a serious offer to patients with metastasised cancer, and we will therefore strongly encourage the scientific society to explore these new possibilities. Our holistic medical research meets both ethical dilemmas and practical difficulties, but it seems evident from the presented case in this paper that the problems might be much less than we expected some years ago (2).

To support the patient in learning from his disease the mastery of coherence of body and life, and using the crisis of cancer to recover the human character and the purpose of life seems turning a personal potential disaster into the greatest gift of all. When it comes down to it, life is not just about surviving; what is more important is to live fully, to learn from the great challenges of life, and to obtain the optimal quality of life while being here.

The limitation of this research is that we are presenting a case study and not a large group of patients, but that is the possibility we have at the moment at the Research Clinic for Holistic Medicine in Copenhagen, which is a private clinic, where the patients themselves have to finance their treatment and the patient flow not as large as in a public medical center.

Acknowledgments

The Danish Quality of Life Survey and the Quality of Life Research Center has been supported by grants from the 1991 Pharmacy Foundation, the Goodwill-fonden, the JL-Foundation, E. Danielsen and Wife's Foundation, Emmerick Meyer's Trust, the Frimodt-Heineken Foundation, the Hede Nielsen Family Foundation, Petrus Andersens Fond, Wholesaler C.P. Frederiksens Study Trust, Else and Mogens Wedell-Wedellsborg's Foundation and IMK Almene Fond. The research was approved by the Copenhagen Scientific Ethical Committee under numbers (KF)V.

100.1762-90, (KF)V. 100.2123/91, (KF)V. 01-502/93, (KF)V. 01-026/97, (KF)V. 01-162/97, (KF)V. 01-198/97 and further correspondence.

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Submitted: October 11, 2008.

Revised: December 30, 2008.

Accepted: January 11, 2009.

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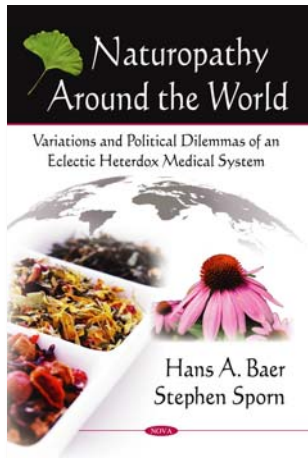


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Variations and Political Dilemmas of an Eclectic Heterodox Medical System

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Whereas various professionalized heterodox medical systems found in Western societies, such as homeopathy, chiropractic, osteopathy, Chinese traditional medicine, and even acupuncture have been the object of considerable historical and social scientific research, naturopathy has been, at best, spotty.

This book constitutes the first effort to provide a broad social historical and ethnographic account, particularly in the United States, Canada, and Australia, but to a lesser extent in Germany, Britain, New Zealand and India. Naturopathy emerged in the early twentieth century under the leadership of Benedict Lust, a German immigrant to the United States who had studied under Father Kneipp (a strong proponent of water cure), as a highly eclectic therapeutic system that drew not only from hydrotherapy, but

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Naturopaths or naturopathic physicians are the ultimate therapeutic eclectics within the broader confines of complementary and alternative medicine. Yet naturopathy is not a monolithic entity but has been shaped by historical developments in the larger plural medical systems and national sociopolitical contexts in which it is embedded. Like other medical systems, naturopathy is a cultural construction with fluid borders within specific countries across the globe.

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Binding: Hardcover ISBN: 978-1-60692-590-4
Pub. Date: 2009 Price: \$79.00

Acknowledgments

Introduction

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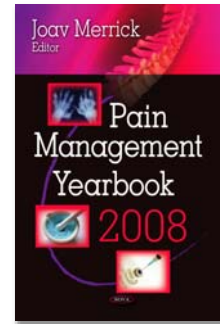
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Pain Management Yearbook

Joav Merrick
Editor



In the year 2008 the new "Journal of Pain Management" was begun under the auspices of the National Institute of Child Health and Human Development in Israel in collaboration with Nova Science Publishers in New York with the hopes of facilitating an outlet for peer-reviewed papers in the areas of pain and pain management from a holistic, practical, and clinical point of view. This yearbook for 2008 contains selected research published from the "Journal of Pain Management" by leading researchers from all over the world.

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Binding: Hardcover ISBN: 978-1-60692-867-7
Pub. Date: 2009 Price: \$145.00

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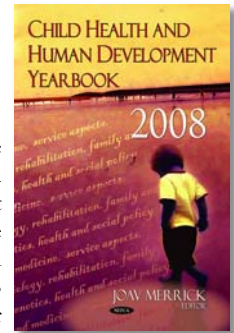
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CHILD HEALTH AND HUMAN DEVELOPMENT YEARBOOK 2008

JOAV MERRICK
EDITOR



The early years in the life of a child are critical for cognitive, social and emotional development. It is therefore important that we make sure that children grow up in an environment, where their social, emotional and educational needs are met. Children who grow up in an environment where their developmental needs are not met are at risk for compromised health, well-being and sometimes also developmental delays. Failure in the first years of life or lack of invested time or resources (both family and society) may have long term effects on not only development, but also the health, welfare and education systems. Society must therefore work to ensure that children develop in safe, loving, and secure environments. They are our future and our success or failure. This yearbook compiles the work done in 2008 with a broad research agenda on a global basis, addressing questions ranging from policy to practice, and spanning the developmental spectrum from human genetics, infancy and early childhood, to adolescence and adulthood.

Binding: Hardcover ISBN: 978-1-60692-979-7
Pub. Date: 2009 Price: \$145.00

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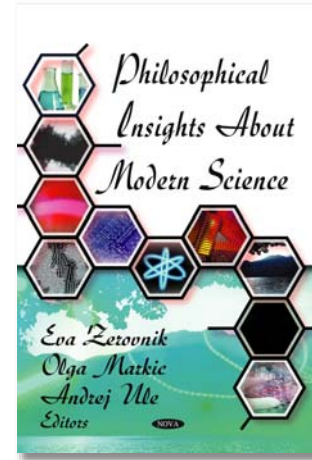
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Philosophical Insights About Modern Science

*Eva Zerovnik
Olga Markic
Andrej Ule*
Editors



Modern science is so much specialized that it seems utopic to try to follow it all at once. This new book is aimed at crossing the gap between specialists and a common understanding of 'modern science'. It would seem desirable that all educated people would know something from the humanities, literature, art but also the newest developments of natural sciences. One aim of this book is to point out the main messages of certain scientific fields, and what is really new and beyond the average educational level, in order to broaden our horizons. Therefore, at the end of the chapters each scientific field possible future contributions and and ethical concerns, if any, are elaborated.

Series: Scientific Revolutions ISBN: 978-1-60741-373-8
Binding: Hardcover Price: \$79.00
Pub. Date: 2009

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