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Does an infrasonic acoustic shock wave resonance of the manganese 3+ loaded/copper depleted prion protein initiate the pathogenesis of TSE?

Mark Purdey

Elworthy, Taunton, Somerset, UK

Summary Intensive exposures to natural and artificial sources of infrasonic acoustic shock (tectonic disturbances, supersonic aeroplanes, etc.) have been observed in ecosystems supporting mammalian populations that are blighted by clusters of traditional and new variant strains of transmissible spongiform encephalopathy (TSE). But TSEs will only emerge in those 'infrasound-rich' environments which are simultaneously influenced by eco-factors that induce a high manganese (Mn)/low copper (Cu)–zinc (Zn) ratio in brains of local mammalian populations. Since cellular prion protein (PrPc) is a cupro-protein expressed throughout the circadian mediated pathways of the body, it is proposed that PrP's Cu component performs a role in the conduction and distribution of endogenous electromagnetic energy; energy that has been transduced from incoming ultraviolet, acoustic, geomagnetic radiations. TSE pathogenesis is initiated once Mn substitutes at the vacant Cu domain on PrPc and forms a nonpathogenic, protease resistant, 'sleeping' prion. A second stage of pathogenesis comes into play once a low frequency wave of infrasonic shock metamorphoses the piezoelectric atomic structure of the Mn 3+ component of the prion, thereby 'priming' the sleeping prion into its fully fledged, pathogenic TSE isoform – where the paramagnetic status of the Mn 3+ atom is transformed into a stable ferrimagnetic lattice work, due to the strong electron–phonon coupling resulting from the dynamic 'Jahn-Teller' type distortions of the oxygen octahedra specific to the trivalent Mn species. The so called 'infectivity' of the prion is a misnomer and should be correctly defined as the contagious field inducing capacity of the ferrimagnetic Mn 3+ component of the prion; which remains pathogenic at all temperatures below the 'curie point'. A progressive domino-like 'metal to ligand to metal' ferrimagnetic corruption of the conduits of electromagnetic superexchange is initiated. The TSE diseased brain can be likened to a solar charged battery on continuous charge; where the Mn contaminated/Cu depleted circadian-auditory pathways absorb and pile up, rather than conduct the vital life force energies of incoming ultra violet, acoustic and geomagnetic radiation. Instead of harnessing these energies for the body's own bio-rhythmic requirements, an infrasonic shock induced metamorphosis of the Mn atom intervenes; initiating an explosive pathogenesis that perverts the healthy pathways of darkness and light; Cu prions are replaced by hyperpolarized Mn 3+ prions that seed self perpetuating 'cluster bombs' of free radical mediated neurodegeneration. TSE ensues.

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Correspondence to: **Dr. Mark Purdey**, High Barn Farm, Elworthy, Taunton, Somerset, TA43PX, UK. Phone: +44-1984-656832;
E-mail: TSEpurdey@aol.com

INTRODUCTION

The conventional consensus on the origins of TSEs maintains that these diseases are caused by 'hyperinfectious'

malformed PrP that is capable of converting healthy PrPc into abnormal, protease resistant prions in the mammalian brain (1) These prions are purportedly transmissible in the external environment via animal to animal contact or via ingestion of TSE diseased/prion contaminated brain tissue, but no evidence exists to date to substantiate this speculative, universally held belief.

The study of the epidemiology of TSEs suggests that the conventional consensus is severely flawed, and that environmental factors must play an as yet 'unrecognised' primary role in the origins of these diseases (2–4).

For instance, Bovine Spongiform Encephalopathy (BSE) has failed to surface in the cattle populations of the Middle East, India, S. Africa, Third World countries, etc., which received substantial tonnages of the BSE incriminated meat and bone meal (MBM) imports from the UK from the 1960s onwards (5). Furthermore, there have been 40,000 + cases of BSE in UK cows that were born after the 1988 ban on MBM going into cattle feed. And more recently (6), 22 cases of BSE have occurred in cows born after the 1996 ban on MBM going into animal feedingstuffs designated for all types of domestic animal.

It has been proposed that TSEs are not caused by 'in vivo' exposure of PrP susceptible individuals to infectious exogenous prions, but are caused by simultaneous exposure of the susceptible individual to a specific combination of environmental prerequisites; high Mn, low Cu, and high intensities of visible/nonvisible acoustic radiations – a package of factors that is shared by geographical pockets around the world where TSE clusters have traditionally emerged, yet remains absent in adjoining TSE-free regions (2,3).

Combined exposure of PrP susceptible genotypes to these environmental prerequisites invokes a 'Jekyll and Hyde' style transformation of the normal native Cu PrPc into its rogue, protease resistant, pathogenic Mn 3+ PrPtse isoform (3).

Healthy Cu prions, electromagnetic conduction and circadian homeostatis

Evidence gleaned from PrP 'knock out' experiments demonstrates a possible functional role of PrPc in the circadian rhythm (7,8). Likewise the clinical and neuropathological profiles of TSE indicate a wide ranging disruption of the circadian–serotonergic–sympathetic pathways (1,9–12).

Furthermore, diurnal–nocturnal oscillations in the levels of Cu and Mn in the CNS have also been shown to be integrally interconnected with the circadian day/night cycle (13).

It is proposed that the electromagnetic homeostatis of the circadian pathways is maintained by the Cu component of the normal PrPc (14,15); where Cu conducts electromagnetic energy along the circadian regulated melatonin–serotonergic sympathetic pathways; conducting that energy in order to activate a wide array of physiological functions; sleep/wake rhythms, sexual cycles, mood/behaviour, heart beat, immune response, gastrointestinal rhythms, growth and repair of cells; including the growth of tumour cells, etc. (see Diagram 1)

Interestingly, the healthy prion protein is intensively expressed (or localised) in those neural/extra neural tissues which are directly under circadian mediated

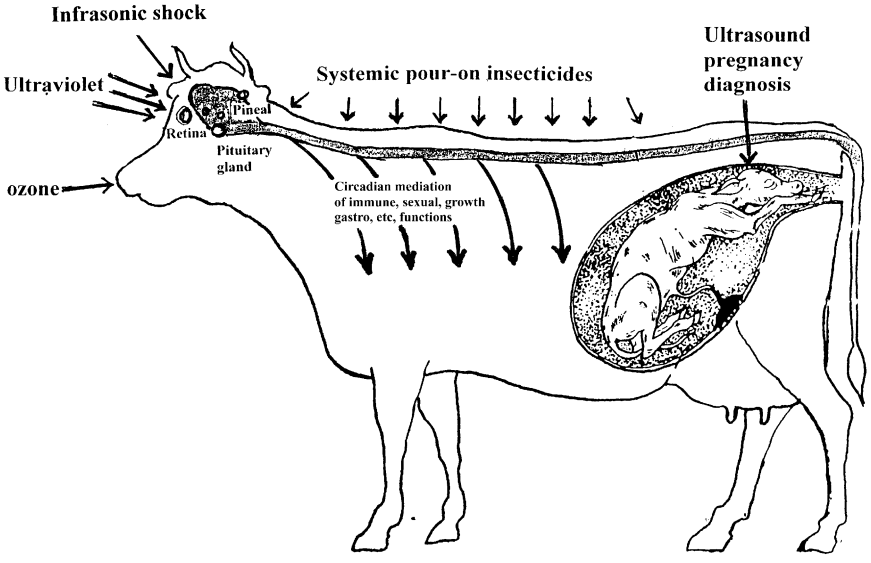


Diagram 1 BSE pathogenesis; environmental electromagnetic/hyperoxidative assault of Mn loaded/Cu depleted CNS circadian–auditory–vestibular pathways of the bovine.

electromagnetic influence – the retina, pineal, hypothalamus, visual cortex, pituitary, medulla, glial cells, sympathetic neurones, spleen, lymphatic, tonsils, appendix, myocardial cells, gastrointestinal membranes, nerve growth factor mediated cells involved in growth and repair, etc. (1,9,16–19).

In this respect, the proposal of an electro-conduction function of the copper prion protein may turn out to offer further scientific insight into mechanisms involved in the electromagnetic meridians/nodes recognised by Chinese medicine; where the healthy Cu PrP performs some regulatory role in maintaining electro homeostatis at the nodal points and along the meridians, whilst the Mn PrP serves to block that conduction.

Mn prions, circadian–vestibular disruption and TSE pathogensis

The origins of TSE stem from a breakdown in the ability of the brain's circadian and auditory–vestibular pathways to deal with unusually intense environmental exposures to visible and nonvisible electromagnetic radiation (EMR) (see Diagram 1).

In this respect, it is interesting that the retina contains both magneto and photo receptors for receiving and transducing several types of incoming visible/nonvisible EMR (20). Since this theory implicates an intensive inflow of these acoustic/ultra violet radiations into the retina and other EM receptors as part of the aetiological interplay, it is interesting that the retina plays host to the initial pathological lesions in most types of TSE (9,21–23), whilst the circadian, auditory and vestibular pathways exhibits the full spectrum of pathological damage in TSEs at the end of the day (1,9).

The incoming flow of ultraviolet and low frequency acoustic radiation, etc., is largely transduced at receptors in the retina (20,24) and at the hair cells in the cochlea, respectively (25). Both visual and auditory pathways have analogous components. Each starts with sensory receptors that connect to early integration stages (in the retina for vision and in the brainstem for hearing), then to a thalamic relay. Both terminate via projections to the superior colliculus of the neocortex where the integration of auditory and visual information occurs (24). Whilst the role of light in mediating the circadian rhythm is well recognised, infrasound has also been shown to exert significant effects on the bio rhythms of the brain (26).

It is a disruption in the Cu mediated conduction of endogenous electromagnetic energy (transduced from incoming light and sound) via the vestibular–circadian pathways, that represents the primary disruption in TSE pathogenesis.

But what causes this breakdown in electromagnetic homeostatis along the circadian pathways, and the resulting onset of TSE pathogenesis?

A three stage pathway of environmentally induced pathogenesis is proposed

(see Diagrams 2 and 3)

1. Foreign cation (e.g., Mn) substitution of copper atoms at the octapeptide repeat domain on PrP (2). This forms a noninfectious protease resistant 'sleeping' prion.
2. Endogenous/exogenous sources of oxidative stress (via phagocytosis, vaccinations, systemic insecticide exposure, ultra violet, ozone, etc.) oxidize Mn 2+ prion in retina, tonsils, astrocytes, lymphatic system, etc. (prion factory sites) (see Diagram 4) into Mn 3+ prions (3). The hyperoxidized status of the CNS in TSE diseased mammals has already been expounded (2,3). Such a scenario is considerably facilitated by the deficit of Cu/Zn/selenium (Se) activated antioxidant enzymes in the bio system (27). Analyses of TSE ecosystems demonstrated low levels of these antioxidant activators; Se, Zn, Cu (2). Alternatively, Mn 3+ species could enter the organism directly via mineral supplements or foodchains that depend upon soils containing natural or pollutant mineral sources

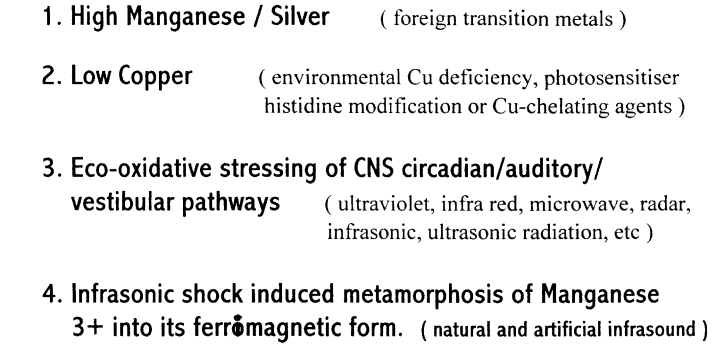


Diagram 2 Key environmental factors in TSE aetiology.

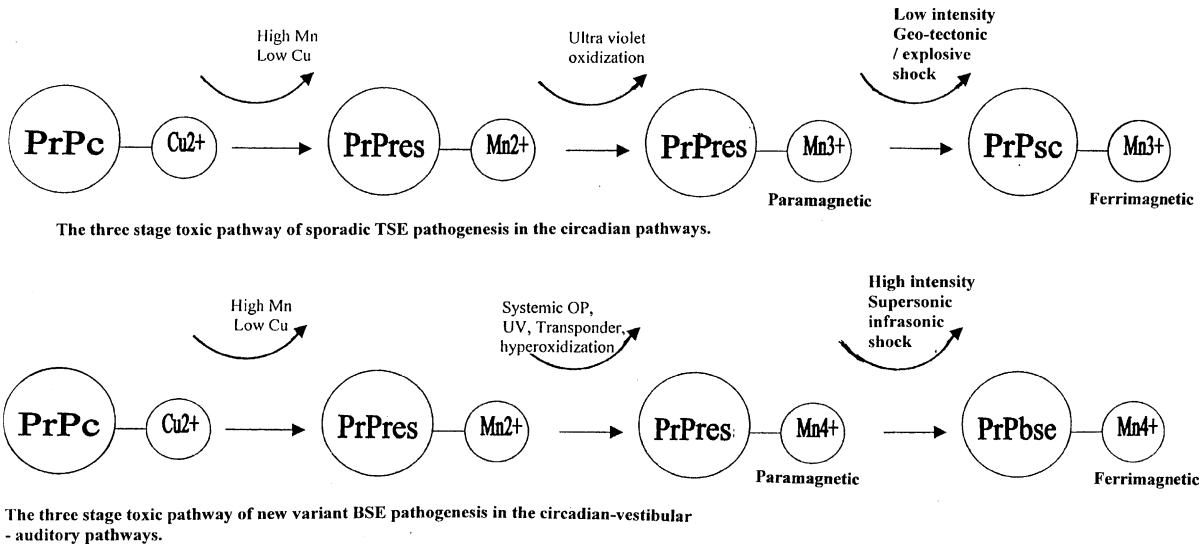


Diagram 3

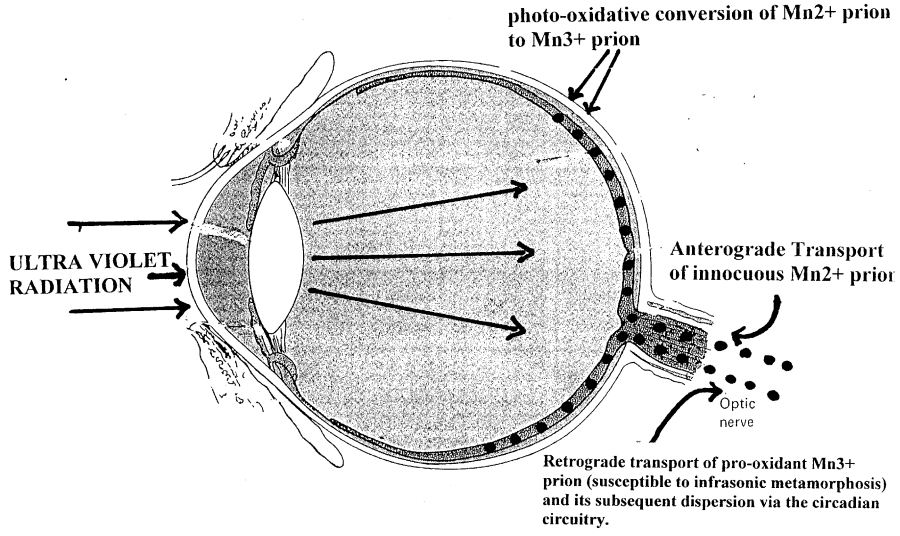


Diagram 4 The retina: the 'Flagship' prion production plant.

of Mn 3+; such as hausmannite, braunite and some perovskites (see Diagram 5).

3. The trivalent species of Mn is well known to absorb and resonate phonons, and, furthermore, a high energy intensive, infrasonic shock is capable of metamorphosing the piezoelectric atomic structure of the Mn 3+ component of the Mn 3+ prion, since trivalent Mn is well known to absorb and resonate phonon energy (28), transforming the atom from paramagnetic to ferrimagnetic status due to the dynamic lattice effects of the Jahn-Teller type distortions of the oxygen octahedra around Mn 3+ – enabling a strong phonon–electron coupling (28). The ferrimagnetic strain of Mn 3+ prion is consequently polarized by the incoming flow of EMF and a contagious, field inducing 'metal to ligand to metal' domino-like pathogenic corruption of the conduits of magnetic superexchange ensues. The increased intensity of magnetic field in the CNS invokes oxidative stress; whereby chain reactions of free radical mediated neurodegeneration burst forth; full blown TSE ensues (see Diagram 6). Polarized prions would remain persistently 'infectious'/pathogenic in the biosystem. It is only when prions have been heated 'in vitro' to temperatures in excess of 500 + degrees that their 'pathogenic' capacity is lost. This is explained by the high temperatures which exceed the specific 'curie' point for Mn 3+; thereby instantly depolarizing the ferrimagnetic charge in the Mn 3+ component of the prion, with a subsequent loss of pathogenic capacity.

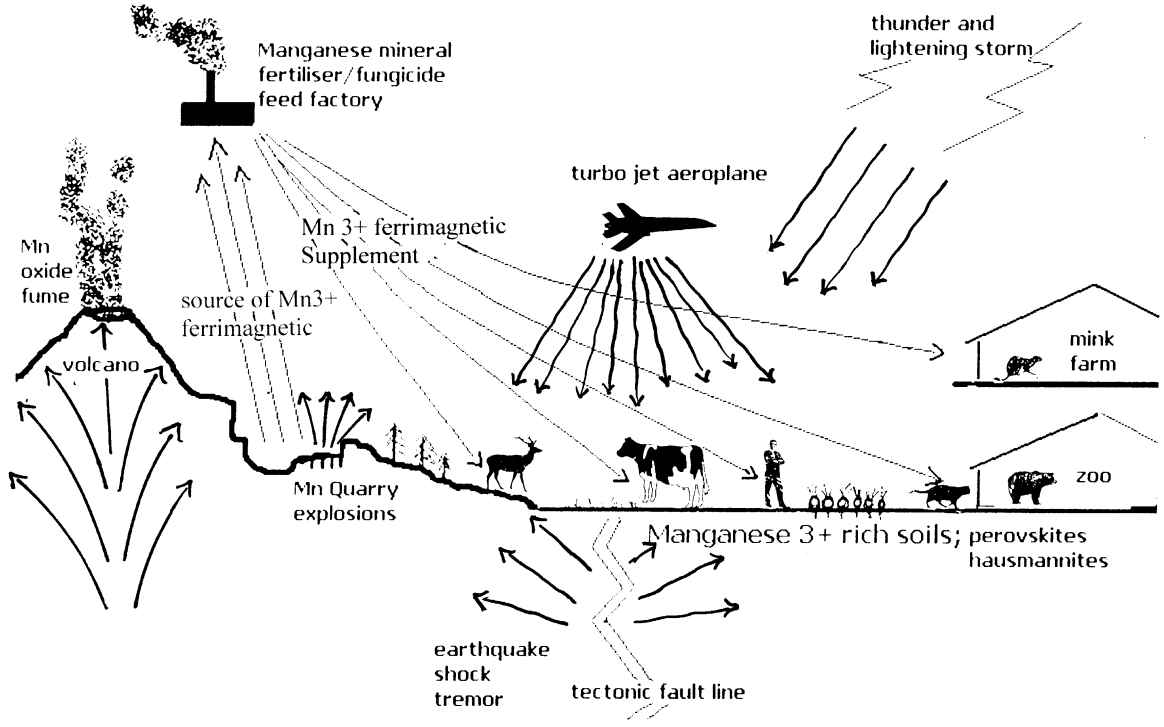


Diagram 5 Environment infrasonic shock induced metamorphosis of soil/air borne Mn 3+ compounds into rogue ferrimagnetic Mn 3+; an environmental genesis of the TSE agent? (←) Low frequency infrasonic shock wave.

Alternative foreign cation candidates to Mn

Other foreign transition metal cations which could potentially bond to Cu histidine ligands should not be discounted as possible alternative candidates for replacing Cu on PrPc, thereby priming the prion for suceptibility to TSE. Environmental studies of TSE clusters have identified the significant presence of silver (Ag) and bismuth (Bi) pollutants (see Tables 1 and 2) in some TSE clusters. Whilst Ag and Bi can compete for histidine ligands (30,31), cobalt, chromium, tin and iron can also affiliate with histidine ligands (27,29,31), whilst molybdenum could conjugate directly to the Cu atoms on PrP 'in situ'.

Contamination of the Cu depleted brain by a particular replacement cation would present its particular strain-type of TSE (2), whose clinical and neuropathological profile would reflect the specific conduction/magnetic susceptibility status of the foreign metal involved. Whilst Ag and Bi are diamagnetic and Mn is paramagnetic (27), both of these metals can also be oxidized, like Mn, into trivalent species rendering them susceptible to phonon/photon absorption, etc. (32). A diverse array of atomic transmutations could be initiated; resulting from a range of interactions with incoming electromagnetic fields from the environment.

An Ag strain of TSE can be envisioned where the diamagnetic silver prion would instigate an abnormal state of 'superconduction' of electromagnetic energy through the circadian pathways – instead of the steady state of conduction provided by Cu prions. This would result in an electrical hyperstimulation at the circadian effectors as well as generating a possible 'gravity-free' moon-like vacuum', where the diamagnetic capacity of the Ag prions along the circadian pathways could initiate a state of two way repulsion between other endogenous or exogenous localised fields (e.g., ferrimagnetic magnetite crystals, etc.) that exist within/without the CNS. Thus, diamagnetic Ag atoms will repel and be repelled by any neighbouring magnetic fields. A kind of magnetic 'black hole' would result, creating a state of levitation encased and trapped inside very localised force fields within the brain; perhaps explaining the mystery 'hollow headed' feeling reported by early stage victims of CJD.

Various disturbances in the electro-magneto equilibrium resulting from the formation of a diamagnetic Ag prion would undoubtably generate a raft of electrical, thermal and radical mediated pathogenic consequences throughout the CNS.

A diamagnetic 'Bismuth' strain of TSE could be similarly invoked. It is interesting that reversible CJD-like encephalopathies have been regularly recorded in humans who have been prescribed Bi-based pharmaceuticals (33). These cases remitted following cessation of treatment, although it could be speculated that the syndrome might have advanced to a fully fledged,

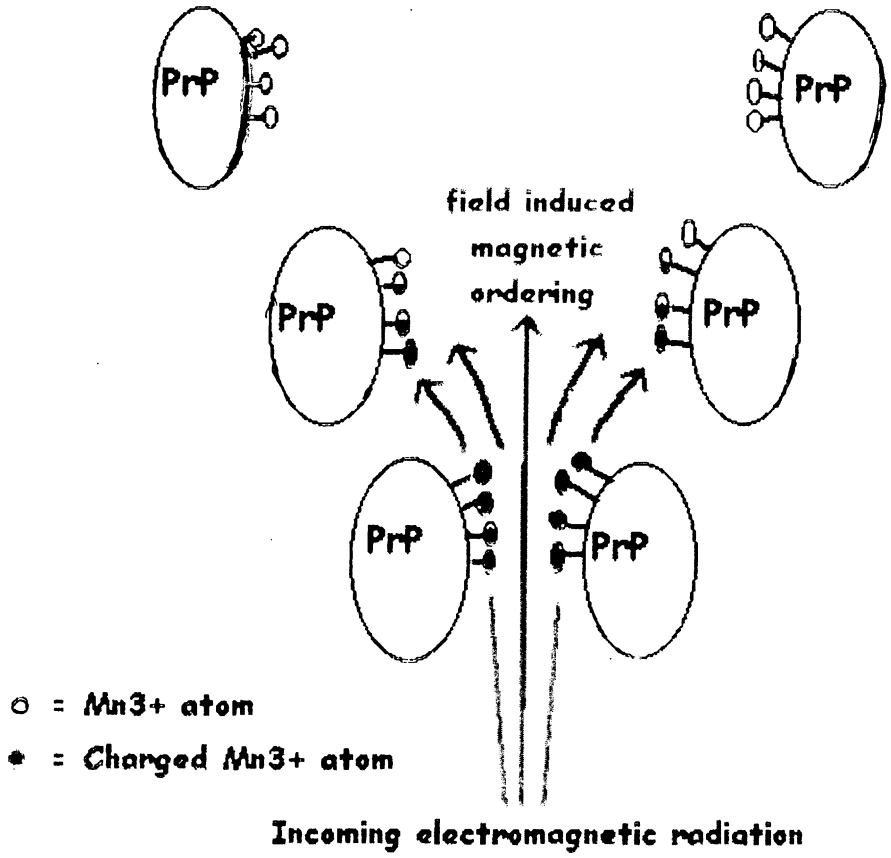


Diagram 6 A rogue ferrimagnetic ordering of Mn 3+ prions progressively corrupts the CNS circadian pathways of magnetic superexchange. A contagious domino-like aggregation of PrP fibrils result, and TSE pathogenesis ensues.

irreversible CJD had the individuals involved lacked Cu availability; thereby enabling a Bi substitution at PrP's vacant Cu domain to proceed.

Supporting evidence for the environmental TSE origin theory

Once these external environmental factors bring about a depleted Cu/Zn and superfluous Mn status in the mammalian brain, then PrPc's Cu domain becomes vulnerable to bonding with Mn in place of Cu. The original postulation of 'a foreign Mn cation substitution at the vacant Cu domain on the PrPc' (2) was put to challenge in a cell culture experiment conducted by David Brown at Cambridge University (34). The results confirmed this hypothesis, where Mn loaded/Cu depleted prion protein cells yielded the protease resistant PrP isoform which characterises the TSE diseased brain.

Alan Prescott et al.'s research at Dundee University (35) has shown that Mn can cause protein misfolding by disrupting membrane dynamics along the secretory pathway. The authors suggest a delicate regulatory mechanism operates to enable healthy protein secretion, and this is exercised between a delicate balance of golgi associated Cu transporter proteins and Mn transporter proteins.

Further research by Boon Seng Wong at Case Western University's National US Prion Surveillance Unit in Cleveland, USA (36), revealed a 10-fold increase of Mn and 50% reduction of Cu in the brains of those who had died of sporadic CJD in relation to controls. The Prions present were bonded to Mn rather than Cu in these sections.

Research by Roumiana Tsenkova at Kofu University (37) investigated the hydration and binding properties of PrP using near infrared spectroscopy. This work concluded that the Cu bonded PrP formed a stable, ordered hydration of the protein – enabling correct folding processes – whereas Mn bonded PrP demonstrated totally different spectral characteristics.

Research at Leeds University using murine PrP (38) has demonstrated that PrPc is rapidly endocytosed following exposure to Cu and Zn, but fails to endocytose in the presence of Mn. This work shows that a cessation of the healthy endocytosis of PrP in the Mn treated cells was instigated by some Mn mediated disruption at the octarepeat region of PrP – presumably binding.

Table 1 Fulfillment of Purdey's Eco-postulates that provide an explanation for the eruption of long standing clusters of sporadic/familial TSEs in specific environments around the world

Cluster region	TSE type	Foreign metal	Cu deficiency/PS hist mod	Infrasonic sources	Ultra violet risks	Topography
Iceland	Scrapie	Mn (volcanic, acid soil)	Low soil Cu High Mo	Geotectonic Auroral disturb Volcanoes Ocean waves Thunder Earthquakes	High altitude ozone thinning	Parabole valley Mountain ridges
Calabria	CJD familial sporadic	Mn (refineries, local food) Ag (water purification)	Low soil Cu Bergamot Dithiophosphate insecticides	Geotectonic Earthquake Volcano Adjacent quarry explosions	Coastal/white sandstone/white rendering glare	Parabole valley Mountain ridge
Slovakia (Orava)	CJD familial sporadic scrapie	Mn (steel, local food, pine tea) Ag (soil)	Low soil Cu Pine terpines	Geotectonic Earthquakes Adjacent quarry explosions	High altitude	Parabole valleys Mountain ridges
Colorado (Front Range)	CWD Scrapie	Mn (pine needle consumption, acid rain, antler promoter feeds) Ag (cloud seeding, water, mines) Bi (bullets, mines)	Low soil Cu Pine terpines	Geotectonic Earthquakes Turbulence Thunder Adjacent quarry explosions Military jets	High altitude	Parabole valleys Mountain ridges
Japan (Fuji)	CJD familial sporadic	Mn (Al–Mn alloy factory, fungicides) Ag (film factories)	Low soil Cu Dithiophosphate insecticide	Geotectonic Volcano Earthquake tremors Oceanic waves Turbulence	Coastal	Parabole valley Mountain ridges
Sardinia (Sopramonte)	Scrapie	Mn (Cu toxicity treatment) Ag (soil)	Low soil Cu Asphodel	Geotectonic Adjacent quarry explosions Military jets	High altitude	Parabole valleys Mountain ridges
New Quinea (E Highland)	kuru	Mn (volcano, Mn–Al alloy scavenging from aircraft) Ag (soil)	Low soil Cu Pine terpines	Geotectonic Bomb explosion at crashed WW2 bombers Thunder Earthquakes	High altitude	Mountain ridges

PS hist mod = photosensitiser induced histidine modification.

Table 2 Fulfilment of Purdey's eco-postulates that provide an explanation for the eruption of vCJD clusters in specific environments within the UK

Cluster	Foreign metal source	Cu deficiency/PS Histidine mod	Infrasound source	UV risk	Location
Queniborough	Mn, Ag, Bi sewage, dye factories Mn fungicide/fertiliser spray	Dyes PrP genetic	Concorde/aeroplane overflights Aero-engine testing plant Granite quarry explosives	Ozone thin Rural	Rural village
Adswood	Mn (brick factory)	Dyes	Concorde/aeroplane overflights	Ozone thin, Adjoining lakes	Town bordering Open country
Kent (weald)	Mn fungicide/fertiliser spray	Hops PrP genetic Dithiophosphate insecticides	Concorde/aeroplane overflight	Ozone thin Rural	Rural villages amongst hops/ orchards/arable
Lymphstone	Mn fungicide, Mn nodules/dust in exposed cliff face	PrP genetic	Concorde/aeroplane overflights	Ozone thin Rural Coastal	Rural village on coastal estuary
Armthorpe	Mn fungicides/fertilisers Mn sewage	PrP genetic Vulcanising Dithio-compounds	Concorde/military jet overflights Opencast coal Mine explosions	Ozone thin Rural *	Rural village adjoining farmland
Tenby	Mn fungicides/fertilisers Mn pottery glazes	PrP genetic	Military jet/Concorde transatlantic overflights Bombing range Tank/rifle range	Ozone thin Rural Coastal	Rural villages adjoining farmland
Burnhamon-Sea	Mn fertilisers	PrP genetic	Military jet/ Concorde transatlantic overflights	Ozone thin Rural coastal	Small town adjoining farmland and coast
Eastleigh	Mn fungicide/fertilisers	Prp genetic	Domestic jet overflights	Ozone thin Rural Nr coast	Village adjoining farmland/airport

Therapy with chlorpromazine has been shown to be beneficial to victims of vCJD. Interestingly, Cotzias demonstrated that chlorpromazine exerts its therapeutic benefits by specifically targeting and combining with Mn 3+, as well as competing for protein ligands with Mn 3+ (*39*).

The overview of the working hypothesis

It is difficult to attribute the full spectrum of clinical and pathological abnormalities encountered in TSEs to the sole pathogenic activities of the prion. Lasmezas et al. transmitted TSE into laboratory animals via intracerebral inoculation of TSE affected CNS homogenate, and the resulting TSE diseased CNS tissues of the recipient animals failed to demonstrate the presence of prions at post mortem.

The hypothetical case for the Mn 3+ component as the pathogenic agent – operating either singly or in conjunction with the prion – addresses these missing links well, since the progressive delayed neuropsychiatric syndrome encountered in cases of Mn intoxication in miners, etc., displays a clinical and neuropathological profile which virtually duplicates the profiles seen in TSE (2).

The simple fact that Cu is employed in electric cabling as a conductor whilst Mn is employed in batteries for absorbing and storing up electric energy may elucidate the underlying cause of TSEs; where healthy Cu prions conduct the vital electro energy (derived from the sun's ultra violet and earth's geomagnetic, infrasonic waves) along the circadian pathways, whilst the metamorphosed Mn prions serve to blockade and permanently store up a historical memory bank of those incoming energies to levels which exceed the explosive 'flash point'. A rogue ferrimagnetic ordering of Mn 3+ initiates a progressive field inducing pathogenic corruption of the circadian mediated pathways of magnetic superexchange, which, in turn, detonates off neuropathogenic cluster bombs of free radical chain reactions (see Diagram *6*).

The fact that Mn 3+ perovskites – as well as chromium compounds, etc., – are actually employed by the audio music tape/compact disc industry as the medium for storing recorded sound, illustrates the capacity of Mn 3+ for sound absorption well.

This new concept of the 'ferrimagnetised metal' as the pathogenic co-partner component of the prion could explain why the so called infectious pathogenic property of prions cannot be destroyed until extremely high temperatures are reached (1,2). In this respect, once the 'infectious agent' is exposed to sufficiently high enough temperatures that exceed the 'curie point' for that cation, then the thermal agitation of atoms is sufficient to drain the permanently magnetised status of the metal. Once the metal has cooled below the curie point, any subsequent re-exposure to external magnetic fields would be sufficient to re-prime the pathogenicity of the remaining prion fragment.

With an overabundance of Mn prions and loss of Cu prions, the oxidative impact of the various electromagnetic energies received at the Cu deficient retina or cochlear hair cells, etc., can no longer be quenched. Consequently the energy flow of incoming UV, infrasound, etc., piles up, being absorbed by the Mn atoms; only to find its photo/phonooxidative capacity misappropriated into converting the innocuous Mn 2+ prions into potentially lethal, prooxidant Mn 3+ or 4+ prion species. So any accumulations of protease resistant, piezoelectric Mn 3+ PrP in the retina finds itself susceptible to an acoustic shock induced metamorphosis at a later date.

Alternatively, instead of an oxidative/acoustic shock induced transformation of paramagnetic Mn 2+ into ferrimagnetic Mn 3+ occurring endogenously within the biosystem, Mn 3+ – or the fully fledged ferrimagnetic Mn 3+ – may enter the organism directly from the external environment; from ecosystems supported by soils that contain Mn 3+ compounds and have been irradiated by intensive acoustic shocks at sometime in the past (see Diagram 5).

Irrespective of the mode of ferrimagnetic Mn 3+ accumulation in the CNS, the Mn contaminated/Cu depleted brain is unable to deal with the incoming flow of EMR from the external environment – particularly when the levels of radiation are at high intensities. The incoming energy is hijacked and perverted into unleashing a 'Jekyll and Hyde' style property of PrP; where the protein transforms from innocuous 'sleeping' to fully fledged 'pathogenic' form. A self perpetuating field inducing/oxidative melt down of neurodegeneration bursts forth, and TSE ensues (see Diagram *6*).

ENVIRONMENTAL PREREQUISITES INVOKE A THREE STAGE PATHOGENESIS OF TSE (SEE TABLES 1 AND 2)

Cu/Zn depletion at the octapeptide repeats on PrP

Following the pioneer soil/vegetation analysis of TSE cluster regions around the world, the prerequisite of Cu (and Cu) deficiency was first identified and proposed as a primary aetiological prerequisite for TSEs (2). It has also been suggested that the geographical distribution of regions of high BSE incidence in the UK correlates with Cu deficient regions (3), whilst a survey on UK farms suffering endemic BSE observed problems with Cu deficiency on all farms studied (40).

The relevant pathogenic mechanism pivots upon the loss of Cu (and Zn) from the octapeptide repeat domains

of the normal PrPc, thereby rendering the domains vacant for substitution by specific foreign cations that can affiliate with these ligands. Loss of Cu/Zn from PrP's domains can be achieved in several ways and need not necessarily result from a straightforward external environmental Cu/Zn deficiency; although this appears to be the case in the clusters of traditional TSEs analysed (2).

Significant exposure to chemical sensitising agents such as bergamot, pine, asphodel plants, hops, synthetic dyes, petroleum, dithiophosphate insecticides was observed in the diets or local ecosystems of all TSE clusters studied (3). These agents actually exert their photo/audio/tactile sensitising affects by interfering with the histidine ligands (41) where they can form long term bonds (42); thereby capping histidine residues on metal transporter/metallo proteins such as PrPc, so that Cu/Zn can no longer access their specific binding ligands – regardless of the level of abundance or deficiency of the free metal within the CNS.

Systemic organodithiophosphate warble fly cattle insecticides containing phosmet, (exclusively used as a high dose 20 mg/kg, 20% conc. solution in the UK) and human headlice insecticides have been putatively implicated in the aetiology of the new variant strains of TSE (nvTSE) in the UK(4). These compounds also interfere with Cu availability by chelating Cu with their free sulphurs or nitrogen to form a mercaptide ring (2). Furthermore, other lower dose systemic pour-on warblecide compounds which contained trichlorophon as their active ingredient were used early on in the UK and Eire, and then later in Germany, Holland, Portugal, Switzerland, Japan, Italy, Spain, France (countries where endemic BSE has occurred at lower incidence rates) (4). Trichlorphon also interferes with histidine residues as part of their delayed toxic mechanism of ageing proteins (43).

Other Cu chelators such as Mn dioxide (44), Ag (45), tributylin and other metal additives/contaminants, some antidepressants, cuprizone, hexachlorophene (46) should be considered as possible candidates for disturbing Cu in the initiation of TSE susceptibility. Molybdenum conjugation to Cu atoms on PrP could also play a role.

An interesting study at Leeds University (38) indicated that the mutation occurring in the octapeptide repeat region of PrP in cases of inherited, familial TSEs, may also implicate a pathogenic mechanism centred upon the disruption of histidine–Cu/Zn ligands, They showed that an 'in vitro' deletion of the four octapeptide repeats or mutation of the histidine residues on PrP abolished endocytosis, indicating that intracellular internalisation and degradation of PrP within the healthy brain is dependent upon the successful binding of Cu or Zn to the repeat region. Interestingly, when manganese was added to these cells in the absence of Cu/Zn, PrP was no longer internalised and endocytosed.

Foreign metal contamination and its substitution at PrP's vacant Cu domain

The manganese strain of TSE

The high levels of Mn recorded in sporadic, familial and nvTSE cluster environments have been published previously (2,3). Environmental sources of Mn have stemmed from airborne emissions of volcanoes, steel/ceramic/brick/dye/glass/munitions/battery factories, lead-free petrol refineries/autocar exhausts, aeroplane take-off flight paths, spraying of liquid Mn based fertilisers and fungicides, etc. Airborne Mn can enter the CNS via the nasal-olfactory route of inhalation (47) – the route of absorption which poses the highest risk for invoking TSE.

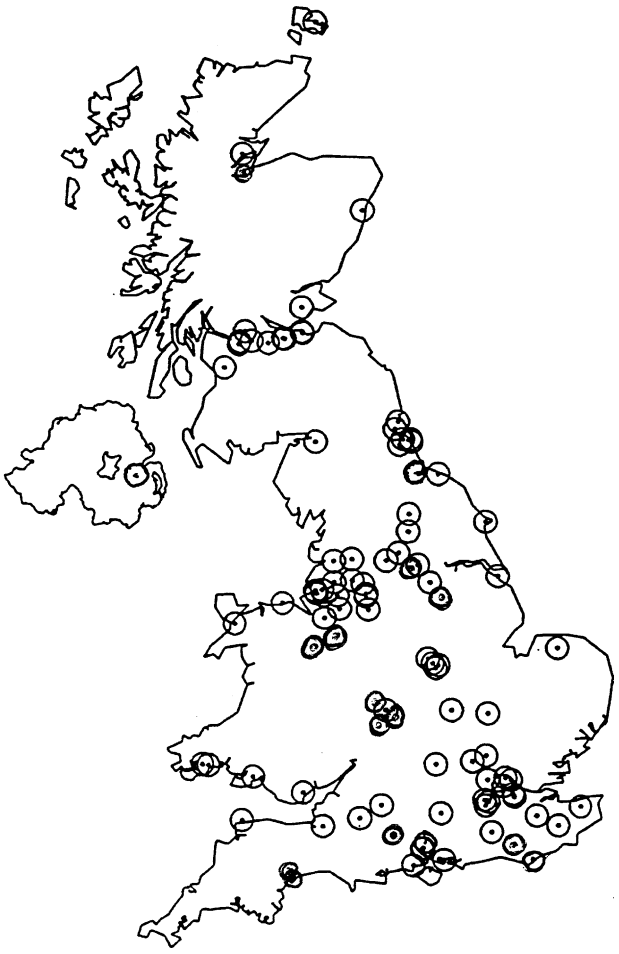
An interesting correlation exists between the areas of Mn deficiency in soils (48) and the distribution of vCJD cases in the UK (49) (see Maps 1 and 2). During the 1980s, It became customary practise to spray Mn deficient farmland with liquid Mn fertiliser sprays up to four times per growing season, thereby subjecting human populations residing in these areas to significant toxic levels of airborne Mn particulates.

It has been proposed that the addition of Mn oxide into artificial calf milk powders at levels up to 1000 times the levels found naturally in cows milk (3), along with the inclusion of Mn oxide in a range of livestock and human free access mineral supplements and feeding stuffs (50) underlies a major source of Mn overloading of the CNS in BSE/vCJD endemic countries. Exposure to high levels of dietary Mn in early/embryonic life exacerbates this problem of Mn toxicity; since the blood brain barrier's regulation of metal uptake into the brain is underdeveloped in the immature mammal (51).

Virtual absence of BSE in beef suckler herds (1) and total absence in 100% of cattle raised on fully converted organic farms (52) can be explained by the fact that these farms employed real cow's milk rather than the Mn fortified artificial milk powder for rearing their calves.

High dietary intakes of Mn enriched pine needles (2,3) and Mn enriched 'addictive' mineral supplements (put down by hunters for 'hooking' deer onto their shooting territories as well as promoting growth of their antlers) amongst Colorado/Wisconsin deer and elk herds may also partly explain the aetiology of CWD in these areas.

Since the 2001 publication (3) a fresh analytical study has been conducted in the familial/sporadic CJD cluster area of the Fuji river basin in Japan (53). The results observed consistently high levels of Mn (av 874 ppm) and low levels of Cu(av 46 ppm) in the soil at all 7 test locations. An aluminium–Mn alloy sheet factory (involved in the construction of fuselages for world war 2 bomber aircraft in the 1940s) was noted at the mouth of the valley, whilst Mn is utilised as a fungicide spray on



Map 1 Geographical distribution of vCJD cases at onset of symptoms at 2001. (source; CJD Surveillance Unit, Edinburgh, UK).

Map 2 Areas in the UK where manganese deficiency can occur in crops, so where spraying of manganese fertiliser occurs.

the top fruit crops which predominate the cultivation of this region.

Interestingly, several of the Japanese bombers manufactured from these Mn–Al alloy materials at Fuji had been shot down in Papua New Quinea during the second world war in the precise region where the Fore tribe reside. A few years after the war, an epidemic of the TSE 'kuru' erupted exclusively in the Fore tribe (1,74). The tribe's folk had scavenged these crashed aircraft (74) utilising the Mn–Al alloy panelling for making tools, bowels and pots, etc. They had also accidentally exploded some bombs (74). Did the Mn and Al atoms leach from the cooking pots into the foods and contaminate their brains. And then the bomb explosions provided the additional infrasonic shock that invoked the 'in vivo' conversion to ferrimagnetic Mn?

The silver strain of TSE

Ag preferentially bonds with Cu ligands on cupro-proteins more than any other replacement metal (45); placing Ag as a prime candidate for substitution at PrP's vacant Cu domain. The significant presence of Ag in TSE risk environments has also been recently observed; where its use in weather modification sprays – for rain/snow making around reservoirs/ski slopes, airport/coastal fog clearance – water purification, surgical instrument/electrode plating, surgical sutures/plates, dental amalgam, anti bacterials, etc. (54), bears a strong epidemiological correlation with the widely accepted predisposing risk factors for TSEs; such as visits to the dentist, surgical operations, outdoor occupations, (1,9) etc.

Recent trends for use of colloidal Ag as a nasal germicide inhalant should be viewed with caution, since Ag, like Mn, will directly enter the brain via the nasal–olfactory route of inhalation (55).

Since Ag is a transition metal like Mn, a similar three stage mechanism of TSE pathogenesis that has been applied to an Mn strain of TSE can also be applied to the development of a 'silver strain' of TSE

Bismuth, cobalt strains of TSE

Bi and Cobalt can also substitute Cu or Zn at histidine ligands (27,29,31), so should also be considered as potential candidates for TSEs.

Of interest is the publication of several reports of a CJD like encephalopathy following ingestion of Bi as the active component for various gastric disorders from ulcers to upsets, as well as for syphilis (33). However, these CJD-like conditions remitted following cessation of treatment with Bi. Perhaps if Cu levels had been simultaneously low in any of these individuals undergoing Bi therapy, then an irreversible TSE would have been initiated.

Bi is also used in the manufacture of metal alloys, bullets, electronic components, superconductors, dye pigments, cosmetics (lipsticks, etc.) and appears as a significant impurity in some phosphate fertilisers (56) used on farmland, whilst cobalt is used in animal/human mineral supplements, magnets, hard steel, electronics, catalysts in petrol refining, batteries, dye pigments, ceramics.

High intensities of eco-oxidants in TSE ecosystems

The association between TSE cluster zones and environments demonstrating high intensities of UV, ozone and other oxidants has already been extensively discussed (3). The high altitude/snow covered/coniferous/mountain or coastal locations that commonly characterises the traditional cluster zones of TSE (2,3) are well recognised for their above average intensities of UV and ozone.

Interestingly a greater majority of both sporadic CJD (57) and nvCJD cases have surfaced in individuals living in remote rural or coastal locations during their period of clinical onset (3) (see Map 2). Levels of UV are considerably lower in urban environments since the canopy of airborne smog particulates overlying towns serves to absorb and deflect incoming UV rays (58). Furthermore, ozone tends to form in rural and high ground areas due to migration of exhaust gases out of the towns into the high UV areas – thus bringing together the entire set of prerequisites required for ozone formation in these areas (59). Atmospheric release of terpines from pine trees in the high UV mountain areas will likewise yield intensive levels of ozone (60).

High intensities of eco-oxidants penetrating the CNS of any antioxidant deprived mammal would set up specific 'prion production plants' (see Diagram 4) in the eco-oxidant reception centres – such as the retina or tonsils – where incoming UV or ozone could interact and oxidize manganese 2+ prions (in situ) into their Mn 3+ or Mn 4+ isoforms. The mass production of trivalent Mn prions would render the organism susceptible to any future infrasonic shock conversion of paramagnetic Mn prions into pathogenic, ferrimagnetic Mn prions.

Has the increased cocktail of oxidants that is contaminating the modern world (increased UV in the populated northern hemispheres due to stratospheric ozone thinning) assisted in the emergence of the more aggressive new strain TSEs over the last years?

Infrasonic radiations resonate in Mn 3+ prions – does infrasound prime the pathogenic prion?

Environmental sources of infrasound and their correlation to TSE clusters

A correlation exists between clusters of traditional TSEs and new variant TSEs and environments where high intensities of natural infrasound and excessive intensities of man made infrasound (from supersonic aircraft) occurs, respectively.

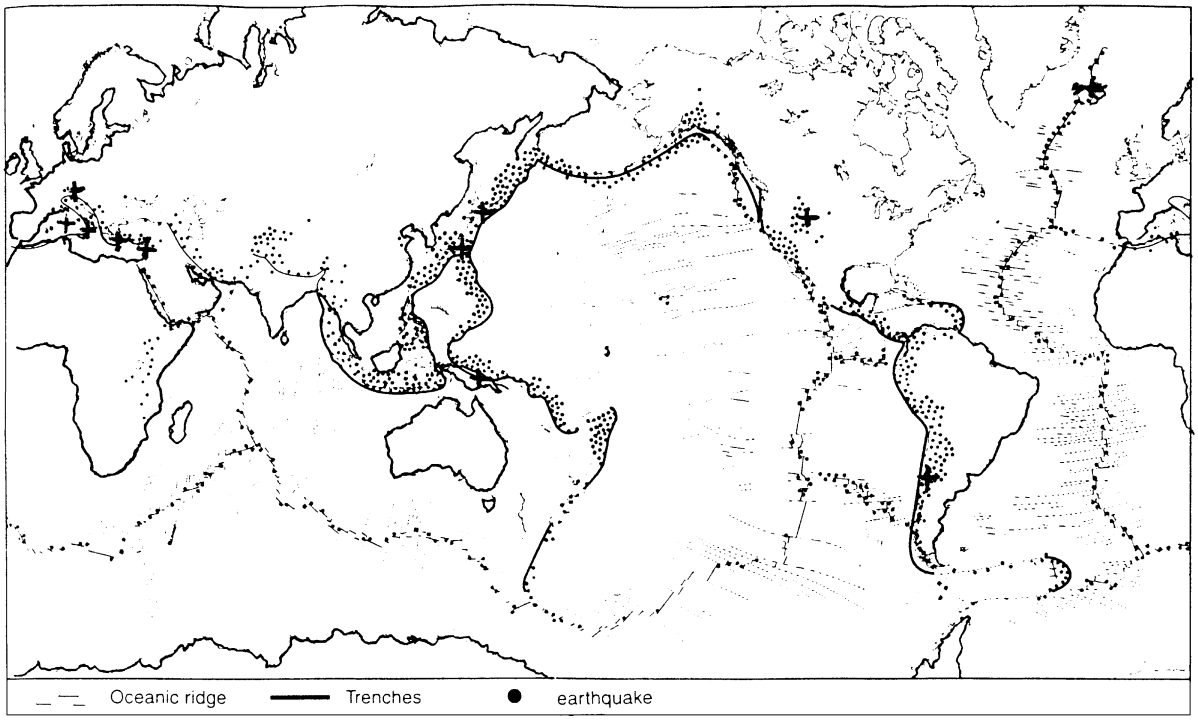
Naturally generated sources of infrasound are either perennial or seasonal. Perennial sources stem from waterfalls (61), sites of geothermal activity (62) and seismic induced movements at tectonic plate junctions (62). Winter seasonal sources of infrasound stem from oceanic waves (63), marine storms (63) and wind storms (64), whereas summer and other seasonally related sources stem from thunder/lightning storms (65), auroral disturbances (66), geomagnetic activity (67), atmospheric turbulence (68). Acute sources of natural infrasound are radiated from volcanic eruptions (69) and the seismic shock waves of earthquakes (70) produced by the tectonic movement of rift plates sited along mountain ranges and coastal locations.

Interestingly, all of the long standing clusters of traditional sporadic/familial TSE are located on the major tectonic fault lines across the globe – notably on the mid atlantic rift and the infamous 'ring of fire' (71) (see Map 3). This recent focused observation of a 'tectonic' connection to TSE cluster locations could offer an explanation for the previously stated more generalised observation that 'all traditional, long standing TSE clusters erupt in areas located in volcanic, pre cambrian, high altitude, mountainous terrain' (2).

Furthermore, the well recognised TSE clusters investigated in Iceland, Colorado, Slovakia, Calabria, Sardinia, Sicily and Japan (3) have all implicated populations residing in parabole shaped mountain valleys where the valley mouth opens into the full brunt of the incoming prevailing winds.

Interestingly, certain topographical landforms are predisposed to serving as acoustic beacons or tannoys of amplified infrasound. For instance, parabole shaped mountain valleys or coastal cliffs can refract and channel incoming prevailing infrasonic waves (radiating from windstorms, oceanic waves, thunderstorms, explosions, etc.) into wind tunnels so that they converge to form acoustic beacons of concentrated infrasound at spot locations (72).

Acute, high volume sources of artificial infrasound are perhaps more relevant in respect of the aetiology of



Map 3 Correlation between locations of long term clusters of sporadic/familial TSEs and the areas of seismic activity along the major global tectonic plate margins. (+) TSE cluster.

TSEs, whilst the lower volume artificial infrasound which radiates from industrial/domestic air conditioners, boilers, transformers, extractor fans, blast furnaces, asphalt plants, stationary/autocar/train engines, ship foghorns, sirens, churchbells, organs etc. (24,61), provides a constant source of low to medium intensity background infrasound in western industrial countries. However, the locations which radiate high decibel acute infrasonic shock bursts from rocket/missile/bomb/nuclear testing sites, quarry/mine explosives or beneath intensively used flight paths of supersonic passenger and low flying military aircraft/helicopters (61) seem to correlate with locations where TSE clusters emerge.

Examples include the recent puzzling outbreak of CWD in an isolated deer herd contained behind the perimeter fences of the White Sands Missile testing facility in New Mexico where infrasonic shock bursts are well known to be high (61,73). Likewise, the deer in the Colorado, Wyoming and Wisconsin clusters of CWD (1) all reside in areas that are located on the epicentres of intensive earthquake activity as well as being chronically exposed to quarry/mine/gun explosions/low flying military jet practise (as well as turbulence derived infrasound (68)), the New Quinea Fore tribesfolk exploded bombs from crashed world war two bombers before they developed kuru (74), whilst the CJD foci in slovakia (75)/calabria (76) and the scrapie foci in Sardinia (77) reside in areas where intensive blasting for open cast stone quarries is practised (as well as being chronically exposed to infrasound derived from tectonic plate margins (71,78). Another intensive cluster of scrapie erupted in sheep grazing land used as a long term military firing range near to Ashoro in Hokkaido, Japan (personal communication; K Yamada, Japanese Organic Farmers Association, Tokyo).

Locations which are subjected to 'shockwave' boom carpets of supersonic/subsonic aircraft overflights – where a high intensity of select low frequency infrasound is radiated from the 'afterburner' employed for high thrust acceleration/deceleration (61,72,79) – correlate precisely with the locations where clusters of new strain BSE and vCJD have emerged in the UK, France, etc. (being regions where a high intensity of Cu chelating warble insecticides and Mn feed supplements have been concurrently used on cattle (2–4)).

INFRASOUND AND THE BIOLOGICAL SYSTEM

Metabolic factors influencing sensitivity to Infrasound and their putative application to TSE susceptibility

Infrasound receptors have been identified in special infrasound sensitive neurones in the cochlear ganglion of

birds, elephants and other infrasound sensitive species (25). These neurones originate from the papilla basilaris (hair cell receptors) and extend into the auditory cortex which ultimately interconnects with the vestibular pathways. Free radicals generated by any phonooxidative stress at these receptors (27) are scavenged by copper/zinc SOD antioxidants (80,81) – once again demonstrating how copper/zinc deficient individuals (e.g., those residing in Cu/Zn deficient TSE ecosystems (2)) may be hypersensitive to the oxidative effects resulting from high burst exposure to infrasonic and other audio frequencies.

Interestingly, the status of magnesium availability and melanin expression have both been shown to play a major role in protecting the mammal against the impact of the whole spectrum of acoustic frequencies (82). In this respect, the low levels of magnesium that have been observed in TSE ecosystems (2) (and the beneficial response of TSE affected mammals following Mg therapy (83) might suggest that 'TSE at risk' animals living in TSE environments are already predisposed to noise sensitivity.

There is a strong correlation between blue eyed, fair haired mammals who lack melanin pigmentation and increased susceptibility to ototoxicity (82), and it is of great interest that the whiter pigmented breeds of cow such as the Friesian/Holstein – that express lower levels of melanin in relation to the other breeds – have endured almost *96*% of the total incidence rate of BSE in the UK when approximately 70% of the total cattle herd in the UK comprise the Friesian/Holstein type (5). Furthermore, An 'on farm' survey of 25 BSE affected farms in Germany and Holland carried out by the author observed that 100% of BSE casualties involved white or yellow–red pigmented cows in those herds.

Interestingly, the yellow–red pigmentation is created by the class of melanocyte that produce the pheomelanins; the type of melanin which is known to react with free iron or manganese ions, forming the deleterious hydroxyl radicals as a result (82) – a mechanism that has been putatively implicated in the progressive neurodegeneration of substantia nigra cells in Parkinson's disease. The fact that melanins are involved in protecting the organism against acoustic shock and light (82) and that interactions between pheomelanin and metals create ototoxic or phototoxic effects (82) suggests that this type of progressive pathogenic mechanism – involving manganese, melanin and sound – could be central to the pathogenesis of TSE in some way.

Considering the ability of infrasonic radiation to penetrate through all biological tissues (61), it can be assumed that intensive bursts of infrasound will potentially exert pathogenic effects at a diverse array of electromagnetic receptors located in the retina, eyelid, pineal, etc., in, as yet, unrecognised susceptible genotypes.

Known health effects of infrasound

Low intensity infrasound from autocar engines has been well recognised to induce car sickness (24,61) – a mild serotonergic–vestibular disturbance involving nausea, giddiness, headache. Furthermore, The infrasound radiated from boilers and air conditioning (24,61) has been controversially implicated in the aetiology of 'sick building syndrome' – an increasingly common mystery condition which affects a high proportion of people working/living in the internal environs of certain buildings.

At higher intensities, infrasound can produce resonances in body cavities such as the chest and stomach, producing lethal damage to internal organs (24). The resonance effects on the brain have not been researched. Some low frequencies radiated from hi-fi equipment have caused sudden unexpected deaths at techno-type dance parties, where infrasonic sensitivity may have been induced by concurrent exposure to abusive psychotrophic drugs which impact serotonergic circuits in the CNS. Furthermore, experiments to develop a military infrasonic weapon by Vladimir Gavreau in France (61) had to be abandoned due the uncontrollable and lethal nature of the infrasonic radiation that could decimate buildings and biological life following a few seconds of application.

Intensive sources of infrasound generated from the application of man made appliances in the modern environment – rocket/missile launches and overflight of supersonic aircraft (61,84–88) which employ the 'afterburner' turbofan thrust technology – pose one the greatest health risks associated with infrasound.

Several field and laboratory research studies which began to substantiate the physiological effects of infrasound/sonic booms on human subjects were carried out by Von Gierke and others during the 1960s/1970s (61,84–88). Pathological effects had also been observed in the middle ear of servicemen who worked on German submarines during world war two and had been exposed to the infrasound radiated by the suction strokes of the engine cylinders (61,89).

Apprehension, fatigue, headache, lowered intelligence, salivation, coughing, voice modulation, increase of middle ear pressure, chest wall/nasal cavity vibration, visual field vibration, interference with respiration, hypopharyngeal gagging, cutaneous flushing and tingling where instantly invoked during several tests on human subjects exposed to two minute bursts of infrasonic frequencies of 5 cycles per second upwards at sound pressure intensities up to 150 dB (85). Other tests had demonstrated the severe impact of infrasound on

the vestibular system resulting in vertigo, feeling of falling, nystagmus, spatial disorientation, tinnitus (61).

With an increase in intensity and lowering of the frequency of the noise radiated from the larger modern afterburners employed on the supersonic passenger aircraft (61), there is a need to carry out updated studies on the possible long term delayed neurological effects of these more intensive sources of infrasound that are permeating our the modern environment.

One intriguing study by Jonathan Hagstrum (72) reported the disruption of pigeon races following permanent loss of homing orientation ability in pigeons who had flown into the 100 km boom carpet of the Concorde supersonic transport on several separate occasions. Concorde's intense infrasonic acoustic shock waves were considered to have disrupted the pigeon's navigational ability to follow naturally occurring infrasonic microseism cues which radiate from steep sided topographical features.

This observation is interesting in that navigational orientation skills of migrating birds, bees, dolphins, sharks and mammals are thought to be centred upon a physiological ability to simultaneously detect specific frequencies of both light and geomagnetic field from the earth (90,91). These radiations are thought to be detected at special blue light 'cryptochrome' receptors in the retina (92) and at magnetoreceptors in the retina, sinus, pineal, midbrain, etc. (20,90,91), which are all integrally interconnected to the circadian pathways.

The magnetoreceptors are biomineralized with ferrimagnetic magnetite (93) (present in humans also (94)), and this metal is thought to form the basis of an internal compass for magnetic field detection in mammals. Perhaps some pathogenic impact of the acoustic shock wave from Concorde had somehow disturbed/metamorphosed the polarization status of the atoms in the metal domains in magnetoreceptors, to the extent that the pigeons permanently lost their navigational abilities?

A SPATIO-TEMPORAL EPIDEMIOLOGICAL CORRELATION EXISTS BETWEEN THE FLIGHT PATHS OF SUPERSONIC AIRCRAFT AND CLUSTERS OF NEW STRAIN CJD/BSE

In respect of the fact that both the clinical and pathological profiles of BSE and vCJD involve disturbances of the circadian–vestibular–auditory pathways (1,9) and that infrasound is known to influence both the vestibular–auditory system (61) and the circadian biorhythms (26), then the emergence of clusters of the modern strain, aggressive TSEs (vCJD and BSE) in locations influenced by highly intensive infrasonic shock bursts may indicate an association with the aetiology of nvTSEs.

For instance, the infrasonic shock frequencies radiated from both sub-sonic flight paths as well as the 100 km sonic boom carpet (72) along the routine, charter and test flight corridors of supersonic aircraft seems to correlate with the spatial distribution of new variant TSEs incidence precisely. In this respect, the intense infrasonic waves emitted from the 'after burner' propulsion turbo fans that are employed during acceleration and deceleration of supersonic civilian and low flying military aircraft (61,79) could provide an explanation for the final pathogenic trigger in the multifactorial aetiology of nvTSEs.

From this perspective, it is easy to see how Britain and France became the exclusive host to virtually all cases of vCJD (49); since they are the countries who exclusively developed the Concorde supersonic passenger aircraft services which have employed the largest afterburner turbofans in use to date.

A spatial correlation exists between the map of the routine flight paths of Concorde (from Paris and Heathrow to JFK airport, New York return) (72,95) and its regular charter flight paths (96) (between UK/Channel Island airports and Heathrow) and the UK map illustrating distribution of BSE/vCJD incidence (6,49) (see Map 4).

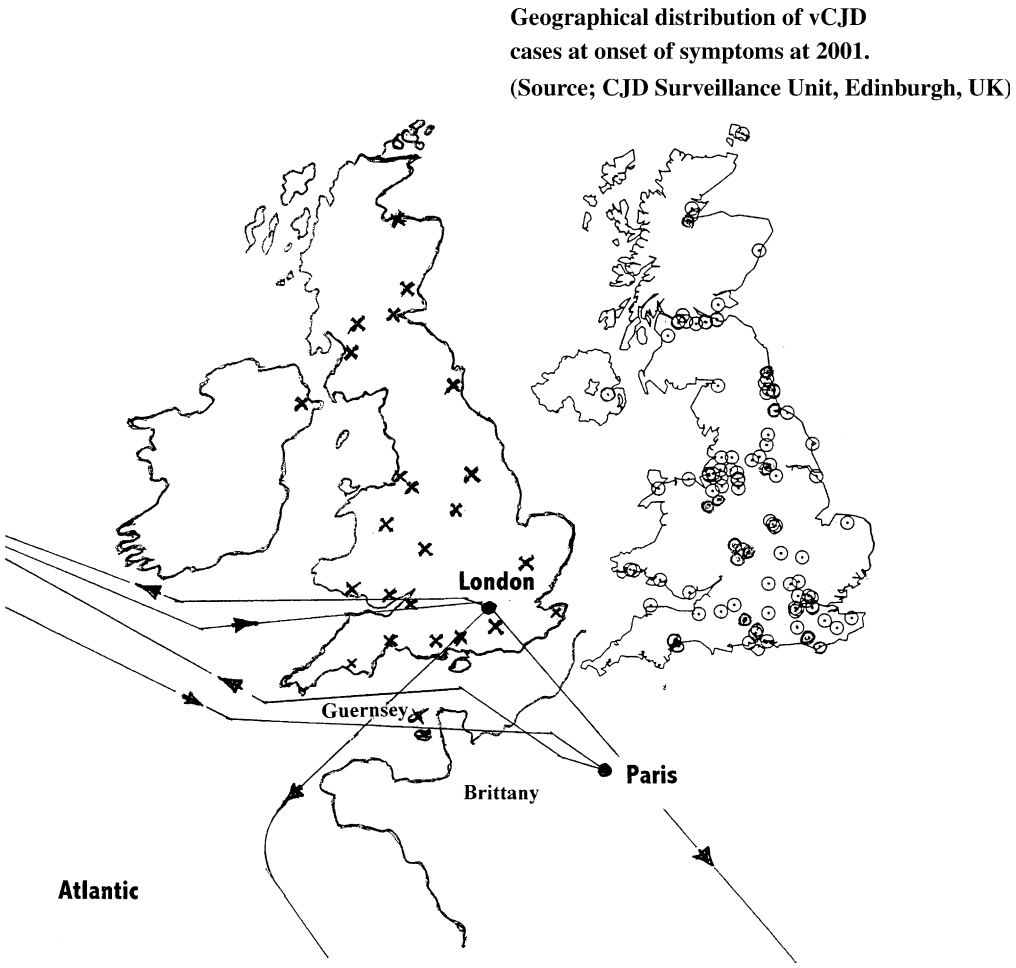
BSE largely originated in the mid south and south west of England, SW Eire (Co Cork), etc. (5,6), being areas over which the original routine transatlantic Concorde flights flew (95); and were therefore directly influenced by the 100 km boom carpet of infrasound radiated by the these overflights. During the early days of Concorde testing/service up until the late 1980s, structural damage to buildings (shattering of windows and ceilings, etc.) (88,95) due to Concorde's sonic boom was regularly reported in the news, particularly in the settlements sited alongside Concorde's flight corridor over the River Severn. Many of the initial public complaints had misattributed the mystery bangs and vibrations of Concorde overflights – which shook the whole of south west England and South Wales – to an earthquake of unprecedented proportion for the UK.

Recordings of the first 97 transatlantic departures of Concorde from Heathrow during 1976 revealed that 72% of those departures breached the max permitted noise levels of 110 PNdB (97). Some departures had recorded as high as 135 PNdB.

Presumably, modifications to the Mach speed, angle of take off and application of the afterburner turbo fans resulted in the easing of these problems to the more tolerable levels experienced over recent years.

As Concorde's regular charter and airshow flights expanded to cover visits to the more northerly airports of the England, N Ireland and Scotland, so the distribution of BSE and vCJD spread likewise (6,49) (see Map 4).

Sections of Northern Brittany lie beneath the initial routine service flight paths of the French Concorde (72),



Map 4 Flight paths of Concorde supersonic aircraft to and from London and Paris Airports; and to Barcelona and Middle East. (×) Special charter flight destination. (←) Daily commercial flight path route.

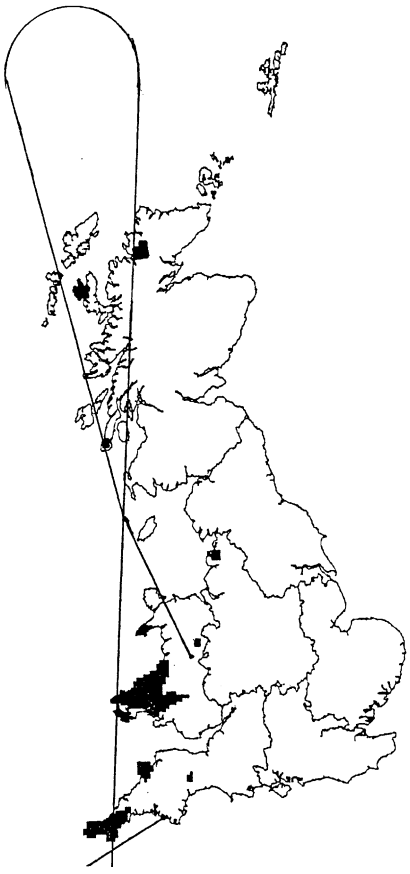
and it was this region that exclusively hosted the first French cases of BSE/vCJD (*98*). In fact, BSE remained exclusive to Brittany for a seven year period (*98*), apart from 3 outbreaks which occurred in the southern regions of France that lay beneath the Concorde route to the Middle East. Brittany is still burdened with the highest incidence rate of BSE in France today (*98*). Furthermore, Guernsey island hosts the highest incidence pocket of BSE in the world (1), and likewise lies directly beneath the flight paths of the French Concorde (72) (see Map 4) at a more distant location from Charles de Gaulle, Paris than Brittany; at which point incoming and outgoing flights are travelling at a higher Mach speed, thus radiating higher intensities of infrasonic shock.

Since the number of Concordes operating within the France and British fleets has increased – as well as an increase in routine flight traffic to destinations other than New York's JFK airport (e.g., to the Middle East and South America), plus increases in Concorde's 'joyride' charter services around the Bay of Biscay (*95*,*96*) – BSE subsequently started to emerge in the more southerly areas of Europe – Southern France (*98*), Switzerland, Portugal, Holland, Belgium, Spain, Italy, Germany (*6*) – being areas which are challenged by an increasing number of Concorde overflights serving an increasing variety of destinations.

The almost exclusive distribution of Italian BSE cases along the Eastern Coastal/Northernmost regions of Italy (*99*) correlates with the flight paths taken by UK and French Concordes along the Adriatic sea (*95*,*96*) on route to the Middle East (Map 8).

The mystery of 'western peninsula' intensive BSE foci solved?

Maps depicting the distribution of high incidence BSE clustering per annum across the UK were presented to the BSE Inquiry by the New Zealand epidemiologist, Professor RS Morris (100)(Map 5). These maps demonstrate that the most intensive category of BSE cluster (0.12–0.50



Map 5 The West Coast Supersonic Turbojet Test Route superimposed over the locations where the most intensive category of BSE cluster surfaced in the UK during 1986–1996 period. (—) West Coast Test Route. (■ 0.12–0.50 cases of BSE per 100 cattle per sq. km (source; Professor RS Morris evidence to BSE inquiry 14/10/99).

cases per 100 cattle per square kilometer) recorded during the UK BSE epidemic are all exclusively located on the westerly tips of remote peninsulas stretching along the western coastline of the British isles. This curious distribution was maintained for every year of BSE incidence that Professor Morris had charted (*1986–1996*). How can such a pattern relate to the feeding of MBM?

Intriguingly, the well used 'West Coast Route' flight path that was routinely used by supersonic jets of the military air forces as well as for testing Concorde aircraft fresh off the production line (88,101) (see Map 5) passes precisely over the centre of all of the highest incidence category of BSE foci denoted on Professor Morris's maps (100).

Military air bases or intensive low flying of military jets are also present/practised at all of these BSE cluster foci that are located at SW Cornwall, Hartland peninsula (Devon), West Pembrokeshire, Lleyn peninsular, Mull of Kintyre, Isle of Skye, Loch Glascarnoch, whilst another practise flight corridor – originally used by the Lightening aircraft (88) – transected the UK's southern counties (see Map *6*) across areas like Maidstone that hosted a vCJD cluster in the late 1990s (4) as well as high rates of traditional CJD recorded there in the 1970s (102).

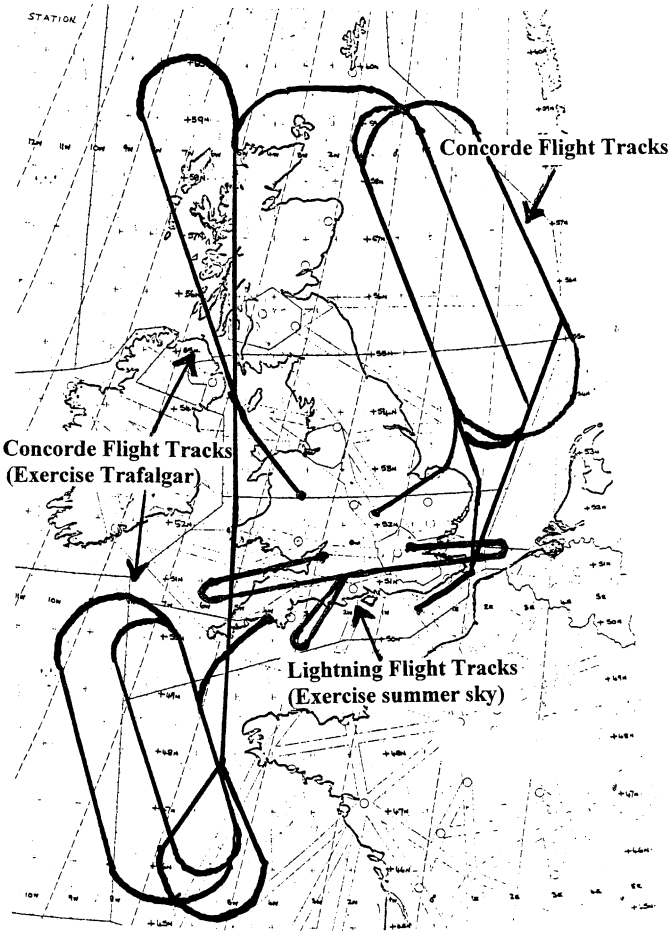
During 'Exercise Trafalgar' Concordes were repeatedly flown along the 'West Coast Route' during the 1970s (see Maps 5, *6*) and sonic boom experiments were carried out on patients of an isolated hospital, on farm/wild animals, on a cliff face and on building structures such as churches, monuments, etc., sited in the few remote western peninsula locations where this route passes over land (88). Given the relatively small total landmass area of Great Britain, the UK authorities executed by far the largest number of sonic boom experiments in areas close to human/animal populated areas (88) in relation to the few other countries who were involved in these types of trial (e.g., the USA and France).

Another epidemiological mystery ignored by the conventional consensus on BSE, which could prove relevant here, involves the significant 5-fold increase in BSE incidence (*6*,103) endured by cattle born during the mid winter period – for every year that BSE has existed. One underlying explanation for this and its relationship to the 'Western Peninsula' epidemiological mystery implicates the lack of copper availability in the farm food chain during the mid winter period – thus suggesting that calves born during this high risk period for Cu deficiency will subsequently acquire heightened hypersensitivity to the background noise of artificial and naturally occurring infrasonic waves.

Magnesium (Mg) levels are also at an all time seasonal low in the biosystem during the cold winter period, and Mg also plays a major role in protecting the organism against the deleterious impact of noise (82). Furthermore, the high rainfall status of these western peninsulas accounts for the acidic nature and correspondingly low Mg/low Cu profile of their soils (48) – a phenomena that further exacerbates the deficiencies of these elements in cattle residing in these regions.

Natural infrasonic waves, known as microbaroms, are generated in the atmosphere by ocean surface waves (*63*,*72*). These are considerably increased during the winter period due to rougher seas (104). In fact, the most westerly peninsulas of the UK would stand in the front line against the prevailing westerly winds that carry the infrasound generated from waves across the atlantic – additionally compounded by the carriage of the more intense shock waves of Concorde's transatlantic flights (104). In addition, strong westerly winds prevail in the stratosphere during winter, so that effective sound velocities are enhanced for waves travelling east and are considerably reduced for those travelling west (104).

This provides an explanation for a seasonally enhanced chronic infrasonic assault on these westerly



Map 6 Supersonic Test Routes used by Concorde, the lightning and other military jets since the late 1960s.

atlantic peninsulas of the UK during the wintertime – areas which are chronically exposed to a high intensity of background natural infrasound whilst being repeatedly 'topped up' by the acute bursts of infrasonic shock waves radiated from the high intensity of supersonic test/military overflights across these remote peninsulas.

Supersonic anecdotes

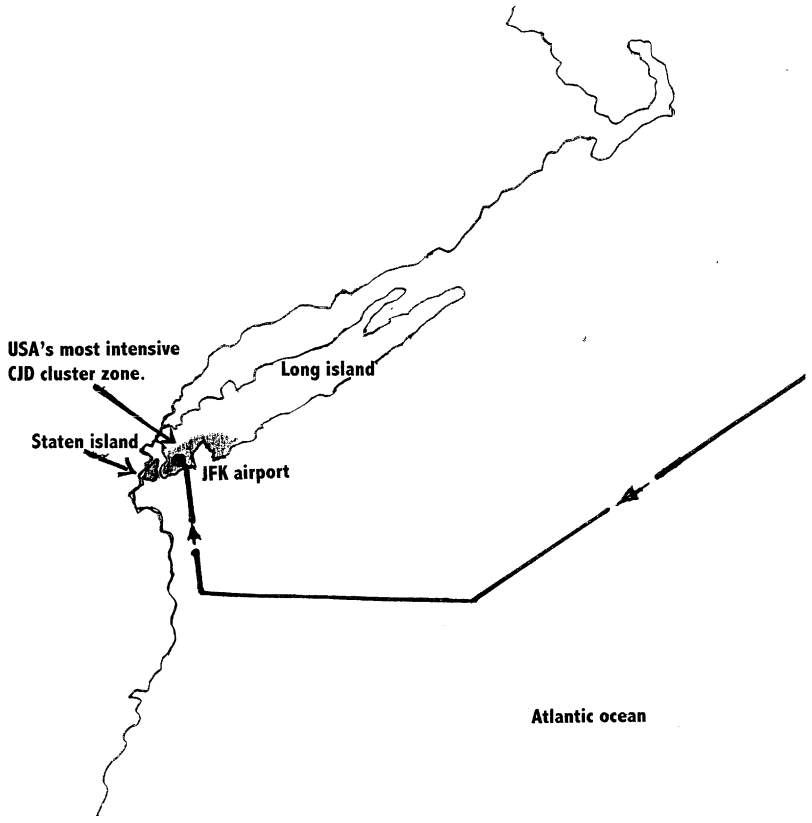
Interestingly, the Staten Island/Long Island environs around intensively used JFK airport – where both the French and UK supersonic transatlantic aeroplanes land; albeit under more stringent noise regulations than those applied in Europe – hosts the highest incidence cluster of traditional CJD in the USA (105) (Map 7).

Study of the environments where vCJD has clustered in the UK – Queniborough, Lymphstone, Adswood, Armthorpe, the Kent Weald, Burnham on Sea, Edinburgh, SE Lancs, Tenby, Eastleigh, etc. (3), have all experienced Concorde or other military turbojet aeroplane overflights connected to landing/taking off from local airports at Kegworth, Exeter, Manchester, Finningley, Heathrow, Bristol, Edinburgh, Liverpool, St Athan, Southhampton, respectively (96). Furthermore, the victims of vCJD in Queniborough had lived less then a kilometre from a hotspot of infrasonic radiation – a former small factory/airfield that was employed in the manufacturing and testing of aeroplane engines, where engines were routinely left running outdoors at full throttle for several hours at a time (personal communication; Queniborough villagers).

Anecdotal correlations which link up infrasonic exposure and TSEs abound; whilst conducting a survey on 15 BSE farms in Bavaria and 5 BSE farms in Holland, the author recorded intensive overflights of military and civilian jet aircraft passing directly over 100% of farms subject to the questionnaire.

A keen lifetime preoccupation of the 19 year old, first case victim of vCJD in the UK was military jet spotting (106). He had joined the RAF before his death.

A cluster of traditional CJD had also emerged in three small villages (East Chinnock, Crewkerne, Stoke Sub Hamdon.) of South Somerset during the 1990s (107).



Map 7 Flight paths of Concorde supersonic aircraft into JFK airport, New York, USA.

These villages lay beneath the incoming/outgoing flight paths of the RNAF Yeovilton airbase.

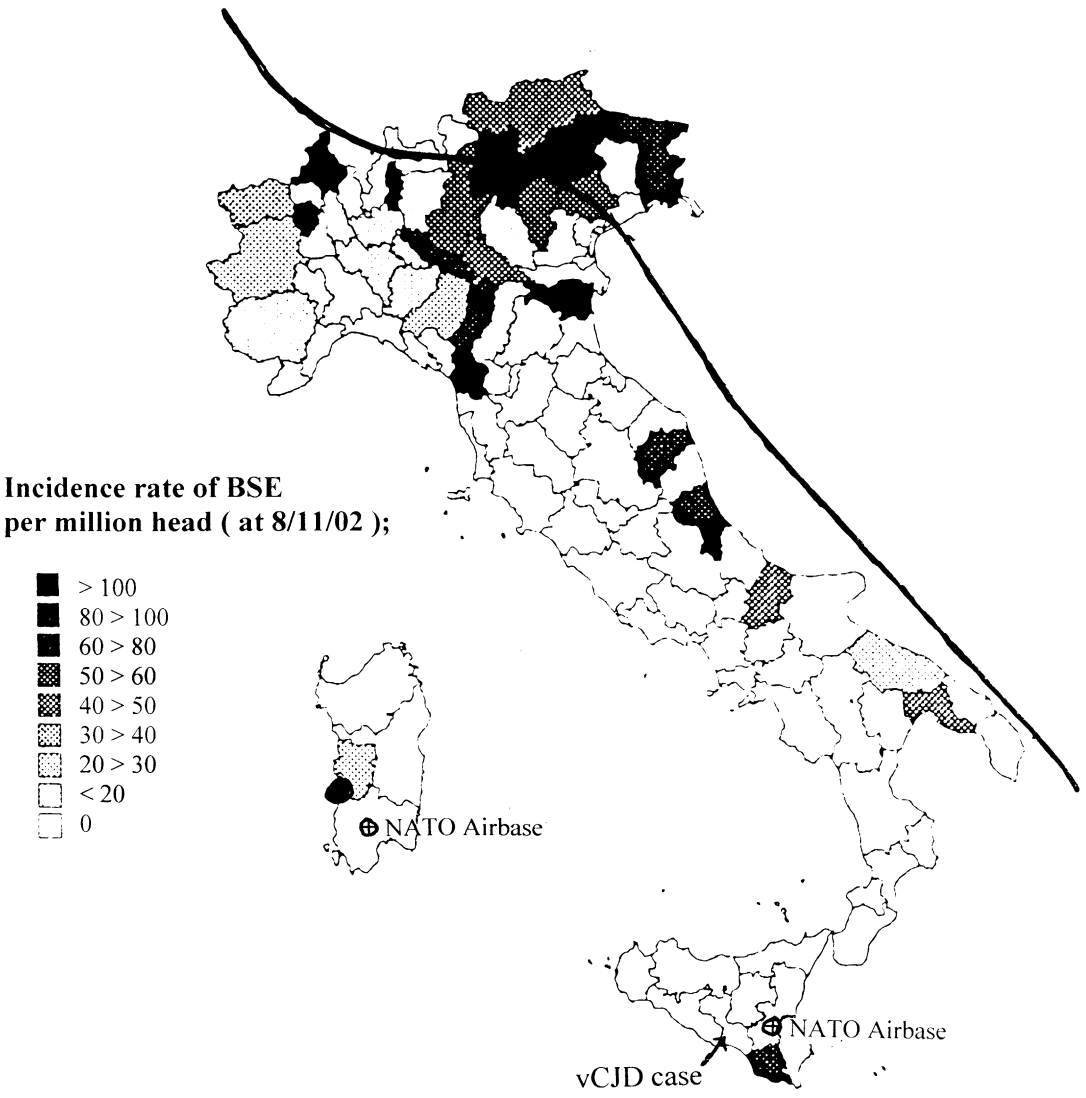
Between the mid 1960s and 1970s, military jets used to practise low flying at supersonic speeds along the specific length of the Front Range slopes in Colorado where deer have become affected with CWD since 1968 (1). After complaints from the residents of Fort Collins, the jet practise zone was largely moved out East along the S Platte river valley and the Nebraska plains – where CWD has subsequently emerged over the last decade.

Likewise, scrapie clusters have recently erupted at Assemini (1999) and Alghero (2002) in Sardinia (99)which are directly beneath the take off flight paths of both NATO military and civilian airbases at nearby Decimomannu, Cagliari and Alghero airports, respectively, whilst all BSE and vCJD cases that have erupted in Sicily (2000–2002) to date involved cattle and a single human (from Agrigento) who all co-resided in the southernmost district of Sicily (99) beneath the flight paths of military aeroplanes serving the nearby NATO airbase at Sigonella (Map 8).

Vicars suffer CJD at one of the highest incidence rates for an occupational group of 11.8 per million head of population (108). Apart from their chronic exposure to the infrasound radiating from church organs and bells, this may also stem from the fact that many churches and cathedrals ironically became the 'in vogue' target for testing the impact of sonic booms on building structures during Exercises Underlord, Gambit, Summer sky and Trafalgar carried out at the end of the 1960s/1970s in the UK (88). One of the prime test targets of Exercise Trafalgar was to 'sonic boom' the cathedral of St Davids in West Wales, since it lies directly beneath the 'West Coast Route' (88). The vicar of St Davids died of CJD in 1996.

A SPATIAL CORRELATION BETWEEN THE TECTONIC PLATE RIFT LINES AND CLUSTER LOCATIONS OF SPORADIC/FAMILIAL TSES (SEE MAP 3)

Clusters of sporadic/familial TSEs investigated in N Iceland, NE Colorado, Fuji (Japan), Slovakia, Calabria, Sicily, New Quinea, etc. (2,3,53,75–77), all lie over major seismic belt/tectonic plate rift lines in common (71,78). In fact, the offshoots from major plate margins, such as the infamous 'ring of fire' and the mid atlantic rift, seem to demarcate locations of traditional TSE clusters with remarkable fidelity (see Map 3). Furthermore, the clusters often appear at specific locations on



Map 8 Distribution of BSE/vCJD in Italy (99) in relation to Concorde and military flight paths/airbases. (—) Concorde route to middle east (95). (●) Military jet practise zone.

the plate boundaries where tectonic activity has historically given rise to bursts of geomagnetic energy and seismic waves which radiate infrasonic energy (62,67) (via volcanic eruptions (69), earthquakes (70), geothermal extrusions (62), thunder/lightning storms (65), etc.) (see Table 1).

Such a correlation gives credibility to the age old shepherds' anecdote which decrees that sheep will contract clinical scrapie after they have been exposed to a thunder/lightning storm (1)! As mentioned previously, these TSE locations are all sited in the key topographical landforms – such as parabole mountain valleys – which can serve as acoustic radiators or beacons; where amplification of infrasonic radiation results from incoming prevailing waves converging through 'wind tunnel' type locations (72).

INFRASONIC DISCUSSION

One of the difficulties of the 'supersonic' facet of this nvTSE origin hypothesis, is the approximate 10 year delayed lag period between the start of the first routine Concorde flights to JFK in 1976 (95), and first military turbojet practises, and the onset of the first reported cases of BSE in 1986 (1).

There are obviously many theoretical scenarios that could be generated involving the possible aetiological involvement of an infrasonic shock induced mutation in some cell line or other which did not manifest itself in a clinical capacity until the next generation. But, relative to this theory, the delayed lag could be explained by the fact that the 'infrasonic' seeding of the first metamorphosed Mn rogue prions took place during the suscep-

tible 'in utero' period, where the seeded bovine/human embryos would fail to develop the full blown clinical phase of the disease until adult life – after a protracted, so called 'incubation period' of free radical mediated neurodegeneration had sufficiently gathered momentum to enable the symptoms of TSE to emerge.

However, it seems more plausible to suggest that additional causal prerequisites which increase mammalian sensitivity to infrasonic shock need to simultaneously come into play. In respect of the theory under discussion, the compulsory high dose usage of the copper chelating warble fly insecticides which did not get underway until the start of the 1980s in the UK (4) (in combination with Mn supplementation in feeds), rendered the brains of cattle more susceptible to this class of infrasonic shock from the external environment.

A more nightmarish, yet perfectly feasible scenario envisions that the infrasonic shock vibrations from jet overflights or quarry/missile explosions, etc., could actually modify the atomic structure of trivalent Mn (e.g., as found in Mn perovskites, Hausmannite, etc.) in the specific types of open environment where these mineral species are found (see Diagram 5). The shock vibrations would metamorphose the paramagnetic Mn 3+ atoms (in the soil/vegetation/atmospheres) into their rogue ferrimagnetic forms; thereby instigating TSE susceptibility in any Cu deficient livestock/human who subsequently ingests/inhales these rogue Mn atoms from the infrasonically adulterated foodchain.

In this respect, it is interesting that TSE outbreaks seem to erupt in ruminant populations residing in overstocked or drought stricken areas where fierce competition has caused close-cropping/overgrazing of the pasture; thereby forcing animals to graze at 'soil level', ingesting greater quantities of soil than animals thriving in circumstances where pasture is more plentiful. Veterinarian Ciriaco Ligios of Sardinia and the veterinary pathologists at CSU in Fort Collins, Colorado, have both observed worn down/soil stained incisor teeth in the sheep/deer heads of scrapie/CWD casualties that are received at their labs for necropsy – putatively suggesting that the soiled/worn down teeth of these TSE animals indicates that a significant intake of rogue ferrimagnetic Mn from the soil could have potentially occurred.

FUTURE RESEARCH

Insight into the primary causal mechanisms underpinning the pathogenesis of TSE would enable the development of the most effective means of prevention, control and pharmaceutical cure for these diseases.

In this respect, a major extensive research programme needs to be executed into retesting/expanding the pilot observations cited in this paper. Furthermore, research that assesses the straightforward application of copper, selenium and zinc as a preventative treatment for TSEs should be put to test on domestic/wild livestock grazing in TSE risk cluster areas; where Cu and Zn would serve as a means of protecting PrP's Cu domain (14,15) against invasion by foreign cations, as well as ensuring an optimum supply of the right metals that catalyse the antioxidant enzyme groups in animals who would otherwise find their CNS unable to defend itself against hyperoxidative assault by incoming eco-oxidants.

Furthermore, electrophilic-electron acceptor pharmaceuticals, such as the porphyrin molecules (109), could be employed to target manganese bonded to PrP's histidine ligands and act as an electron acceptor; thereby reducing the potentially pathogenic Mn 3+ prion back to its sleeping Mn 2+ prion form. Pharmaceutical chelators that are specific to Mn 3+, etc., could also be tested as a means of reducing the load of Mn in the CNS.

Factors such as the magnetic susceptibility and resonance of the 'metamorphosed' Mn atoms bonded to prions in TSE is of critical importance when considering factors controlling 'the duration of incubation period' and 'severity of symptoms' in the TSE disease process. Therapies which could somehow depolarise or destabilise the magnetic charge of the foreign metal species bonded to pathogenic prions could be developed as a means of treating TSE.

Above all, surveillance programmes should be instigated which conduct analyses for the full range of metals that could be present in TSE affected brain material as a matter of urgency. Such a programme would quickly identify the precise metal species that serves as the copartner on the pathogenic prions in the different strains of TSE.

Comparative spectroscopy/magnetic status studies of metals drawn from topsoils exposed to infrasonic shock vibration and metals drawn from topsoils in infrasonic-free regions would make an interesting study. Furthermore, Mn 3+ prion cell cultures could be exposed to infrasonic shock waves to gauge whether infectious pathogenic prions are generated as a result.

The growing number of 'in vitro' laboratory trials that have confirmed the high Mn/Low Cu facet of this TSE environmental origin theory, along with the positive recommendations made by the BSE Inquiry/EU Commission in respect of instigating further research into this theory (2), indicates that the continued refusal of the various UK government departments to award grant support, let alone encourage research into the environmental perspectives of TSEs is little short of gross negligence.

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