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2 Chronic barium intoxication disrupts 3 sulphated proteoglycan synthesis: a hypothesis 4 for the origins of multiple sclerosis

5 Mark Purdey*

6 High Barn Farm, Elworthy, Taunton, Somerset TA43PX, UK

Received 20 November 2003; accepted 23 December 2003

Summary High level contamination by natural and industrial sources of the alkali earth metal, barium (Ba) has been identified in the ecosystems/workplaces that are associated with high incidence clustering of multiple sclerosis (MS) and other neurodegenerative diseases such as the transmissible spongiform encephalopathies (TSEs) and amyotrophic lateral sclerosis (ALS). Analyses of ecosystems supporting the most renowned MS clusters in Saskatchewan, Sardinia, Massachusetts, Colorado, Guam, NE Scotland demonstrated consistently elevated levels of Ba in soils (mean: 1428 ppm) and vegetation (mean: 74 ppm) in relation to mean levels of 345 and 19 ppm recorded in MS-free regions adjoining. The high levels of Ba stemmed from local quarrying for Ba ores and/or use of Ba in paper/foundry/welding/textile/oil and gas well related industries, as well as from the use of Ba as an atmospheric aerosol spray for enhancing/refracting the signalling of radio/radar waves along military jet flight paths, missile test ranges, etc.

It is proposed that chronic contamination of the biosystem with the reactive types of Ba salts can initiate the pathogenesis of MS; due to the conjugation of Ba with free sulphate, which subsequently deprives the endogenous sulphated proteoglycan molecules (heparan sulfates) of their sulphate co partner, thereby disrupting synthesis of S-proteoglycans and their crucial role in the fibroblast growth factor (FGF) signalling which induces oligodendrocyte progenitors to maintain the growth and structural integrity of the myelin sheath. Loss of S-proteoglycan activity explains other key facets of MS pathogenesis; such as the aggregation of platelets and the proliferation of superoxide generated oxidative stress. Ba intoxications disturb the sodium–potassium ion pump – another key feature of the MS profile. The co-clustering of various neurodegenerative diseases in these Ba-contaminated ecosystems suggests that the pathogenesis of all of these diseases could pivot upon a common disruption of the sulphated proteoglycan-growth factor mediated signalling systems. Individual genetics dictates which specific disease emerges at the end of the day.
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Introduction: the barium facts 29

Barium is a divalent alkali earth metal that is naturally present at elevated levels in certain soil types, oil/coal deposits and seawater [1,2]. Ba ores are exploited for many industrial, agricultural and medical applications [1,2]. The insoluble Ba sulphate is used as a suspension in contrast radiogra- 30
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*Tel.: +44-1984-656832.

E-mail address: tsepurdey@aol.com (M. Purdey).

36 phy in human and veterinary medicine, whilst the
37 soluble Ba salts – acetate, sulphide, carbonate,
38 chloride, hydroxide, nitrate – are highly toxic and
39 used extensively by industry, the military and ag-
40 riculture [3] for the manufacture of paper, pesti-
41 cides, rubber, steel/metal alloys, welding rods,
42 paints, fabrics, leather, fuel additives [4], TV/
43 electronic components, bomb/gun explosives,
44 flares, atmospheric aerosol sprays for refracting
45 radar/radio waves, cloud seeding weather modifi-
46 cation sprays, radar absorbing paints, ceramics,
47 glazes, glues, soaps, depilatories, cements, bricks,
48 drilling muds, dyes, inks, glass, water purifiers,
49 magnets [1,2].

50 The distribution of MS clusters correlates 51 with workplaces and environments that 52 are associated with elevated levels of Ba

53 Occupational groups that have been identified as
54 the highest risk for the development of MS, involve
55 those involved in paper manufacturing, wood pro-
56 cessing, leather, metal (especially zinc-related in-
57 dustries), welding, printing, textiles, electronics
58 and agriculture [5–12]. Intriguingly, Ba salts are
59 utilised as key ingredients in the fillers, glues, inks,
60 pesticides, welding rods, etc., that are employed
61 in *all* of these MS risk industries [1,2]. Further-
62 more, simultaneous exposure to the solvents that
63 are also used in these industrial processes would
64 exacerbate the problem of Ba exposure by in-
65 creasing the permeability of the blood brain barrier
66 [9], thereby enabling an increased uptake of Ba
67 into the brain.

68 Some MS epidemiological studies have shown
69 that examinations involving X-ray film exposure of
70 the gastro intestinal tract represent a significant
71 risk indicator for the development of MS [9,11].
72 Assuming that this observation represents more
73 than mere coincidence, then the customary use of
74 Ba sulphate in contrast radiography may represent
75 the pertinent aetiological factor here, rather than
76 the exposure to the actual X ray itself. In this re-
77 spect, several studies have shown that toxic
78 amounts of Ba can be absorbed across the gastro
79 tract [1,2,13,14] following use of this supposedly
80 insoluble compound in radiography, whilst other
81 cases of Ba intoxication have resulted from the
82 accidental use of the more soluble Ba carbonate
83 compound [15] in radiography. Furthermore, It is
84 likely that Ba would be absorbed considerably more
85 efficiently across the 'leaky' gut membranes of
86 those suffering from Crohn's or Ulcerative Colitis
87 (IBS syndromes), and it is this class of patient who

would represent a higher proportion of those being
subjected to this type of exploratory radiography.
On the other hand, the association between X ray
examinations of the gastro tract and MS develop-
ment could be more to do with the fact that both
MS and IBS sufferers share the same genetic pre-
disposition that determines susceptibility to both
IBS and MS [16]; thereby discounting the possibility
of an association between the aetiology of MS and
Ba use in radiology.

The highest prevalence of MS has traditionally
blighted the subsistent, rural populations scattered
across the Northern hemisphere; e.g. in Saskatch-
ewan, Nova Scotia, Iceland, Orkney island, North
Eastern Scotland, N Ireland, Norway, Sweden,
Finland [9,12,17], whilst, more recently, high in-
cidence MS foci have started to emerge nearer to
the equator in countries like Sardinia [18]. It is
interesting that the soil types of these localities
involve the limestones of Saskatchewan/Nova
Scotia, the pre cambrian granites, basalts, mica
schists of Iceland/Faroes/N Ireland/Scandinavea
and the old red sandstones of Orkney/NE Scotland
[17,19,20] which all naturally carry high levels of
Ba [1,2] and low levels of 'free' sulphur. Further-
more, in the case of the Sardinian, Canadian,
Scottish MS cluster regions, the local geological
veins are sufficiently rich in Barytes ore to support
the mining of Ba. Other studies have suggested
(without any analytical support) that elevated
levels of lead or molybdenum are common to the
soil types associated with MS clusters [19,21], but
the results of the author's own geochemical anal-
yses have failed to support these hypotheses.
Whilst lead levels were moderately raised in two of
the locations tested, the widely recognised co-
presence of Ba in lead rich strata [1,2] could rep-
resent the pertinent factor that has been over-
looked.

The low sulphur facet of the abnormal mineral
profile within MS ecosystems (see Table 2) is also
highly relevant in respect of determining the levels
of reactive Ba which can ultimately be absorbed
into the biosystem. Low levels of available 'free'
sulphur in the soil will considerably exacerbate the
problem of Ba/Sr toxicity, since sulphur readily
conjugates with Ba and Sr; thereby acting as a
'toxic sink' and preventative against Ba intoxica-
tion [22].

The coastal position of many of the MS high risk
populations onto the North Atlantic may be asso-
ciated with their dietary intake of seafoods, such
as shellfish and molluscs, which are known to bio-
concentrate Ba to excessive levels [1,23]. Seawater
of the northern Atlantic is notoriously high in Ba
due to the local seabed geology [1], whilst the

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144 additional intensive use of barium drilling muds in
145 the North Sea oil rig drilling industry – particularly
146 around the coast of NE Scotland – has considerably
147 exacerbated the problem of elevated Ba in the
148 marine foodchain since the 1980s [1]. In this re-
149 spect, the customary consumption of whale meat –
150 as well as shellfish and mussels – amongst the MS
151 risk populations could have unwittingly exposed
152 them to excessive bioconcentrations of Ba due to
153 the whale's dietary intake of algae/plankton which
154 bioconcentrate Ba from the surrounding seawater
155 to excessive levels in their cell membranes [1].
156 Reference should also be made here to the exclu-
157 sive reliance of the UK animal feed industry upon
158 the North Sea as its key source of 'fish meal' pro-
159 tein – a common component of concentrated
160 cattle feeds during the 1980s/1990s. Such a prac-
161 tice might have played an aetiological role in the
162 BSE epidemic which emerged in UK bovines, cats
163 and zoo animals during the 1980s/1990s – TSEs
164 representing one of the other classes of neurode-
165 generative disease that exhibit a tendency to co-
166 cluster alongside MS in these Ba-contaminated
167 ecosystems.

168 The billeting of the military in the MS affected
169 communities [8] of the Faroes, Iceland, Saskatche-
170 wan/Alberta borders, Guam, the Gulf war zones,
171 etc, has been associated with the onset of MS and
172 other neurodegenerative epidemics, and this could
173 be correlated to the sudden contamination of the
174 local atmospheres following detonations of Ba based
175 explosives [1,2] during military conflicts or exer-
176 cises, or due to other military uses of Ba such as radar
177 ducting aerosols [28]. Other routes of Ba exposure in
178 the MS clusters involve the proximity of the indi-
179 vidual's home, workplace or water supplies to
180 quarry explosions or the spreading of spent Ba drill-
181 ing mud across farmland – a waste product of the
182 fast expanding oil and gas well industry that was
183 observed in the Alberta/Saskatchewan MS clusters.

184 **Eco-analyses of MS clusters: materials** 185 **and methods**

186 The author has conducted a research programme
187 that analysed the levels of 46 elements in the soil/
188 vegetation/water collected from several of the key
189 MS cluster regions around the world.

190 **Soil sample collection/analysis method**

191 Each soil sample comprised a 300 g sample drawn
192 from a mix of 20 columns of dry soil bored with a

stainless steel auger; each column having been 193
bored at equidistant spaces along a W shape 194
spanning an area of approximately 5 acres, the 195
area being representative of the region harvested/ 196
populated by the MS affected individuals under 197
study. Each column was drawn from the top soil to 198
a depth of 6 in. having taken care to avoid inclusion 199
of root material/surface organic matter and col- 200
lection of samples near to gateways, roadsides, 201
animal dung, disturbed/excavated or polluted 202
terrain. The 20 columns were collected into a 203
plastic bag, then mixed into an even homogenate, 204
from which a further sample of no more than 300 g 205
was drawn and placed into a small polythene bag, 206
then sealed, labelled and transported to the labo- 207
ratories at the Department of Geology, Royal Hol- 208
loway, University of London, Egham Hill, Surrey 209
TW20 0EX, where samples were dried after arriving 210
at the laboratory in forced air flow cabinets. The 211
temperature was maintained below 32 °C during 212
the 12-h drying period and the air was constantly 213
dehumidified. The soil samples were then ground 214
to pass a 2 mm mesh using a hammer mill. The mill 215
was flushed between samples using a small portion 216
of the next sample. Each sample was analysed by 217
standard mass spectrometer analytical procedure. 218

Vegetation sample collection/analysis 219 **method** 220

Each plant tissue sample comprised a 200 g sample 221
representing tissue collected from approximately 222
10 pickings/diggings taken at equal spacings in a W 223
shape (where possible) across an area of approxi- 224
mately 5 acres that was representative of the re- 225
gion harvested/populated by the MS affected 226
individuals under study. Samples were picked dry 227
and at an appreciable distance from roadsides, 228
gateways, animal manure, mechanically disturbed 229
or 'spot' polluted terrain. The tissue was packed 230
directly into plastic bags, lightly sealed, labelled, 231
refrigerated and then transported to the labora- 232
tories of the Department of Environmental Sci- 233
ences at Derby University, Kedleston Road, Derby 234
DE22 1GB, UK. Each sample was placed in a plastic 235
sieve and thoroughly washed in deionised water. 236
After removal of any roots or soil, the samples 237
were spread evenly on a drying tray and dried in a 238
90 °C oven to constant weight, and then ground by 239
Christy Norris mill, a small portion of the next 240
sample being used to flush the mill, before col- 241
lection of the ground material. The samples were 242
then prepared for analysis by dry ashing for non 243
volatile elements and wet digestion in aqua/regia 244

245 for volatile elements (e.g. selenium). Analyses was
246 by standard ICP scan.

247 Results of eco-analyses of MS clusters 248 (see tables)

249 Working to a mean reference level of Ba in soils at
250 250 ppm and Ba in pasture vegetation at 10 mg/kg
251 [24,25], levels of barium (and/or strontium) were
252 recorded in the excessive/high ranges in the veg-
253 etation (mean: 74 ppm) soils (mean: 1428 ppm) of
254 all MS cluster environments analysed to date,
255 whereas levels remained in the normal ranges
256 (means; 19 and 349 ppm, respectively) within ad-
257 joining MS-free control regions (see Tables 1 and
258 2). Levels of free sulphur were recorded in the low
259 range in the vegetation of the MS cluster regions.

260 Weymouth, Massachusetts cluster

261 One high incidence cluster involved 40+ cases of MS
262 that have recently emerged in a middle class pop-
263 ulation living in a 3 sq. mile block of suburban
264 'dormitory' housing that is sparsely scattered
265 around the former US military naval airbase at
266 South Weymouth in Massachusetts [26]. A local
267 survey [26] had established that 70% of the MS
268 cases involved people who had been living beneath
269 or near to the incoming/outgoing flight paths of the
270 jet aeroplanes. Samples were drawn close to the
271 homes of the MS victims and the results indicated
272 that Ba, and to a lesser extent Zinc, were the only
273 elements that showed a significant deviation from
274 mean reference levels – Ba was 16-fold elevated in
275 the vegetation and 12-fold elevated in the soils –

see Tables 1 and 2. The levels of Ba recorded 276
normal in the identical soil types of the MS-free 277
adjoining area, suggesting that the high Ba re- 278
corded beneath the MS affected jet flightpath zone 279
derives from a pollutant source that is linked to the 280
activities of the aircraft – such as a Ba based sys- 281
tem of atmospheric cloud seeding for fog disper- 282
sion, or from the common practise of adding Ba 283
into jet fuels for capturing sulphur, suppressing 284
exhaust smoke [4], as well as creating a Ba ion 285
atmospheric aerosol [27,28] ducting path – for 286
enhancing/refracting radio and radar signals during 287
military jet practise or battlefield operations. 288

Aberdeenshire clusters 289

The three MS cluster foci in Aberdeenshire, NE 290
Scotland identified in the Shepherd thesis [12] 291
during the 1970s are located in the specific areas 292
where paper milling and/or granite quarrying was 293
exclusively prevalent. Furthermore, the drinking 294
water which supplied these MS populations used to 295
be drawn from springs that issue from the Ba rich 296
Dalradian quartzose mica schist geological series. 297
Another possible source of Ba contamination may 298
have stemmed from the aerial dispersal of Ba based 299
aerosols – such as the barium strontium titanate 300
compounds used for enhancing radar/radio wave 301
transmission [28] – along the flight paths of the 302
military jet 'low flying' test zones that operate 303
over these specific MS affected valleys in Scotland. 304
The author recorded high levels of Ba in all of these 305
Aberdeenshire MS cluster ecosystems, which in- 306
cluded levels of Ba at 46 and 694 ppm in the veg- 307
etation and soils lying beneath the flight path 308
entering the local military airbase at Lossiemouth. 309

Table 1 Levels of Ba, Mg, S in pasture vegetation drawn from MS cluster and MS-free adjoining region (Ba in mg/kg dry basis; Mg and S as %)

Cluster	Disease	Ba (range)	Ba source	Mg%	S%	No sample
Weymouth (Ma)	MS, ALS	160 (110–210)	Aeroplane fuel additive	.11	.22	×10
Randolph (Ma)	MS-free	14 (11–17)	Soil	.16	.38	×5
S Guam	MS, PD, AD	53 (30–91)	Volcano/WW2 bombs	.22	NR	×4
N Guam	MS-free	24 (21–27)	Soil	.41	NR	×2
Sardinia	MS, TSE	45 (124–13)	Soil/barytes/explosives	.23	.19	×13
S Sardinia	MS-free	14 (10–23)	Soil	.46	.47	×5
SW Saskatch	MS, TSE	50 (35–64)	Soil/bomb testing	.17	NR	×6
Vermont	MS-free	24 (12–46)	Soil	.30	.47	×20
Fort Collins, Co.	MS, TSE	56 (10–147)	Soil/cement/gypsum	.25	.19	×40
Aberdeenshire	MS	82 (42–121)	Soil/granite/paper mill	.24	.26	×10
Mean MS		74		.20	.21	
Mean MS-free		19		.33	.44	
Mean ref. range [25]		10 (0.5–40)		.37	.35	

Table 2 Levels of Ba/Mg in soils drawn from MS cluster and MS-free adjoining regions (Ba in ppm/MgO as %)

Cluster	Disease	Ba (range)	Ba source	Mg%	No samples
Weymouth (Ma)	MS, ALS	5017 (1745–8290)	Aeroplane fuel additive	0.49	×10
Randolph (Ma)	MS-free	396 ()	Soil	0.53	×5
S Guam	MS, PD, AD	601 (191–1170)	Volcano/WW2 bombs	1.73	×5
N Guam	MS-free	144 (66–302)	Soil	1.37	×4
Sardinia	MS, TSE	696 (478–1369)	Soil/barytes/explosives	0.78	×14
S Sardinia	MS-free	367 (290–454)	Soil	1.57	×6
SW Saskatch	MS/TSE	905 (591–2282)	Soil/bomb testing	0.69	×8
Vermont	MS-free	474 (326–762)	Soil	1.4	×20
Fort Collins, Co.	MS/TSE	568 (345–1091)	Soil/cement/gypsum	0.69	×40
Aberdeenshire	MS	786 (560–1570)	Soil/granite/paper mill	0.58	×12
Mean MS		1428		0.82	
Mean MS-free		345		1.22	
Mean ref. range [25]		250 (100–500)		1.00	

310 Other co-cluster locations

311 The author has also observed excess levels of Ba
312 and strontium (Sr) in specific districts within
313 Sardinia, Saskatchewan, Fort Collins (Co), Iceland,
314 NE Scotland and NE Leicestershire (UK) where a
315 high incidence of MS has co-clustered with other
316 types of neurodegenerative disease; particularly
317 the transmissible spongiform encephalopathies
318 (TSEs) and amyotrophic lateral sclerosis (ALS)
319 [29,34] – possibly suggesting that an exclusive type
320 of environmentally induced pathogenesis is shared
321 by all of these neurodegenerative conditions; one
322 that is determined by the prevalence of an abnormal
323 package of eco-factors in these co-cluster
324 environments.

325 South Pacific clusters

326 Elevated levels of Sr/Ba were recorded in the
327 miocene volcanic terrain which supports the vil-
328 lages on the southern tip of the isle of Guam [30] –
329 the area representing the ‘epicentre’ of the well
330 recognised cluster of ‘Guam syndrome’ involving
331 motor neurone disease, Alzheimer-type dementia
332 (AD), parkinsonism (PD) and MS that simultaneously
333 emerged in those individuals who were commonly
334 exposed to some insidious neurotoxic agent during
335 their early life [31,32]. Whilst the incidence rate of
336 these Guam syndromes used to run at 50× the
337 mean international rate for these conditions, the
338 outbreaks have significantly declined over recent
339 years, suggesting that the causal candidate/s were
340 present during the 1940s–1950s window period
341 [31,32]. Levels of Sr and Ba in the disease-free,
342 non-volcanic north of the island were nearer to
343 normal.

An additional source of artificial Ba contamina- 344
tion was introduced into the specific regions of the 345
South Pacific which subsequently became the 346
neurodegenerative cluster environments. This in- 347
volved the detonation of Ba based explosives [1,2] 348
during the intensive US bombing raids of world war 349
two, when the coastlines of the Japanese occupied 350
Guam, Rota island, Irian Jaya and southern Japan 351
were specifically targeted by the US aircraft carrier 352
assaults of june/july 1944. This may explain why 353
the high incidence clustering of neurodegeneration 354
simultaneously surfaced in the populations who 355
were occupying all of these specific conflict regions 356
[31,32] – where their syndrome represents a de- 357
layed neurotoxic response to the detonation of Ba 358
based explosives. Furthermore, the New Guinea 359
‘Fore’ tribesfolk who developed an epidemic of 360
‘Kuru’ TSE in the 1950s had accidentally exploded 361
several bombs whilst looting the WW2 bombers 362
which had crash landed in their highland territories 363
during the 1940s [33]. Furthermore, the Fore folk 364
had also scavenged the metal fuselage sheeting (365
painted with barium based radar absorbing pig- 366
ments) from the planes and utilised them for tools 367
and cooking pans. 368

The biochemistry of a Ba initiated MS 369 pathogenesis 370

Whilst 90% of Ba absorbed into the biosystem is 371
deposited in the bones, the remaining 10% is ab- 372
sorbed into the soft tissues such as the brain and 373
cardiovascular system [1,2]. In this respect, it is 374
not surprising that cases of Ba intoxication fre- 375
quently simulate inflammatory and neurotoxic 376

377 conditions of the nervous system such as Guillain
378 Barre syndrome, fish poisoning (ciguatera) and
379 periodic paralysis [3].

380 During circumstances of calcium shortage, Ba
381 can replace Ca causing the Ca channels to 'scram-
382 ble' into a state of rapid fire, inducing an overdrive
383 of the cholinergic and monoaminergic neuronal
384 systems [1].

385 Chronic exposure to the reactive, soluble Ba
386 salts could initiate the pathogenesis of MS [3] via a
387 straightforward pathogenic mechanism based upon
388 the capacity of Ba ions to readily conjugate with
389 sulphates in the biosystem [1–3] – via an electro-
390 static and non electrostatic interaction with the
391 carboxylate/water molecules (see Fig. 1). The re-
392 sulting loss of free sulphur deprives the sulphated
393 proteoglycan molecules of their essential sulphur
394 component, whereby the synthesis of a metaboli-
395 cally viable proteoglycan molecule is impaired
396 [35]. Furthermore, Ba can also knock out S-proteo-
397 glycans when Ba reacts *directly* with S-proteo-
398 glycans to yield the Ba sulphate; an interaction
399 which is exploited by biochemists for analysing the
400 sulphate content of the proteoglycans [36]

401 Once the syndecan, perlecan and glypican types
402 of sulfated heparan proteoglycan are deficient
403 within the biosystem, then the proteoglycan-de-
404 pendent fibroblast growth factor-2 (FGF) signalling
405 system is disrupted, causing a collapse in the pro-
406 liferation of the oligodendrocyte/astrocyte type 2
407 progenitor cells that are essential precursors of the
408 mature oligodendrocyte/astrocyte glial cells
409 [37,38]. In this respect, a Ba-induced disruption in
410 the synthesis of these sulphated proteoglycans,
411 blocks the vital participation of these molecules as
412 co-receptors for the growth factors and extracel-

413 lular matrix molecules which specifically regulate
414 the signal that induces oligodendrocyte/astrocyte
415 progenitor proliferation, migration and adhesion
416 phenomena; which, in turn, blocks the develop-
417 ment and structural maintenance of the multila-
418 mellar myelin sheaths [37,38] – the central
419 pathogenic mechanism of MS pathogenesis. Fur-
420 thermore, the Ba-induced disruption in the for-
421 mation/maintenance of astroglial cells, as well as
422 the oligodendrocytes, could explain why TSEs are
423 co-emerging alongside MS in the animal/human
424 populations who are residing within these high Ba
425 ecosystems; for a disturbance in the metabolism of
426 astroglial cells is a consistent feature of TSE
427 pathogenesis [39].

428 Ba contamination would also impair the supply
429 of free sulphur required for the disulphide bonding
430 of the peptides that are structurally assembled into
431 the building blocks of the myelin sheath [35]. Fur-
432 thermore, the loss of the S-proteoglycans would
433 disrupt cell cell signalling and the subtle confor-
434 mational changes surrounding the all important
435 amino acids in the tryptophan peptide of the my-
436 elin basic protein that enables serotonin (5HT) to
437 bind [40]. Since 5HT binding to this peptide is
438 regulated by the co binding of both FGF and sul-
439 phated proteoglycans to local tyrosine kinase re-
440 ceptors [35,41], it is easy to envision how a Ba-
441 induced impairment of proteoglycan signalling
442 could disrupt the cell to cell signalling that enables
443 5HT to bind to its peptide domain on myelin basic
444 protein. The resulting cessation of the signal leads
445 to a 'shut down' in the phosphorylation which is
446 normally required to induce the subtle conforma-
447 tional changes within the tryptophan peptide that
448 determines the successful binding of 5HT to myelin

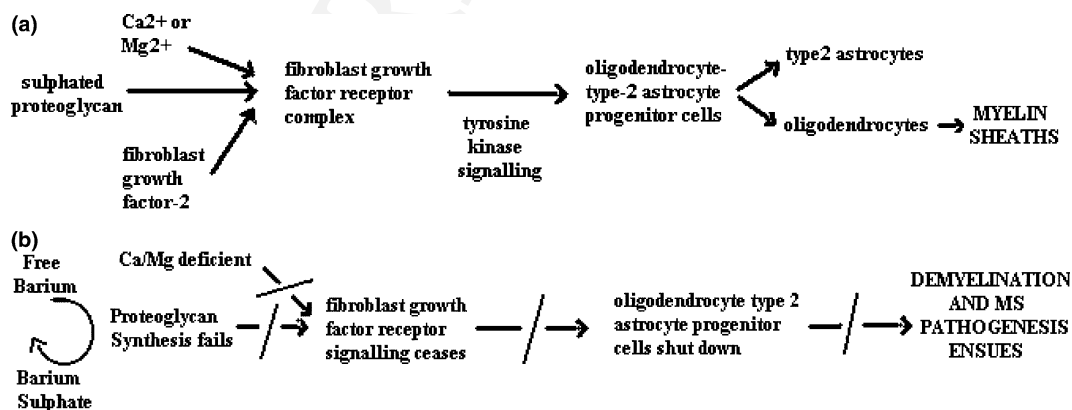


Figure 1 (a) Healthy proteoglycan metabolism. A co-requirement for sulphated proteoglycan, Mg/Ca cations and fibroblast growth factor type 2 in the regulation of the tyrosine kinase receptor complex, which, in turn, regulates the proliferation of the oligodendrocyte progenitors which mediates the synthesis of the myeline sheath. (b) Barium disrupted proteoglycan metabolism and MS pathogenesis. A barium induced sulphur starvation and Mg deficiency disrupts the proteoglycan mediated proliferation of progenitor cells and the production of the myelin sheath.

449 basic protein [40]. Such an aberration could lead to
450 a successful replacement binding by some oppor-
451 tunist alien 'heavy weight' molecular mimics [41]
452 (e.g. Lysergic acid diethylamide, Mescaline, am-
453 phetamine, cannabis, etc.), where the overall
454 molecular weight of the newly formed 'alien-amino
455 acid' complex is excessive; thereby invoking a
456 lymphocyte mediated auto immune attack on the
457 myelin protein – the key feature of MS/experi-
458 mental autoimmune encephalomyelitis [40,41,44].

459 A Ba-induced depletion of endogenous S-pro-
460 teoglycan turnover would also lead to platelet ag-
461 gregation due to a similar style block in 5HT binding
462 and a disruption of cell cell communication with
463 the platelet adhesion molecule [42,45]. Loss of cell
464 surface proteoglycan binding to superoxide dismu-
465 tase would result in the proliferation of superoxide
466 generated oxidative stress [45]. There is evidence
467 for both increased platelet aggregation [44] –
468 caused by a block in 5HT uptake [43] – and in-
469 creased superoxide generated oxidative stress in
470 the pathogenesis of MS [46].

471 Ba intoxication induces a disturbance of the so-
472 dium–potassium (Na–K) ion pump leading to ex-
473 tracellular hypokalemia [1–3], where the Ba ions
474 competitively block passive cellular potassium (K)
475 ion efflux, whereupon continuous activity of the
476 Na–K ion pump leads to an accumulation of K and
477 extracellular hypokalemia – an imbalance in the K
478 channels is evident in the pathogenesis of MS [44].

479 Discussion and conclusions

480 The sulphur-capturing facet of Ba intoxication of-
481 fers a credible explanation for the key demyelin-
482 ating feature of MS pathogenesis [43]. In this
483 respect, the involvement of other sulphur-captur-
484 ing organic chemicals and metals, like Mo, Sr, Zn or
485 tributyl tin [3,23], should also be considered as
486 alternative candidates for initiating the breakdown
487 in the proteoglycan-FGF signalling systems that is
488 putatively involved in the pathogenesis of MS.

489 The key tenet of this hypothesis pivots upon the
490 Ba-induced breakdown in the proteoglycan-FGF
491 signalling systems which normally maintain the ol-
492 igodendrocyte and type 2 astrocyte progenitor cells
493 [37,38]; thereby ultimately disrupting the synthe-
494 sis/maintenance of the myelin sheath. This tenet is
495 readily testable in the cell culture model, where
496 oligodendrocyte/astrocyte type 2 progenitor cells
497 are exposed to levels of Ba that reflect concen-
498 trations that would be expected to penetrate the
499 brain following chronic atmospheric exposure to Ba
500 in welding fumes or military radar/radio ducting

aerosols, or following dietary exposure to Ba con-
taminants in foods and water. The possibility of a
nasal-olfactory route of airborne Ba intake into the
brain [47] should also be born in mind when as-
sessing the dose range in the protocol.

Postmortem analyses of MS affected brain in
order to establish the distribution and concentra-
tion of Ba/Sr/Mo depositions would also be useful.

If the results of any future challenge continue to
substantiate the preliminary observations that un-
derpin this hypothesis, then benefits could be
gained from developing therapeutic treatments
with Ba chelating agents that can cross the blood
brain barrier; or, alternatively, by direct treatment
with the classes of S-proteoglycan that will re-
plenish the biosystem of the specific types of S-
proteoglycan that have been depleted during the
initiating stages of the disease. Pioneering therapy
with S-proteoglycans is currently being adminis-
tered to a vCJD in Northern Ireland.

The already established evidence for a disturbed
proteoglycan-FGF co-receptor signalling system in
the pathogenesis of several types of neurodegen-
erative disease (AD, PD, MND, TSEs, etc.) [42,48] is
advanced by this preliminary report on the novel
discovery of elevated levels of sulphur-capturing
Ba/Sr elements, combined with low sulphur, in the
cluster environments of these neurodegenerative
diseases. These observations suggest that chronic
or acute-on-chronic Ba/Sr intoxication could play a
primary role in the multifactorial aetiology of these
diseases.

Furthermore, the analytical observations of the
author and others have observed low levels of
magnesium (Mg) and Ca in the ecosystems that
support these neurodegenerative cluster communi-
ties [30,31,49]. This observation of low Ca/Mg
provides a further pathogenic explanation for the
shut down of the proteoglycan-FGF co-receptors;
in that these receptors have a co-dependence upon
the presence of Ca and Mg cations if a viable
binding of the FGF to its tyrosine kinase receptor is
ultimately able to succeed [42]. In this respect an
overall multifactorial hypothesis is postulated
which decrees that any population that is depen-
dent upon an ecosystem that is characterised by
this *aberrant mineral template* – involving high
levels of Ba/Sr and low levels of Mg/Ca/S – is
compromised into a position of high risk of devel-
oping MS, AD or TSE. Whilst many other environ-
mental, stress, idiosyncratic and genetic factors
are involved in the aetiological interplay, it is those
factors which influence the permeability of the
blood brain barrier function – thereby permitting
excess uptake of Ba/Sr into the brain – which are
of paramount importance in determining our sus-

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557 ceptibility to these diseases. Individual genetics
558 determines which particular class of neurodegen-
559 erative wasting disease emerges at the end of the
560 day.

561 Considering the diverse array of Ba usage within
562 the modern environment [1,2], it is suggested that
563 chronic, or acute-on-chronic exposure to the in-
564 soluble salts of Ba could represent a hitherto un-
565 recognised mode of delayed neurotoxicity that is of
566 major public health significance. Further research
567 needs to be channelled into investigating the pro-
568 posed aetiological association between these re-
569 active alkali earth metals and the origins of MS, as
570 well as the other types of neurodegenerative con-
571 ditions such as AD, ALS, TSE.

572 Acknowledgements

573 To Dr. David Grant (Aberdeen) for enlightening
574 discussion and education surrounding the bio-
575 chemistry of proteoglycan molecules. This work
576 was unfunded.

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