



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

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**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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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].

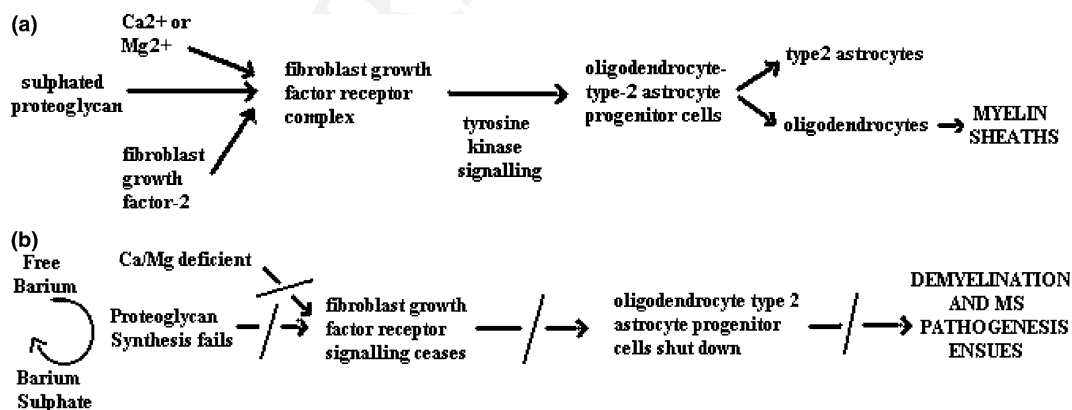
380 During circumstances of calcium shortage, Ba  
381 can replace Ca causing the Ca channels to 'scram-  
382 ble' into a state of rapid fire, inducing an overdrive  
383 of the cholinergic and monoaminergic neuronal  
384 systems [1].

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.

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