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DENTAL INFECTION AND DISEASES OF THE NERVOUS SYSTEM

Part I: *The venous system as a route
for spread of bacterial products in the pathogenesis of
disseminated encephalomyelopathy*

By

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INTRODUCTION

The literature is exceedingly rich concerning the pathogenesis of different forms of disseminated encephalomyelitis. In the form labelled as disseminated sclerosis the *role of infection* has been discussed by many authors, i.a. *Pierre Marie* (29), *Dawson* (12), *Pette* (45), *Steiner* (52, 53), *Neumayer* (39), *Ferraro* (16).

To review the tremendous literature with regard to the role of infection as a pathogenic factor in all different disorders of the nervous system and in ophthalmic and otologic diseases is beyond the scope of the present paper.

In previous papers (54), I emphasized signs of *common bacterial infections* with streptococci, staphylococci and *E. coli* in disseminated sclerosis and suggested that the lesions of the central nervous system might be caused by *bacterial products* from foci of infection.

The purpose of this *part I* of the present investigation is

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mainly to review some long-established but still neglected facts concerning the vertebral and cephalic venous systems and to discuss their role in spread of microorganisms and their products from foci of infection.

In the following *part II* a detailed account of the clinical material with case reports will be published. At present only a short communication of the material is given.

SHORT SURVEY OF MATERIAL¹

The present investigation is based on data from my clinical material which consists of 400 cases. The 185 cases, labelled as disseminated sclerosis with "pluri-symptoms" from the central nervous system, fulfilled the following diagnostic criteria: bouts, two or several, with exacerbation and remission, in the case history, and signs of two or several disseminated lesions in the central nervous system at clinical examination.

The other 215 cases had different neurological "mono-symptoms" of cranial or cerebral localisation. Thus 10 cases of optic neuritis, 15 cases of eye muscle paresis, 25 cases of peripheral facial paralysis, 40 cases of vertigo rotatorica and 60 cases with epileptic fits (*epilepsia tarda*); 65 cases of headache were also included in the present material.

Each *case history* was taken with special regard to *common infections*. As previously reported (54) it was again found that disseminated sclerosis remarkably often made its appearance following upon an infectious disease, a severe throat infection, quinsy, a puerperal infection, a septic abortion, acute enteritis, exacerbation of an anal fistula or of a chronic rectal abscess, et cetera.

In the routine *laboratory examination* were included sedimentation rate, differential leukocyte count, serologic determination of antistreptolysin (AS) and antistaphylolysin (AS_t)

¹ A detailed account of the roentgenological and bacteriological investigation of dental apical osteitis in patients with disseminated sclerosis and other diseases of the nervous system will be published in co-operation with Åke J. R. Möller, L.D.S., Alf Öhman, L.D.S., Lars-Åke Hansson, M.B. & Eva Lundstedt, L.D.S.

titers. The normal limit and evaluation of these titers have been discussed in earlier papers (54).

Dental examination.

In all patients a case history was taken with regard to earlier and present dental infections, including a complete roentgenological dental examination.

It was interesting to note that the patients often spontaneously reported the history of dental infection or dental abscess preceding their first symptoms of disseminated sclerosis, in the form of e.g. visual disturbance, diplopia, vertigo.

As earlier published (*Störtebecker, Öhman, Möller and Hansson* (58), 1958) out of 150 cases of disseminated sclerosis roentgenologically examined 94 per cent (141 cases) showed signs of dental apical osteitis.

A very high frequency of *dental apical osteitis* was found in the present material at roentgenological examination.

With regard to the possibility of dental infection one has to keep in mind *impacted teeth* with *pericoronitis*. The parodontosis, too, might represent serious foci of infection.

The fact is that a chronic dental apical infection may exist during a long period before giving a roentgenologically perceivable apical damage. This circumstance induces a great difficulty in evaluating the roentgenograms and necessitates therefore a bacteriological examination of the suspected teeth.

Bacteriological examination of dental apical osteitis.

A special surgical technique (*Möller* (34, 35, 36), *Möller & Öhman* (37, 38, 61)) is employed when the samples are taken from patients with apical osteitis; this to avoid contamination from microbes present in the oral cavity. The samples are cultivated so that the presence of any cultivable micro-organisms might be demonstrated (*Möller*).

Many different micro-organisms, aerobic and anaerobic ones, have been cultivated from dental apical osteitis in the patients with disseminated sclerosis.

Electroencephalography.

EEG has been performed before and after clearance of foci of dental infection (see later).

DISCUSSION

Concerning the dissemination of micro-organisms and their products within the body

Discussing the role of foci of infection two main factors are important:

The *mode* of dissemination of micro-organisms and their products within the body from foci of infection.

The *kind* of micro-organisms and their products spread from foci of infection.

Concerning the mode of dissemination only the following routes will be mentioned: 1. *Arterial* route; 2. *Venous* system; 3. *Lymphatics*; 4. *Nerve* trunk.

1. *Dissemination of micro-organisms and their products by the arterial route.*

After their entry into the circulation bacteria and bacterial products may spread by the arterial blood stream to different organs of the body.

Depending on the kind of material spread and the defence mechanisms of the body either a polyarteritis or a local arteritis might develop, followed by a peri-arterial inflammatory reaction or even an infectious metastatic abscess.

In this way acute or chronic inflammatory changes may be produced in many different organs, e.g. the brain (encephalitis, brain abscess), spinal cord (myelitis), skin, muscles and joints (dermatitis, myositis and arthritis), heart (endocarditis, myocarditis with infarction from coronal arteritis), lungs (asthma), kidneys (nephritis), thyroid (thyroiditis, hyperfunction), pancreas (pancreatitis, diabetes), spleen and bone marrow (hematopoetic diseases, leukemia).

2. *Dissemination of micro-organisms and their products by the venous systems of the central nervous system.*

The main venous systems which belong to the central nervous system consist of the *vertebral* venous system and the *cephalic* venous system, communicating with each other.

The vertebral venous system.

It is interesting to note that the *vertebral veins* have been described more than 400 years ago. According to the English anatomist *Harris* (1941) (22) they have been known since the time of the Italian *Gabriel Falloppio* (1523-1562), and *Thomas Willis* (1664) (60) gave a clear account of the spinal veins and described the internal longitudinal anastomoses of the spine as "vertebral sinuses" and depicted their communications with the occipital sinuses of the dura mater.

Bock (1823) (7) demonstrated most completely the rich venous plexuses of the spinal canal, and he pointed out that the *sacral* branches of the internal iliac veins, as well as the *lumbar*, *thoracic* and *cervical* veins *communicate freely* with the veins within the spinal canal *through the anterior spinal foramina*. He also described in detail all the communications with the cranial venous sinuses.

These long-established facts, familiar to the anatomists, seem to have been almost unknown to the pathologists and clinicians of this century until *Batson* (1940) (4) proposed that metastases may reach the brain by way of the vertebral vein complex.

Batson *roentgenologically* demonstrated in cadavera the pathway for spread of possible infection or neoplastic cells from the dorsal vein of the penis and pelvic veins via the bone-protected vertebral venous system of the spinal column up to the skull, and completely by-passing the inferior vena cava and the lungs.

Injection experiments in *living monkeys*, with simulated abdominal straining, show that the venous flow from pelvic veins may be into vertebral vein system (*Batson* 1940) (4).

The results in Batson's experiments in the live animal seem clear-cut, but still medical men were unaware of the pathological and clinical implications of the vertebral venous system. Thus e.g. the neurosurgeon *Percival Bailey* (1948) (3) considered Batson's observations to be illogical.

Studies by *Anderson* (1951) (2) gave further supportive evidence of possible routes for spread of metastases via the vertebral venous system from distant primary foci to the cerebrum. He demonstrated the close relationship of this venous system with the veins of other structures, such as the prostate, kidneys and adrenals, lungs, breast and thyroid.

Knowledge of the vertebral venous system in spread from urogenital foci of infection has been given by several authors (1, 32, 40) and of interest is the investigation of pelveo-spondylitis by *Romanus* (1953) (48).

The roentgenologists *Helander & Lindbom* (1955) (23) in an excellent study *in man* of sacrolumbar venography, by injection of contrast medium through a catheter in the femoral vein, confirmed that the blood may be forced up through the vertebral veins during the physiologic circumstance of straining (Valsalva's experiment).

With regard to this last-mentioned investigation in man I would like to mention that even chronic infected varicose veins and phlebitic lesions of the lower extremities should be regarded as foci of infection.

Concerning the role of the vertebral veins in metastatic processes as a pathway for the *spread of disease between remote organs* the following observation of *Batson* (1942) (5, 6) is noteworthy. After the injection of coloured latex emulsion of the deep dorsal vein of the penis in cadavera the sub-papillary *venous plexuses* of the skin of the *face* are also injected (cf. butterfly erythema). Experiments which indicate the free communications present.

The cephalic venous system.

The normal and morbid *anatomy* of the veins and dural sinuses of the brain, well known to older anatomists, has been

elucidated especially by aid of roentgenological examination (i.a. *Johanson* 1954) (25).

The *spread of infections* via the cephalic venous system has been stressed i.a. by *Sicher* in his "Oral Anatomy" (1952) (51), from whom the following is quoted:

The complications of the system of veins in the head and neck are still enhanced by the fact that *intracranial* veins, draining the blood of the brain, and *extracranial* veins are connected by *multiple anastomoses* which permit a *flow of blood in both directions*.

The anastomoses between the veins of the brain, which is enclosed in a rigid bony capsule, and the extracranial veins are safety outlets. Their existence prevents a rise of the intracranial pressure which would occur if the internal jugular vein, the main drainage of the cerebral blood, were compressed. In this case the venous blood of the brain can escape in many directions.

These communications are, however, a *potential danger because an infection*, involving primarily an extracranial vein, for instance one of the facial veins, *may spread to the intracranial veins and involve the meninges*. The danger of a *retrograde spread of infection* is the graver, because the veins of the face have few, if any, *valves*, which in other veins prevent a backflow of blood.

In addition one has to remember that the intracranial veins, collecting the blood of the brain, are not collapsible. The rigidity of the walls of the sinus prevents any change in their lumen and renders them *open ways for the spread of infection*.

The *communications of the ophthalmic veins* with the anterior and posterior facial veins are of special importance in the pathology of facial infections.

Where palpebral and nasal veins join at the inner corner of the eye, the angular vein constantly is in *wide communication* with the superior ophthalmic vein.

The *superior ophthalmic vein* which opens into the cavernous sinus *forms thus a wide link between the anterior facial vein and the intracranial sinuses* of the dura mater.

A *second important anastomosis*, between the veins of the orbit and the posterior facial vein, connects the posterior end of the inferior ophthalmic vein with the *pterygoid plexus* of veins, from which the posterior facial vein receives most of its blood. The anastomosing branch passes through the inferior orbital fissure and *links* the system of the *posterior facial vein* with the *cavernous sinus*, *behind* the orbit (Sicher) (51).

The *flow of blood* in this valveless venous system may be altered by changes of posture of the body. One-sided position of the head during rest and sleep, or a bending forward may direct the flow in other pathways than is the case in the upright posture of the head.

Other factors of importance are coughing, sneezing, vomiting and the fact that almost everybody during hard straining automatically and simultaneously is biting his teeth.

Furthermore we ought to keep in mind that bacteria or their products passing by the venous drainage through the cephalic or vertebral venous system afterwards reach the general circulation and follow the arterial blood stream out into the body.

Thus a part of the central nervous system where beforehand a periphlebitic lesion has been induced, represents a locus minoris resistentiae, and may be superponed by another lesion of bacterial products spread by the arterial route.

3. *Dissemination of micro-organisms and their products by lymphatic pathways from dental foci of infection.*

The knowledge of spread of bacteria and bacterial products from dental foci via lymph vessels is of great importance.

Sicher (1952) (51) i.a. comments with regard to lymph vessels draining the pulp and periodontal tissue the following: The lymph vessels draining the incisors and the cuspids of the upper and lower jaw run anteriorly; those draining the molars are directed posteriorly. The bicuspidis are situated in a critical area and their lymph may be drained anteriorly or posteriorly.

The dental lymph vessels from the *anterior* part of the

upper jaw pass through the anterior superior alveolar canals and emerge into the face through the infraorbital foramen.

The *posterior* maxillary lymph vessels collect at the maxillary tuber after passing through the posterior superior alveolar canals.

From the infraorbital foramen the *anterior* maxillary lymph vessels follow the *anterior facial vein*. The *posterior* lymph vessels find their way along contributaires of the *posterior facial vein*.

The lymph of all teeth, with the possible exception of the lower central incisors, reaches, as a rule, the *submandibular* lymph nodes. However, some dental lymph vessels, arising in the molar region of the upper and lower jaw, may reach directly one of the anterior superior *cervical* lymph nodes, which otherwise are secondary to the submandibular and submental nodes.

It is a general rule that some of the lymph vessels which take their origin close to the midline *cross* to the other side. The median parts of the lips, of the tongue, and of the palate are, therefore, drained to both sides.

It is clear that this behaviour of the lymph vessels influences the propagation of infections or malignant tumors and that the therapy has to take this circumstance into consideration (*Sicher*) (51).

Invasion of bacteria or bacterial products into lymph vessels may induce involvement of the veins. The abovementioned localisation of the dental lymph vessels close to the facial veins may, in case of dental foci of infection, give spread of bacterial products into the facial perivenous spaces.

There are two main types of propagation of a facial ascending phlebitis or periphlebitis to the cavernous sinus. *One path* leads, as mentioned above (*Sicher*) (51), from the anterior facial vein by way of the ophthalmic veins through the orbit. The *other path* leads from the posterior facial vein through the pterygoid venous plexus to the cavernous sinus without orbital involvement.

Spread of inflammatory involvement along the perivenous

space of facial veins may thus induce *intracranial* periphlebitic lesions.

The simple *palpation* of the neck and scalp with finding of an enlarged or tender lymph node might indicate a dental apical osteitis situated on the corresponding side.

4. *Dissemination of micro-organisms and their products along nerve trunks.*

This route of transportation has been studied i.a. by *Payling Wright* (42, 43, 44), who has given excellent reviews of this item. According to him it is clear that the idea that nerve trunks form potential conductors of pathogenic agents to the brain and spinal cord had already found a place in Pathology more than a century ago.

This mode of dissemination in e.g. rabies, tetanus, poliomyelitis has been emphasized by several authors. Implantation of "neurotropic" virus in a scarified cornea on rabbits and its pathway by the trigeminal nerve has been studied by i.a. *Marinesco & Draganesco* (30, 31) (1923, 1932), *Goodpasture & Teague* (19) (1923).

Further *Teague & Goodpasture* (59) (1923) produced in guinea pigs and rabbits an experimental disease, analogous clinically and pathologically to zoster in man, by inoculating the tarred skin with the virus of herpes simplex.

Their excellent experiments (59) illustrate that peripheral lesions may induce lesions of the central nervous system and that the cause of the central lesions may be traced if we examine the possibility of spread from the periphery along the corresponding nerve trunks.

The conditions are present for spread of micro-organisms and their products from a *dental apical osteitis* in man along the trigeminal nerve to the Gasserian ganglion and the base of the skull. The possible pathways along small perineural venous plexuses ought to be considered.

Acute inflammatory local reactions, as well as chronic fibrotic adhesions might be evoked around the nerve trunk and the

ganglion, i.e. causing symptoms of paresthesia, headache and trigeminal neuralgia.

Whether spread of bacterial products from *common dental foci of infection* along the nerve trunk might cause other diseases of the central nervous system is still open to further investigation.

Kind of micro-organisms and their products spread from foci of infection.

The following items have to be considered: *Firstly* the spread of micro-organisms themselves, *secondly* the spread of toxic products of bacterial metabolism, *thirdly* the time factor or the duration of exposure to the injurious action of bacterial products.

Traumatizing of an infected area may account for *spread of bacteria*. Thus from uro-genital foci spread of bacteria was shown by positive blood culture in 45 per cent of patients immediately after transurethral prostatic surgery (10).

From dental foci of infection spread of bacteria was reported almost 25 years ago, by *Okell & Elliott* (41) who found bacteremia within a few minutes after extraction of a tooth.

With every movement of *mastication*, pressure on a tooth with an apical osteitis must tend to force bacterial products from the osteitis into the surrounding periodontal tissues and further out into the body.

At every meal there exists a possibility of spread of *bacterial products* from dental foci of infection. Some people, too, bite their teeth during night. Traumatizing, hard chewing, as well as intercurrent infections, especially located in the vicinity, as a sinusitis or a throat infection, might alter the local tissue response and produce a flare up of a dental apical infection.

The *mode of the injurious action of bacterial products* varies i.e. according to their specific enzymatic or toxic qualities, e.g. hemolytic, proteolytic, cytotoxic, neurotoxic. The growing bacteria, through their metabolic activities, may liberate

substances which are highly injurious to the cells of the host (e.g. minute amounts of the botulinus toxin induce severe paralytic and myasthenic symptoms).

With regard to the possible injurious action of *common bacteria and their products* some observations have to be considered. The studies of the carcinogenic effect of cyclic hydrocarbons are too well known to be commented here, but a few data which might be of interest in this connection will be mentioned.

25 years ago it was shown that bile acid, through the step of dehydronorcholene, may be converted into potent carcinogenic substances. *Cook & Haslewood* (9) (1934) commented that their experiments "thus show how it is possible for a natural product of animal metabolism to be converted into a carcinogenic compound by simple transformations of a biochemical character (oxidation, reduction, dehydration, decarboxylation, dehydrogenation)".

The carcinogen methyl-cholanthrene i.a. by implantation into the brain evoked gliomas (*Seligman, Shear & Alexander* (49), 1939).

Almost 20 years ago the interesting discovery was made that the *common intestinal bacteria*, *E.coli*, when cultivated on a medium containing dehydronorcholene, formed a substance producing neoplasma in rats (*Druckray, Richter & Vierthaler* (13), 1941). These authors also reported the finding of a local sarcoma after a latent period of 18 months from injections of extract of *E.coli*.

Henschen (24) has seen an interesting case (21) where at the neurosurgical intervention a cerebral tumor of *mycotic* origin was found. Some months later the autopsy revealed a glioblastoma of the same cerebral localisation.

Among more recent works of the metabolism of microorganisms, their production of enzymes and toxins, it is of interest to note that the metabolism of carcinogenic hydrocarbons may be influenced by soil bacteria (e.g. *Lijinsky & Quastel* (27), 1956).

Discussing the possible injurious action of bacteria one

might remember e.g. achlorhydria and cancer ventriculi, lack of normal vaginal flora and cervix cancer.

An important observation is that common bacteria, e.g. *E.coli*, cultivated on a medium of primary carbohydrates, as acetates, *can synthesize very complex cyclic hydrocarbons* (Ehrensward (15), 1958).

With regard to the *time of exposure* it is noteworthy that if the duration of exposure is long enough, even minute amounts may be highly injurious; e.g. Shear (50) (1936) observed that 0.4 gamma of dibenzanthracene in pellets implanted subcutaneously on mice gave a local neoplasma which started growing after an exposure time of 13 months.

The chronicity of a dental apical osteitis implies that this kind of foci of infection might give an *exposure* of the human body *to bacterial products during several years*, day after day. Even if the doses of bacterial products spread within the body are very minute, the long duration of exposure may induce a serious injury.

One might really ask if civilized man, harbouring dental apical osteitis, jeopardizes his health.

Mode of tissue defence against micro-organisms and their products.

The vascular phenomenon of inflammatory reaction is a defensive tissue response to the action of a wide variety of infectious or other injurious agents.

With regard to the local protective reaction of the tissue we have to consider different cellular factors in defence, especially the problems of non-immunity or immunity, the formation of different antibodies, antitoxins, etc.

The eventuality of allergy, local tissue sensitization and anaphylactic reactions, must be taken into account evaluating the histopathologic picture of perivascular lesions in disseminated encephalomyelitis.

The concept of infectious-allergic or toxic-allergic etio-pathogenesis of acute and chronic disseminated encephalo-

myelitis has been elaborated i.a. by *Ferraro* (16), who concluded that the ultimate pathogenic mechanism responsible for the clinico-pathologic changes will remain an allergic one.

My opinion, however, is that in most cases the bacterial products themselves are fully potent to induce a defensive tissue reaction with a perivascularitis.

*The pathogenesis of periphlebitic lesions in
disseminated sclerosis.*

From a histopathological point of view the periphlebitis, with secondary demyelination and gliosis, seems to be characteristic of disseminated sclerosis. According to i.a. *Broman* (8), *Fog* (18) the perivascular inflammatory reaction of the central nervous system is always localized to a vein, thus it is a *Periphlebitic lesion*.

Despite numerous investigations, no satisfactory explanation of the pathogenesis of the plaques in human disseminated sclerosis has hitherto been given.

If we classify the various neurological symptoms of disseminated sclerosis according to their localization, it might be easier to trace the cause of each separate lesion.

Symptoms localized to the orbito-facial region.

Periphlebitis retinae (*Haarr* (20)), chorioiditis, optic neuritis, eye muscle paresis with diplopia, might well be explained in view of my opinion that a periphlebitic lesion is caused by dissemination of bacterial products from a chronic dental infection, by i.a. spread through the ophthalmic veins to the cavernous sinus. Of special interest is the periphlebitis retinae because of its localisation, at least 3 to 4 papillary diameters from the papilla (*Haarr* (20)). The possibility of spread of a periphlebitis from the ophthalmic vein along the venae vorticosae should be considered in those cases. I have also seen papillary edema, choked discs, and pseudotumor cerebri probably caused by spread of periphlebitis from dental foci, containing i.a. hemolytic streptococci. The typical disturb-

ance of the visual field starting with one-sided defect nasal downwards may be caused by spread of bacterial products inducing a periphlebitis of the superior ophthalmic vein which crosses over the optic nerve before reaching the cavernous sinus.

Based on my experience from the present material I recommend to scrutinise the samesided teeth, especially in the upper jaw, with regard to possible foci of infection in all cases of eye involvement.

Peripheral facial paralysis might be caused by spread of bacterial products rather through lymphatics than by the venous route.

Symptoms due to lesions with cerebral localisation.

A chronic toxic encephalopathy may be caused by the more or less constant drainage of bacterial products from dental apical osteitis out into the venous circulation of the brain, especially via the cavernous sinus.

Periphlebitic lesions may spread into the brain parenchyma and induce demyelination, gliosis and scars, which may give rise to epileptic fits. Depending on their localisation the lesions may evoke motor or sensory disturbances, auditive or visual hallucinations, psychic symptoms, et cetera.

In this connection it might be of interest to mention the studies of *Lumsden* (28) concerning the distribution of plaques in different types of demyelinating encephalopathies and their correspondance to the venous drainage areas.

Spread of bacterial products from the cavernous sinus along the superior petrosal sinus to the small veins of the cochlea and labyrinth might induce toxic lesions of the inner ear (e.g. cases of Ménière).

Venous communications exist and conditions are present for spread of bacterial products in many different directions of the brain.

On the base of the skull there are rich venous plexuses in the pituitary and diencephalic region. Periphlebitic or toxic lesions

localized to this part might cause many different symptoms, i.a. endocrine or metabolic disturbances, imbalance of the autonomic nervous system, the blood pressure etc.

Extensive toxic periphlebitis might in some cases even induce thrombosis, cerebral softening, with hemiparesis or hemiplegia. The infectious origin should especially be kept in mind if these cerebral symptoms occur in people without hypercholesterolemia.

Symptoms due to lesions with spinal localisation.

A toxic myelopathy may be caused by spread of bacterial products from foci of infection of many different viscera, especially of the uro-genitary tract, in man from *prostatic infections*, by the route of the vertebral venous system.

The communication between the cephalic and vertebral venous systems might give dissemination of bacterial products into all parts of the central nervous system from dental foci, as well as from urogenital foci (e.g. ascending paralysis and cranial sinus thrombosis after septic abortions are well-known facts). Batson (5) (1942) also pointed out the possibility of spread of air emboli which sometimes follows the diagnostic perirenal insufflation of air.

The *principle of the shortest pathway*, however, should be kept in mind searching a focus of infection which might induce a periphlebitic lesion.

In a case of optic neuritis it is more likely to find the focus of infection in the neighbourhood, in a dental apical osteitis or a sinusitis, than in a far away uro-genital infection.

In a material (58) of 150 cases of disseminated sclerosis, 5 patients were already edentulous at examination and had not shown symptoms localized to the orbitofacial region after the time they had undergone dental clearance. Yet, they had shown symptoms of spinal localisation and i.a. infections in gallbladder and genito-urinary tracts.

With regard to the pathogenesis of symptoms of *spinal localisation* in disseminated encephalomyelitis, the highest pos-

sibility for spread of bacterial products via venous plexuses in the *female* is from the uterine cavity.

The *uterine cavity* has a large venous drainage that may reach the vertebral venous system. Thus in females suffering from salpingo-endometritis a spread of bacterial products might cause periphlebitic lesions of the spinal cord.

I have seen cases where the initial symptoms with continuous paresthesia in the lower extremities (lumbo-sacral localisation) started the first day of a menstrual bleeding. The possibility of spread of bacterial products is enormously high at each menstruation when the mucosa is detached from the uterine wall, that is being left with partly open vessels through which bacteria or bacterial products by the venous drainage might spread to the pelvic veins and further to the vertebral venous system. With regard to the age incidence of disseminated sclerosis in women and spinal symptoms it is also of interest to note that its peak correspond to the fertility period.

Disseminated sclerosis viewed as multiple perivascular lesions of the central nervous system due to the injurious action of bacterial products spread from different foci of infection.

The clinical picture labelled as disseminated sclerosis is so polymorphous that several authors have thought it inappropriate to consider disseminated sclerosis as a *morbus sui generis*.

This opinion was held already by *Pierre Marie* (29) (1884) who stressed that disseminated sclerosis was due to vascular disturbances caused by many different diseases of infectious origin.

Ferraro (16), 1958, i.a. points out that the toxic or infectious etiologic component may be different in various groups of cases.

He (16) too, comments with regard to the different neurological symptoms appearing in bouts: A latent phase of 10 to 30 years seems quite a long time to establish any definite relationship between the initial episode and the relapse.

The role of allergy in the etiology of disseminated sclerosis is en vogue and i.a. based on the concept that experimental allergic encephalomyelitis should be analogous to human disseminated encephalomyelitis. This interpretation seems rather loose, and in this connection I would like to mention the fact that perivascularitis is also found in the musculature of guinea pigs with experimental allergic encephalomyelitis (*Ferraro & Roizin* (17) 1953). Both from a histopathological and clinical point of view I consider these findings (17) of perivascularitis elsewhere than in the central nervous system to be noteworthy. Several earlier clinical reports (e.g. *Querido* (47), *Dansmann* (11), *Störtebecker* (55, 56)) described cases with inflammatory perivascular changes simultaneously in both the musculature and in the nervous system.

To clear up the etiology in those cases it is necessary to differentiate the types of perivascularitis, the peri-arteritic and the peri-phlebitic ones, as their pathogenesis varies depending on the different mode of dissemination of toxic substances.

Concerning the pathogenesis of perivascular lesions in disseminated encephalomyelitis it seems to be no doubt that their causative factors may differ, even with regard to each separate lesion of the central nervous system.

It is, therefore, too artificial to link all these heterologous neurological symptoms, of different origin and even occurring at intervals of several years, together under a common heading, labelled disseminated sclerosis.

Prigal (46) (1956) in a critical review of allergy and disseminated sclerosis makes the sound conclusion that disseminated sclerosis may be a syndrome due to a variety of causes.

It is time to abandon the questionable entity of disseminated sclerosis, as well as many other obscure disease entities. In medicine we should try to trace the etiology of each separate neurological symptom and treat its causative factors.

Discussion of therapeutic measures and their evaluation.

About 50 years ago the theory was advanced that *dental foci of infection* were implicated in the causation of a number

of systemic conditions, particularly in diseased conditions of the joints. Countless teeth were removed in an effort to cure or relieve various systemic disorders.

In an extensive review, with "evaluation of the effect of dental foci of infection on health", *Easlick* (14) (1951) commented that "over the years close observation of the benefits derived from the promiscuous removal of teeth led members of both the dental and medical professions to question the soundness of the theory".

Thus the theory of dental infection gradually lost caste, and now has reached low ebb.

It is always difficult to judge the results of therapeutic interventions. The *clinical picture* supplemented by laboratory examinations may help us in evaluating our treatment.

If, coinciding with the clearance of dental foci of infection, *firstly* the patients get relief of their present neurological symptoms, as i.a. vertigo, headache, epileptic fits, and if, *secondly*, new neurological symptoms do not appear, we might be allowed to conclude that the patients benefit from the therapy.

In the present material clearance of dental foci of infection gave a clinically striking therapeutic effect.

As a guidance to therapeutics I have used some *laboratory examinations*, by aid of which we may get a view of the course of the disease.

Serological determination of the antistreptolysin titer. Normalisation of raised titer values followed clearance of foci of infection; a finding that supports the view that i.a. hemolytic streptococci might play a role in the pathogenesis of disseminated sclerosis.

A pathologic differential leukocyte count, too, normalized subsequent to clearance of dental foci of infection.

A pathologic cerebrospinal fluid, with pleocytosis and a positive colloidal curve, showed normalisation after dental

clearance in cases, where other foci of infection, too, had been eliminated.

EEG. In order to evaluate any therapeutic measure of a cerebral disease and to follow its course the EEG may be of valuable aid.

The EEG-findings correlated to the local site of dental apical osteitis. Patients with a pathological activity on EEG often showed a dental apical osteitis on the same side as the dominance of abnormality on EEG. A tendency to a focal abnormality with frontal or fronto-temporal localisation on EEG corresponded often to a finding of a dental apical osteitis in the upper jaw. This observation showing abnormalities on EEG, implying cerebral lesions, *homonymously linked* to the local site of a dental apical osteitis, might seem too schematic.

Yet, the pathways of bacterial products from a dental apical osteitis into the cephalic venous system may well explain the different findings on EEG in cases with apical osteitis located to the upper and to the lower jaw.

I would like to mention that the clearance of the dental foci of infection induced clinical improvement, and that regression of EEG-abnormalities has been observed. An impressive effect was seen in cases of vertigo, headache and epilepsy, coinciding with treatment of dental foci of infection.

Bearing in mind the *propagation* of bacterial products from dental foci of infection and the *existing pathways* for spread to the central nervous system, I have correlated the cerebral lesions of the cases to their corresponding foci of dental infection.

The EEG has been of valuable aid to me in tracing dental foci of infection and in planning the treatment of the corresponding foci of dental infection, instead of extracting suspected teeth on loose grounds.

It is peculiar to note how difficult it sometimes may be to convince patients, even highly educated ones, how dangerous

it is to harbour chronic dental apical osteitis beneath their golden dental crowns.

Instead they go away to benefit the *climate* of the Canaries, Belgian Congo or an oasis in Sahara, where the natives live in freedom of disseminated sclerosis.

Yet, they get new bouts of their disease during the stay at those places. Why? I have seen i.a. 3 cases of disseminated sclerosis who all brought with them their chronic dental apical osteitis (verified on roentgenological examination).

Each masticatory movement, even in such a nice climate, gives rise to a flow of bacterial products from dental foci of infection out into the body by different routes.

I am fully aware of the general high frequency of dental apical osteitis among the population of modern civilized countries, and my opinion is that just those dental foci of infection cause a great deal of different diseases characteristic of occidental civilisation.

I would stress that chronic dental infection (apical osteitis) is so tremendously frequent among the population of western civilisation, that in cases showing nervous symptoms of cranio-cerebral localisation, it is from a therapeutic point of view in the first hand advisable to search the etiologic factor in a homonymously located dental apical osteitis. Whether one conceives, or not, that dental apical infections may induce symptoms from the nervous system, as disseminated sclerosis, vertigo, epilepsy, headache, as well as from other organs of the body it is in any case advisable to treat dental apical osteitis from a prophylactic point of view.

CONCLUSIONS

with regard to dental infection in the pathogenesis of cranio-cerebral symptoms in disseminated sclerosis.

In view of my opinion that bacterial products from chronic dental infection (apical osteitis) play an important role in the pathogenesis of cephalic symptoms in disseminated sclerosis, several problems (26, 33) might be cleared up.

The cause of the uneven geographical distribution of disseminated sclerosis, its rarity among natives in the tropics and subtropics and its high prevalence among people of modern civilisation, might easily be explained, as well as the following characteristics of disseminated sclerosis; lack of evidence of patient-to-patient transmission, rarity of twin and conjugal occurrence, inability to transfer the disease from human beings to experimental animals, lack of response to heavy dosage of chemotherapeutics and antibiotics by oral or parenteral administration. I would like to mention the well known fact that dental apical osteitis is only accessible to local therapy.

SUMMARY

The *mode of dissemination of micro-organisms and bacterial products* from foci of infection has been reviewed, with special regard to spread along the vertebral and cephalic venous systems of the central nervous system.

The *dissemination of bacterial products from dental foci* of infection into the *cephalic venous system* is commented. Spread of bacterial products from dental foci along the ophthalmic veins through the orbit to the cavernous sinus may count for same-sided *periphlebitic* lesions of retina, optic nerve, eye-muscles or their nerves.

Further spread of bacterial products, inducing periphlebitic lesions and chronic irritation of the brain parenchyma, may give rise to a *toxic encephalopathy*.

My opinion is that cranial and cerebral symptoms, artificially labelled together under the heading of i.a. disseminated sclerosis, may be due to bacterial products spread along the venous cephalic system from foci of chronic dental infection, causing e.g. periphlebitis and toxic encephalopathy. The pathogenesis may be analogous in many cases of vertigo, headache, epilepsy.

In view of this, a bacterial toxic periphlebitis or local toxic encephalomyelopathy might induce any neurological symptoms of the central nervous system, Depending on its localisa-

tion, the lesion will utter motoric, sensoric or psychic manifestations.

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