J. Afr. Ass. Physiol. Sci 5 (1): 29-40, July 2017

Journal of African Association of Physiological Sciences

Official Publication of the African Association of Physiological Sciences
http://www.jaaps.aapsnet.org

Research Article

Mg/Ca ratio in fertilization and agricultural soils, Mg percent of liming agents and human mortality in Finland during 1961-90

Timo Töysä[1] and Osmo Hänninen[2]

Specialty General Practice, Rehabilitation Hospital Vetrea, Pohjolankatu 15, FI-74100 Iisalmi, and [2]Department of Physiology, University of Eastern Finland, FI-70211 Kuopio, Finland

Keywords:
CHD, non-CHD, Mg, Ca, Se, Si, soil, fertilization, recycling

ABSTRACT

Background: Mg is a cofactor in more than 300 enzymatic reactions and its deficiency has been reported to be associated with cardiovascular diseases. Human Mg balance depends on food composition, food processing and Mg variation in foodstuffs, which can be roughly prognostigated by Mg proportion in fertilization and soil. Strong increase of NPK (nitrogen, phosphorus and potassium) in mineral fertilization (fm) included relative delay in Mg supplementation and dilution in plant available silicon (Si) via recycled nutrients (rcl). (Silicon is not included in essential fertilizers in Finland.) **Methods:** We have assessed old data on Ca and Mg in agricultural soils and approximate data on fm, rcl, as well as Mg % of liming agents (Mg-%.lim) and total (TOT), CHD and non-CHD (nCHD) death-rates of humans by R squares and graphics, in order to clarify their associations and possible causality. **Results:** Mg/Ca ratio in total fertilization (ft =fm + rcl) was decreasing in 1951-64 and after that mainly increasing. Soil (Mg/Ca) in 1961- 2000 responded on (Mg/Ca).ft with delay of ca 5 years. During 1961-90 (Mg/Ca).fm "explained" CHD by 74-89 %, non-CHD by 87 - 96 % and TOT by 90 - 94 %. (Mg/Ca) fertilization ratios "explained" better female than male CHD, but TOT and non-CHD more similarly. Soil (Mg/Ca) "explained" male CHD by 94 %, but all other death-rates weaker than (Mg/Ca).fm. Different smoking habits could explain this sex difference. All given associations were highly significant ($p < 0.001$). **Conclusion:** Mg/Ca changes in fertilization preceded respective changes in soil Ca by five years. They explained in general better than the soil value changes in death-rates, except M.CHD with obvious "tobacco delay". Effects of silicon and its association with rcl/ft ratio are discussed.

INTRODUCTION

Tissue Mg

It is known that Mg is a cofactor in more than 300 enzymatic reactions and can affect on vascular health in many ways, but evaluating of Mg status is difficult and chronic changes of Mg status are poorly understood (Elin, 1994).

There are few studies concerning tissue Mg (T-Mg) and CHD: Schechter et al. (2000a) have reported on decreased T-Mg in sublingual epithelial cells, Jeppesen (1986) on decreased T-Mg in femoral muscles and Gyllestad et al. (1992) on estimated decrease by iv Mg loading test in connection with CHD.

Approximation of T-Mg via dietary surveys includes several difficulties: Mg availability depends on composition of foodstuffs, mineral composition variation inside foodstuffs and food processing: Different foodstuffs contain different amounts of nutritional factors, but estimation of Mg content of daily food with the aid of food composition tables can be misleading because of the bias between the tables and results of chemical analyses (Koivistoinen et al., 1970). Additionally, food processing can affect on mineral element concentrations of foodstuffs, e.g. wheat meal contains 0.21 - 3.0 g Mg/kg depending on the grade of refining (Koivistoinen et al., 1980). Additionally. T-Mg depends on regulatory factors: Mg-absorption and urinary excretion. Absorption is increased by vitamin D (Charles et al., 1984) (and exposition to sunshine). Silicon can increase intracellular Mg uptake and fortify its antihypertensive effects in hypertensive rats (besides of its suppression

*Address for correspondence:
E-mail: timo.toysa@fimnet.fi

on gene expression of angiotensinogen and anti-inflammatory properties) (Maehira et al., 2010). Mg loss (U-Mg) can be increased by neurohormones aldosterone, angiotensin II and plasma renin activity (Lin et al., 2005), alcohol (Laitinen et al., 1992) and hyperglycemia (McNair et al., 1982). Sex hormones can reduce T-Mg (Pasternak et al., 2004). Sleep deprivation can obviously decrease T-Mg (Tanabe et al., 1998). Genetically dependent noradrenaline activity can decrease P-Mg (Amyard et al., 1995). P-Mg is not a reliable measure of Mg balance, because P-Mg is less than 1 % of body Mg (Elin, 1994) and P-Mg can change quickly under conditions of acute stress (catecholamine release) without effects on Mg excretion (Ryzen et al., 1990). The T-Mg decrease caused by neurohormones can be relieved by β-blocker (Lin et al., 2005) and decrease caused by sex hormones can be diminished by vitamin E (Laitinen et al., 1992). Mg-deficiency can reduce vitamin D activity (Rude et al., 2006). In cows high dietary potassium (K) and crude protein (N) can decrease P-Mg and cause symptoms of Mg-deficiency (Kemp, 1960).

Magnesium and CHD risk factors

"A crucial step in the pathogenesis of atherosclerosis is believed to be the oxidative modification of low density lipoprotein (LDL). The oxidation of LDL is a free radical driven lipid peroxidation process and the aldehyde products of lipid hydroperoxide breakdown are responsible for the modification of the LDL apoprotein" (Esterbauer et al., 1993)

Normal P-Mg - in contrary to hypomagnesemia (P-Mg 0.48 mmol Mg/L) - can protect cardiac muscle against ATP reduction, lipid peroxidation and LDH (lactate dehydrogenase) release during affection by reactive oxygen species (Manju and Nair, 2006) - i.e. Mg can work like an "on-demand antioxidant". Nuoranne (1978) wrote that "pigs may suffer from Mg deficiency despite the fact that the food Mg content is distinctly higher (0.16 %) than that recommended by international norms (0.05 %) for feeding. -- a prompt lowering of food Mg level can cause a manifest increase in ASAT, LD (i.e. LDH) and BASP (AFOS) values within 2 to 3 days in pigs". Masoudkabir et al. (2011) have reported that liver transaminase activity can reflect the severity of CHD. Mg deficiency can reduce blood ATP and increase several folds the activity of plasma GGT (gamma-glutamyl transpeptidase activity) in rats (Hsu et al., 1982). Niccoli et al. (2013) wrote that GGT, a marker of oxidative stress, could predict human CHD progression independently of lipid-lowering therapies.

Mg can affect on the main CHD risk factors: Mg supplementations can decrease blood pressure (Witteman et al., 1994). Acute Mg deficiency can provoke inflammatory cytokine production (Malpuech-Brugère et al. 2000), which can increase cholesterol synthesis (Memon et al. 1993). Oxidized LDL can increase LDL/HDL ratio in plasma (Bourdon et al., 2006) (and so total cholesterol/HDL cholesterol ratio). Additionally, to the effects on CVD risk factors, Mg deficiency can increase mortality by dynamic mechanisms: coronary artery spasm and cardiac arrhythmia (Bloom 1986). Mg deficiency can increase platelet-dependent thrombosis (Shechter et al., 2000b) - i.e. Mg can be included in antithrombotic agents.

Mineral elements in soil and nutrition

Mineral composition variation in food has been known for decades (Koivistoinen et al., 1970), but the association between soil mineral elements and nutrition has been, with a few exceptions, monitored less closely in human than in veterinary medicine or agricultural sciences. The equivalent sum of Ca, Mg, K and Na per dry weight of soil in standard circumstances is approximately constant, and by changing their ratios in soil it is possible to change their ratios in plants (Itallie van, 1938). Generally is known that in most soils concentrations of Na and K are small relative to Ca and Mg and Mg < Ca (e.g. Toysa, 2015), why (in regression analyses) Mg/(Ca+Mg) or Mg/Ca ratios can be benefited instead of Mg/(Ca+Mg+K+Na). Based on old studies (Sippola and Tares, 1978 and Kähäri & Nissinen, 1978) soil Mg/Ca ratio has been reported to explain ca 70 % of areal timothy Mg/Ca variation (Toysa, 2015).

In time-related surveys on agricultural soil Mg/Ca in 1961-90 has been associated inversely with human CHD, stronger by men than by women (Toysa, 2016a). This was somewhat surprising, because women should make up the population of golden standard for assays of the effects of soil mineral elements, because it is, as generally known, less contaminated by tobacco or alcohol, especially at the first half of the period 1961-90. (N.B. in Toysa (2016a) Fig 2 is slightly biased, but the data in Table 2 are correct). By favoring dolomites (Jokinen, 1981) in liming agents (here included in mineral fertilizers) negative Mg balance of soil was changed positive in the 1970's. Silicon is not generally included in fertilizers (Epstein, 1999), why decrease in rcl/ft ratio has been decreased plant (available) Si.

The aim of this assay is to clarify associations of fertilization factors [(Mg/Ca).fm and (Mg/Ca).ft] with soil factor [(Mg/Ca).sm] and their associations with female and male death-rates - statistically in the period

Table 1. Age adjusted TOT and CHD mortality of 35-64 y old females and males, Ca and Mg (.sm) in agricultural soils, mineral fertilization (.fm) and approximate Mg-% of liming agents during 1951-2000 In Finland (in order to help comparison with previous articles soil values are given as kg/ha and Eq/ha)

	F.TOT	F.CHD	M.TOT	M.CHD	Ca.sm	Mg.sm	Ca.fm	Mg.fm	Ca.fm	Mg.fm	Mg-% of liming agents
	%		1/100,000		mEq/L	mEq/L	kg/ha	kg/ha	Eq/ha	Eq/ha	
1951	727	122	1467	410			35	3.4	1764	280	2.5
1952	713	113	1373	388			35	3.4	1767	279	2.5
1953	683	104	1363	363			48	4.3	2417	352	2.5
1954	653	96	1308	371			53	4.6	2665	378	2.5
1955	637	103	1363	385			51	4.4	2559	366	2.5
1956	630	92	1323	368			56	4.8	2799	393	2.5
1957	647	86	1348	358			57	5.7	2837	468	2.5
1958	603	88	1303	361			60	5.9	3002	488	2.5
1959	587	90	1268	383			71	6.7	3522	547	2.5
1960	583	92	1303	392			71	6.6	3519	547	2.5
1961	583	98	1303	421	69.3	15.5	76	7.0	3782	578	2.5
1962	583	107	1338	468	69.3	15.5	58	5.9	2896	484	2.5
1963	570	103	1348	472	69.3	15.5	86	7.7	4286	633	2.5
1964	557	99	1343	501	69.3	15.5	95	**8.2**	4726	678	2.5
1965	550	101	1368	501	69.3	15.5	89	7.9	4430	646	2.5
1966	540	97	1318	505	71.5	14.6	77	7.1	3826	581	2.5
1967	527	105	1343	515	71.5	14.6	71	6.7	3555	547	2.5
1968	523	98	1343	512	71.5	14.6	75	6.8	3734	557	2.5
1969	524	91	1371	495	71.5	14.6	77	6.9	3841	570	2.5
1970	491	88	1299	477	71.5	14.6	78	7.0	3884	575	2.5
1971	484	90	1350	506	73.5	15.6	88	8.2	4395	672	2.5
1972	456	85	1256	470	73.5	15.6	84	8.7	4179	720	2.6
1973	427	84	1235	465	73.5	15.6	93	11.0	4652	901	3.2
1974	442	82	1242	462	73.5	15.6	64	8.7	3204	720	3.9
1975	430	81	1183	453	73.5	15.6	98	15.3	4885	1258	4.5
1976	416	80	1190	469	71.5	15.6	109	18.6	5459	1535	**5.1**
1977	401	73	1185	469	71.5	15.6	77	14.3	3818	1176	5.6
1978	377	73	1119	442	71.5	15.6	107	21.0	5327	1726	6.1
1979	378	74	1070	416	71.5	15.6	106	22.7	5270	1870	**6.5**
1980	357	63	1026	390	71.5	15.6	136	29.5	6789	2426	**6.5**
1981	352	65	1015	392	72.2	17.4	82	19.5	4108	1607	7.0
1982	342	59	974	376	72.2	17.4	124	27.8	6172	2291	7.0
1983	352	56	939	349	72.2	17.4	203	46.7	10115	3846	7.0
1984	327	56	938	347	72.2	17.4	144	33.7	7196	2774	7.0
1985	329	56	960	347	72.2	17.4	196	45.2	9791	3720	7.0
1986	333	54	931	322	74.8	19.3	140	32.3	6990	2659	7.0
1988	336	58	890	291	74.8	19.3	160	37.1	7980	3051	7.0
1987	338	53	893	280	74.8	19.3	137	32.2	6827	2647	7.0
1989	326	45	887	275	74.8	19.3	144	35.0	7188	2879	7.0
1990	318	43	864	254	74.8	19.3	159	36.6	7920	3014	6.0
1991	314	37	829	236	80.8	21.7	121	26.3	6018	2169	6.0
1992	310	35	801	223	80.8	21.7	88	19.4	4386	1595	6.0
1993	306	33	765	202	80.8	21.7	141	30.2	7028	2485	6.0
1994	287	31	728	191	80.8	21.7	139	29.4	6930	2422	6.0
1995	291	29	727	181	80.8	21.7	127	28.2	6345	2319	6.0
1996	273	27	701	171	82.5	20.8	149	32.0	7416	2633	6.0
1997	284	23	685	157	82.5	20.8	156	31.8	7800	2616	6.0
1998	272	28	683	150	82.5	20.8	141	28.9	7008	2379	6.0
1999	268	23	672	146	82.5	20.8	141	28.7	7026	2361	6.0
2000	277	25	641	149	82.5	20.8	105	22.0	5217	1807	6.0

1961-90 and (more approximately) visually in 1951-2000.

METHODS

We have used old data: Age adjusted TOT and CHD death-rates in 35-64-y. females and males, are from Valkonen and Niemi (1982), Valkonen and Martikainen (1990) and Statistics Finland (2014). Soil data, consumption of mineral fertilizers and the use of arable land are collected from the same Finnish sources as earlier presented (Toysa, 2016a; Toysa, 2016b): Soil data from Eurofins Viljavuuspalvelu Oy (2015); Mg and Ca supplementation from liming agents for 1972-80 from Jokinen (1981) and for 1951-71 and for 1981-1999 from Lauronen (2007). Data for Mg from other sources from Heinonen (1956), Jokinen (1981), Statistics Finland (1991) and Statistics Finland (2001). Ca from nitrates from FAOSTAT (2017a). Ca from phosphates approximated by Sillanpää (1978) by using formula of superphosphate (lower approximation); data on area of arable land from Statistics Finland (1961) and FAOSTAT (2017b).

Publication of Toysa (2016b) needs following additions and revisions: Web addresses of FAOSTAT (2017a, fertilizers, and 2017b, arable land) have been changed during the last year. Supplementation of liming agents in print version is available for the whole period 1951-2000 (Yli-Savola, 2002). Despite of great annual variation the production of liming agents from different mines and quarries was similar in 1950-71, so mean Mg-% was rather unchanged that time (Lauronen, 2007). Because of Mg-rich calcites were included in calcites before 1976 Mg from liming agents in 1972 has been estimated to be 4.6 kg/ha (revised by the basic data from Lauronen, 2007) instead of 4 kg/ha (Jokinen, 1981). That's why Mg-% of liming agents (Toysa, 2016b) need 0.5 %-unit addition from 2 to 2.5 % in 1951-71. Mg-% for 1976, 1979 and 1980 has been calculated by Jokinen (1981) and (FAOSTAT, 2017b). Values for 1973-75 and 1977-78 are linearly interpolated. Mg-% for 1981-89 has been approximated to be 7 % and for 1990-2000 6 % (Lauronen, 2007). Ca from nitrates [Ca(NO3)2 and Ca(NH4)(NO3) is revised (reduced by 50 %) to 0.7 (range 0.0-2.6) kg Ca/ha. The same value as in 1961 (0.7 kg/ha) has been approximated for 1951-1960. Mg from mineral fertilizers other than liming agents (ca 0.85 kg/ha) in 1956 was ca 0.85 kg/ha lower than in 1957, when the production of dolomitic nitro chalk (Oulu salpetre) begun in Oulu (Heinonen, 1956). This "non-liming-agent mineral Mg" for 1951-56 (0.80 - 0.91 kg/ha) has been approximated by the relative consumption of phosphates (Sillanpää, 1978), for 1970-80 from Jokinen (1981), 1981- 90 from Statistics Finland (1991), for 1991-2000 from Statistics Finland (2001). Values of "non-liming-agent mineral Mg" between 1957-70 are linearly interpolated. (Discussable Mg deposition 0.77 kg/a (Jokinen, 1981), was included in mineral Mg fertilizers, as earlier (Toysa, 2016b). (Table 1).

Ca.rcl and Mg.rcl are rough approximates as earlier (Toysa.2 2016) (Tabl. 2).

Table 2. Recycled plant nutrients (approximated)

	Ca	**Mg**
kg/ha/a	15	6.5
Eq/ha/a	746	535

Calculations concerning explanatory power (R squares) and significances have been performed with IBM Statistics 23 program. In Tables 3, 4 and 5 explanatory power is given in percents (R square x 100).

RESULTS

Fig. 1, 2 and 3 show the approximate development in Ca and Mg fertilization in 1951-75. (N.B. the Fig's 1, 2 and 3 are rounded off – given as three year means). In 1951 Ca.fm was > 2-fold to Ca.rcl, Mg.fm only about half of Mg.rcl. In 1951-64 Ca.fm increased by 168 % and Mg.fm by 144 %, which decreased (Mg/Ca).ft ratio by 32 %. In 1975 (Mg/Ca).ft received again the level of 1951.

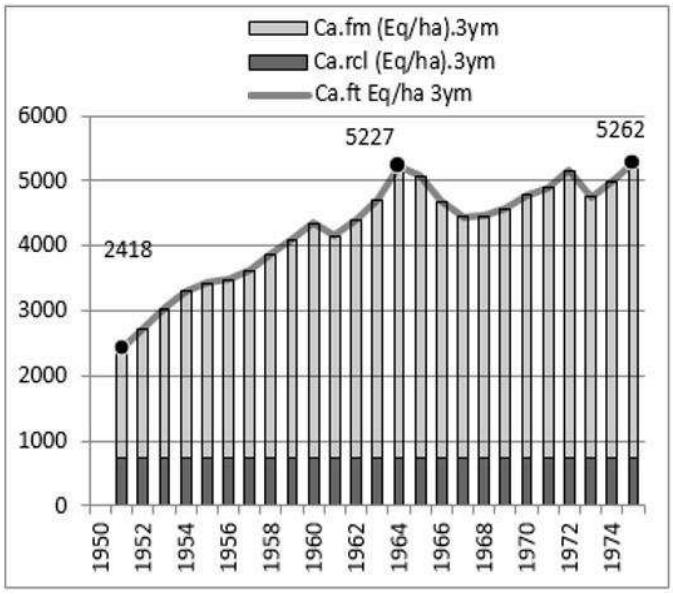

Fig. 1 Estimated development of Ca.ft, Ca.fm and Ca.rcl in 1951-72. Ca.fm increased by 168% and Ca.ft by 116% in 1951-64

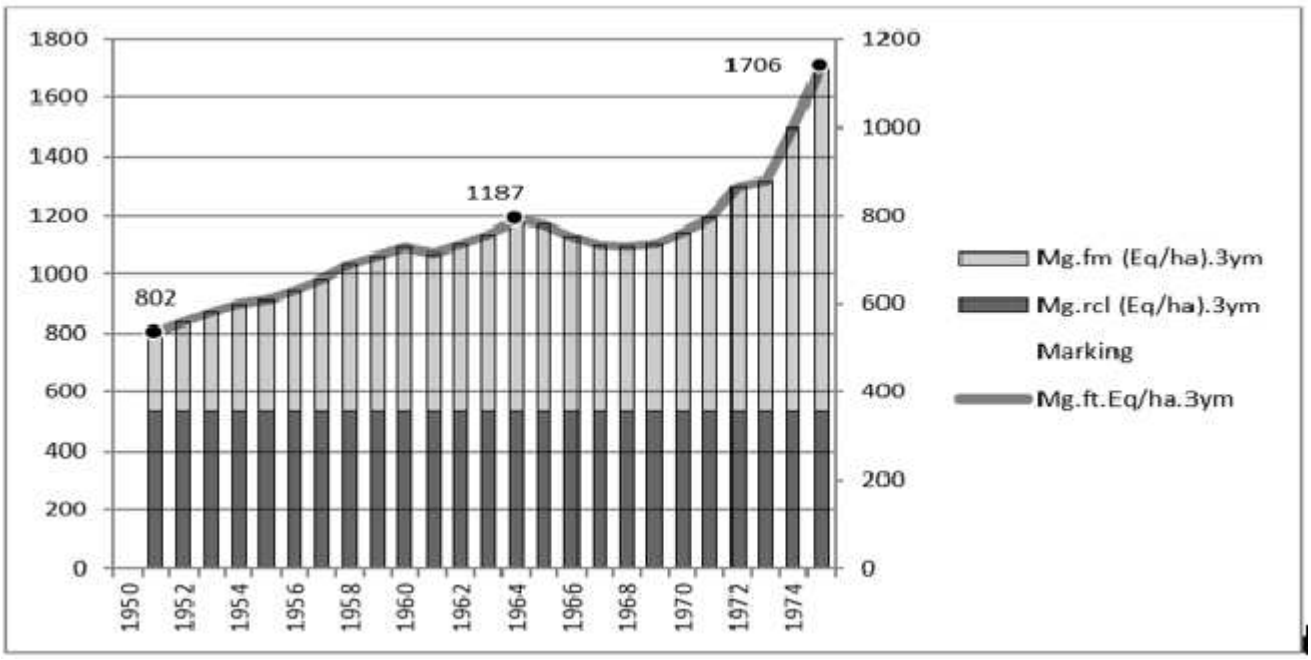

Fig. 2. Estimated development of Mg.ft, Mg.fm and Mg.rcl in 1951-72Mg.fm increased 144 % and Mg.ft 48 % in 1951-64

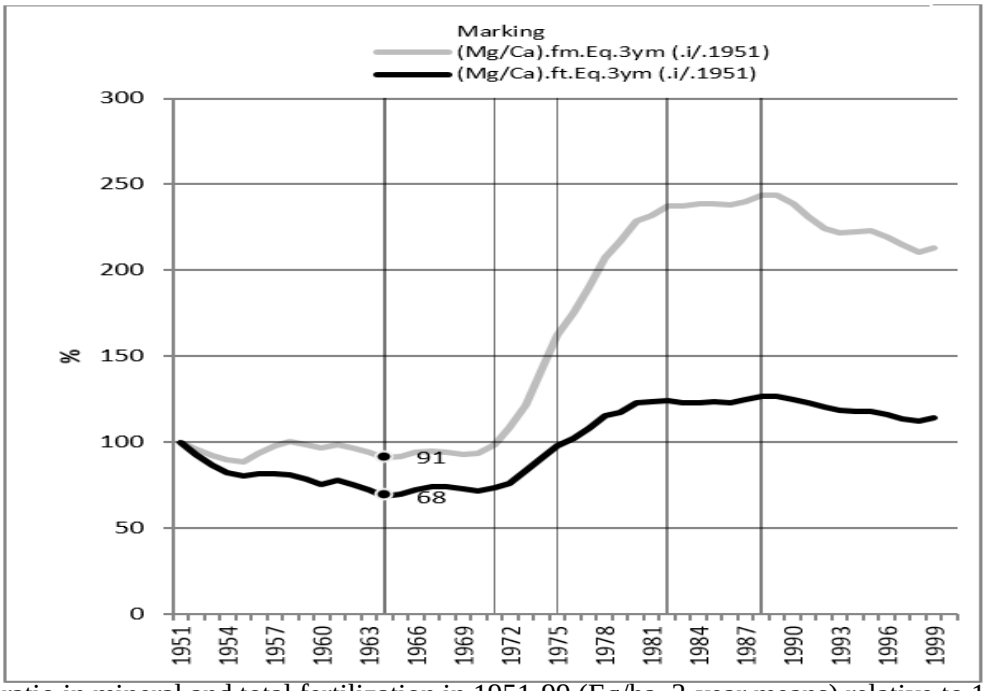

Fig .3. Mg/Ca ratio in mineral and total fertilization in 1951-99 (Eq/ha, 3-year means) relative to 1951

Fig. 4 shows (Mg/Ca) changes in fertilization and agricultural soils, as well as in male and female CHD and non-CHD mortality relative to their values in 1957. Original soil values are rounded off by fixing their mean periodical values (1963, 1968, 1973) and linearly interpolated the intermediate annual values and labeled as "(Mg/Ca).sm.ipol". Period when (Mg/Ca).ft went below the level of 1957 (in 1958-73) is better associated (inversely) with F.CHD epidemic 1958-72 than with M.CHD epidemic in 1957-83. (Mg/Ca).ft and (Mg/Ca).fm fertilization ratios are increasing in 1964-81, stabilizing in 1981-90 and after that slightly decreasing. In 1967 begun rapid decline in female CHD and a slower decline in male CHD. In non-CHD we see a rapid decline between 1969 and 1983 and stagnation in 1983-90. In F.CHD we see a rapid decline since 1987.

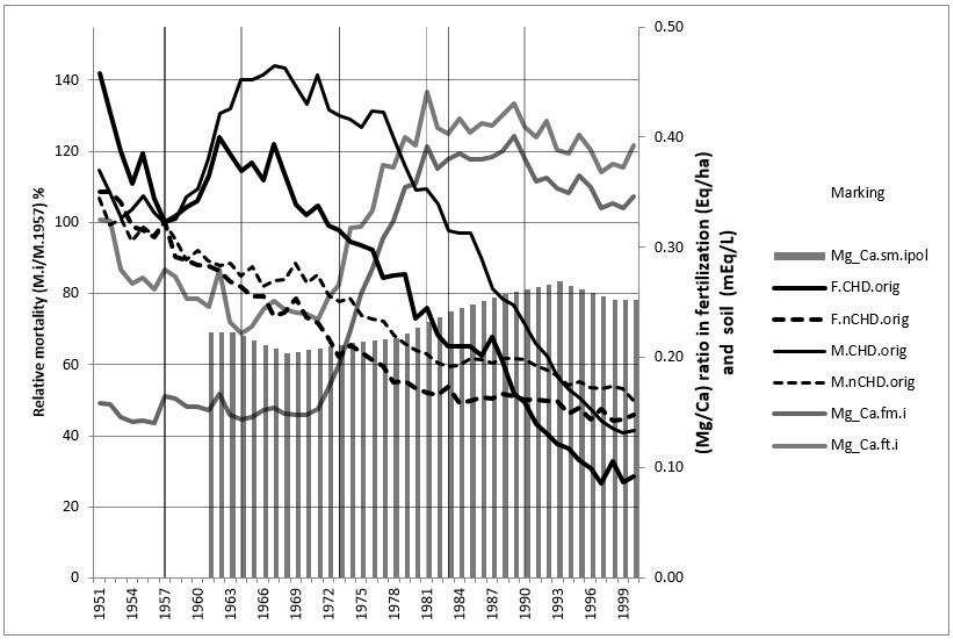

Fig. 4. Mg/Ca ratio of fertilization and agricultural soil and their associations with CHD and non-CHD mortality of middle-aged men and women in Finland 1951-2000

In Fig. 5 the (Mg/Ca) ratios of total fertilization (Eq/ha) are calculated as 5 year means (5ym) and given as percents. Then every year in each 5 year period has got the same value as calculated for their central years (1963, 1968, 1973) - " (Mg/Ca).ft.[5ym (58,63,68…)].i (%)" - and then additionally the same values are moved 5 years forward, which gave " (Mg/Ca).ft.[5ym (58,63,68…)].(i-5) (%)" - fertilization values five years earlier than their respective soil values: on this curve mean fertilization of 1951-55 is on period 1956-60 and fertilization values of 1956-60 are on 1961-65 and so on. Fig. 5 supports the conclusion: "soil (Mg/Ca) ratio responded to (Mg/Ca).ft fertilization ratio by 5 years delay", or annual (Mg/Ca).ft preceded changes in (Mg/Ca).sm ratio by 5 years.

Regressions by (Mg/Ca) of soil and fertilization

In regressions of soil values have benefited interpolated (Mg/Ca).sm values "(Mg/Ca).sm.ipol" as in Fig. 4. For fertilization values have been selected (Mg/Ca).fm instead of (Mg/Ca).ft because of simplicity and additional uncertainty caused by deficient data concerning on Ca.rcl and Mg.rcl after the 1950's and high compliance between (Mg/Ca).fm and (Mg/Ca).ft in 1961-90. Table 3. shows the percentages (R squares x 100) of TOT, CHD and non-CHD mortality "explained" by (Mg/Ca).sm.ipol in 1961-90. (Mg/Ca).sm.ipol explained better the death-rates (TOT, CHD and non-CHD) of men than women. All the associations were significant ($p < 0.001$).

Table 3. Proportions (%) of TOT, CHD and non-CHD mortality explained by (Mg/Ca).sm.ipol in1961-90

Mortality	Female	Male	Mean	F/M
CHD	70	94	82	0.75
Non-CHD	46	62	54	0.75
TOT	52	81	66	0.64

Table 4 and shows the percentages (R squares x 100) of TOT, CHD and non-CHD mortality "explained" by (Mg/Ca).fm. (Mg/Ca).fm explained female CHD by 91 % and male CHD by 73 %, but association with female and male TOT and non-CHD were rather similar. Mortality associations with (Mg/Ca).fm (Table 4) were in general stronger than with (Mg/Ca).sm.ipol (Table 3), with one exception: M.CHD associated stronger (by 94 %) with (Mg/Ca).sm.ipol (Table 3) than with (Mg/Ca).fm (by 74 %) (Fig. 4, Table 4). All the associations were significant ($p < 0.001$).

Figures 6-11 show regressions of female and male CHD, non-CHD and TOT mortality by (Mg/Ca).fm and Mg-% of liming agents (Mg-%.lim) with respective original values. Fig. 12 shows regression of CHD by (Mg/Ca).sm.ipol. Abrupt changes in Mg-% are caused by coarse approximate basic data benefited as such. Vertical markings are added on 1969, 1981 and 1985 in order to help comparison of figures.

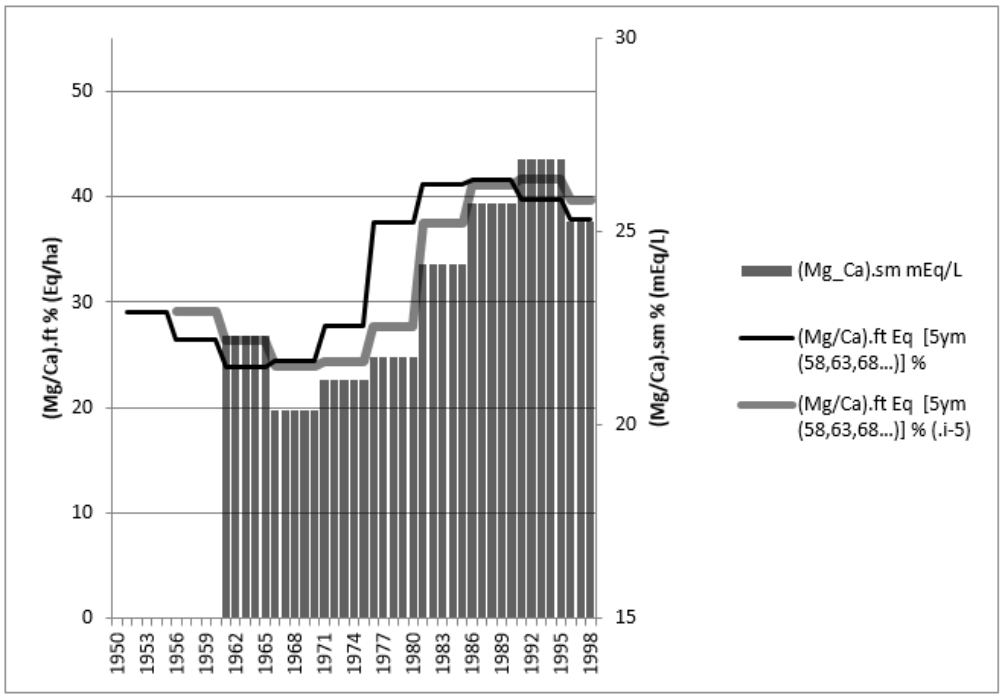

Fig. 5. Mg/Ca ratio in fertilization [(Mg/Ca).ft] (5 years means of 1963, 1968, 1973,...) as such and five years before and in agricultural soil 1961- 2000

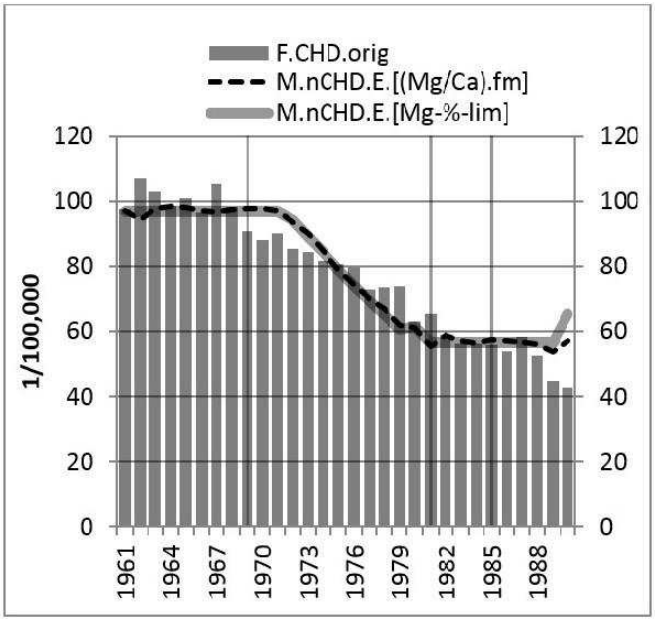

Fig. 6. Female CHD and its regression by [(Mg/Ca).fm] and [Mg-%.lim]

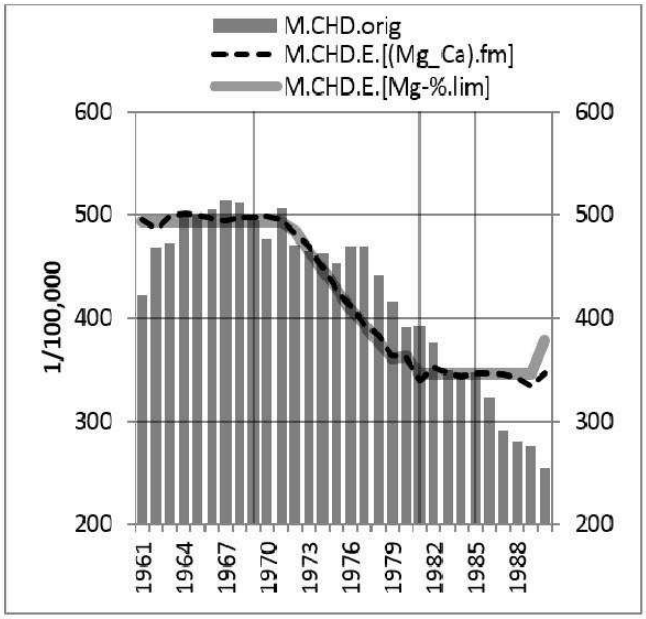

Fig. 7. Male CHD and its regression by [(Mg/Ca).fm] and [Mg-%.lim

Fig. 6 shows female CHD and its regression by [(Mg/Ca).fm] and [Mg-%.lim]. Associations got weaker after 1987 while Fig. 7 shows male CHD and its regressions by [(Mg/Ca).fm] and [Mg-%.lim]. Associations got weaker after 1985.

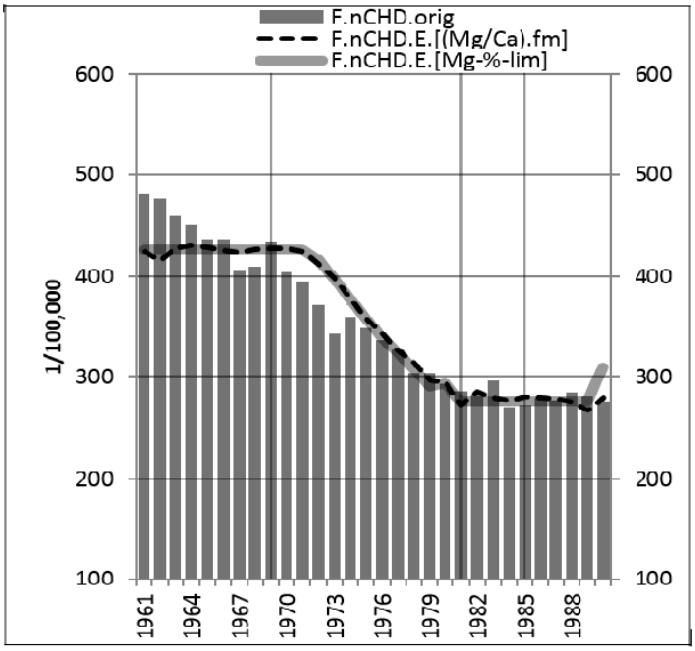

Fig.8. Female non-CHD and its regression by [(Mg/Ca).fm] and [Mg-%.lim]

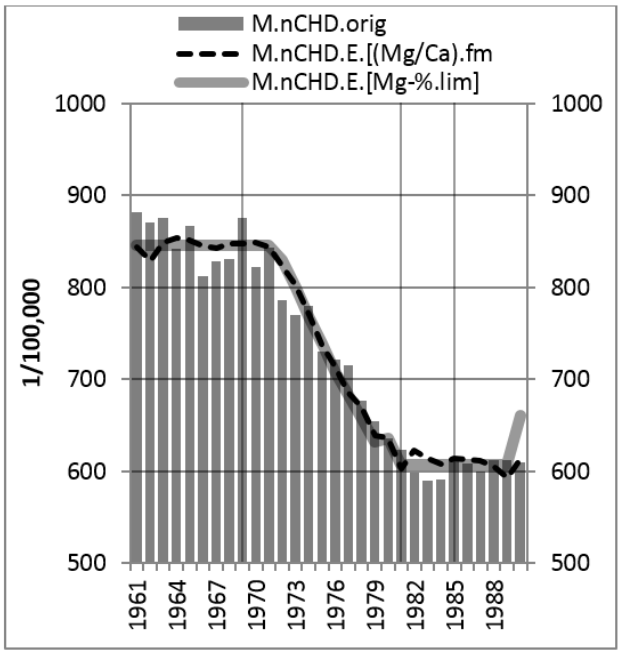

Fig. 9. Male non-CHD and its regression by [(Mg/Ca).fm] and [Mg-%.lim]

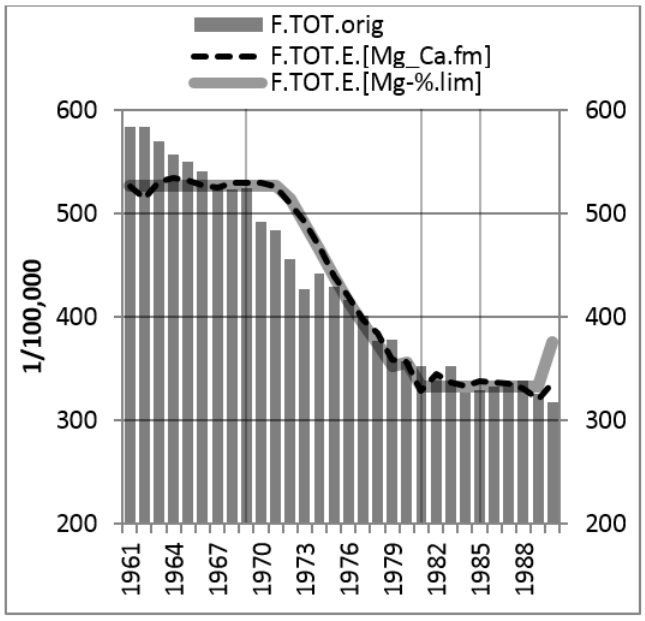

Fig.10. Female TOT and its regression by [(Mg/Ca).fm] and [Mg-%.lim]

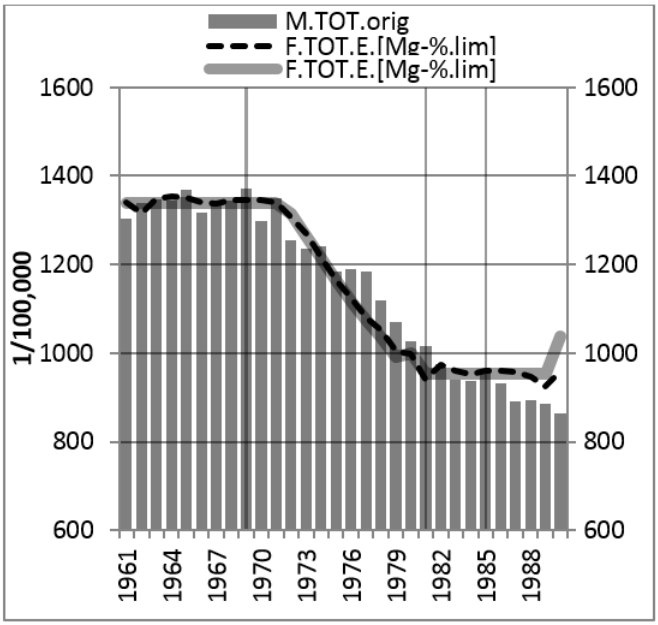

Fig.11. Male TOT and its regression by [(Mg/Ca).fm] and [Mg-%.lim]

Fig. 10 shows female TOT and its regression by [(Mg/Ca).ft] and [Mg-%.lim]. Stagnation is seen in changes during 1981-88, while Fig. 11 shows male TOT and its regression by [(Mg/Ca).fm] and [Mg-%.lim]. Associations get weaker after 1985. Fig. 12 shows male CHD and its regression by [(Mg/Ca).sm.ipol] with standard deviations.

DISCUSSION

This study shows that (Mg/Ca).ft ratio was changed in fertilization in 1950-90 and Mg/Ca ratio of soil followed it with delay of about 5 years (Figures 4 and 5). Earlier has been reported that time-related changes in (Mg/Ca) ratio of soil [e.g.(Toysa.2.)] associated inversely with male and female CHD and this

association was stronger by men. On the other hand, fertilization ratio [Mg/(Ca+Mg+K).fm], which is very closely related with (Mg/Ca).fm (Toysa.3.), has been reported to be associated inversely with male CHD. Anyhow in regional analyses association of soil and timothy (Mg/Ca) with CHD has shown insignificant associations (Toysa.1.). Food Mg content has not been different in East Finland, with higher CHD mortality, to West Finland (Koivistoinen et al., 1970). This regional "ineffectiveness" of Mg in East Finland could possibly be explained by additional factors as temperature, vitamin D (Töysä.5., Hänninen, 2014) and silicon (Si) (Toysa.4.) and does not disclose the effects of time-related changes in Mg availability to plants, animals and humans. Plant available Si, and so intracellular Mg-uptake (Maehira et al., 2011), could be affected by changes in rcl/fm ratio and by regional differences in groundwater Si. The Si effect could possibly partially explain the surprisingly high increase in need of Mg in pig fodder from the recommended international norms (Nuoranne 1978).

Table 4. Proportions (%) of TOT, CHD and non-CHD mortality explained by (Mg/Ca).fm in 1961-90.

	Female	Male	Mean	F/M
Mortality	(Mg/Ca).fm	(Mg/Ca).fm		
CHD	89	74	83	1.19
Non-CHD	88	96	92	0.91
TOT	90	94	92	0.96

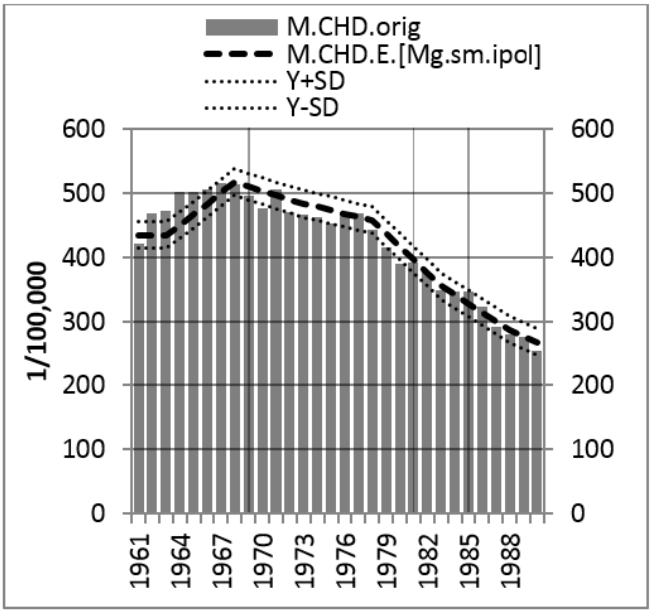

Fig. 12. Male CHD and its regression by [(Mg/Ca).sm.ipol]

Time limits for the begin of the period of assessment has been caused by soil data, which is available only since 1961. 1990 was selected to be the end point, because supposedly developed treatments begun to cause "bias" on environmental effects on those times. In the 1950's the consumption of all mineral fertilizers (not only Ca) was low and Mg deficiency was obviously not very common (Heinonen, 1956). This can obviously explain the exceptional F.CHD-(Mg/Ca).fm association (Fig. 4) in 1951-55. Fig.4 shows that F.CHD, opposite to M.CHD, is better associated with (Mg/Ca) ratio in fertilization than in soil. The immediate "response" of M.CHD to soil (Mg/Ca) (Figures 4 and 12) is suspicious and suggesting on preceding causative factor (i.a. fertilization) and does not disprove our supposition that the death-rates of female population, less contaminated by smoking in 1951-70 (Patja, 2016), has been better human indicator of environmental health than the death-rates of males. High (Mg/Ca) association with non-CHD mortality - especially by males - could be based on the effects of the more than 300 enzymes catalyzed by Mg (Elin, 1994) and on lower variation in male death rates and, of course, on simultaneous improvement of social security, insurances, food quality and rest.

The statistical assessment above excluded interactions of other cations on Mg uptake, Mg losses via leaching and yield, efficacy in recycling (e.g. urbanization), import, export, as well as medical treatments and guidance. It is possible that other functions of mineral elements [F(Ca,Mg,N,P,K,Se)] of fertilization and soil or their combinations could better than (Mg/Ca).ft or (Mg/Ca).fm simulate or explain mortality changes.

Rapid decline in female death-rates in 1968-73 (Fig. 6, 8 and 10) could possibly be based on other changes in agriculture (improved post-harvest processing of grain and grass) and livestock breeding, e.g. increased supplementation vitamins and minerals, e.g. Mg (Nuoranne et al., 1980), selenium (Koivistoinen and Huttunen, 1986), which simultaneously improved health of livestock, too (written for to be published). It is possible that some part of the reduced Si effects (Maehira et al., 2010), associated with reduction in rcl/ft fertilization ratio, could have been compensated by Se.

Smoking as measured by tobacco consumption increased to the middle of the 1970's, but after that (influenced by North Karelian project) decreased radically, but could not stop the moderate increase in female smoking until ca 1990 (Patja, 2016). Smoking changes could explain relative differences between

male and female CHD in the 1970's and 1980's (Fig. 6 and 7) and mask (associated with great annual variation) the Se effect by women in 1986 and 1987.

CONCLUSION

Mg/Ca changes in fertilization preceded respective changes in soil ca by five years. They explained in general better than the soil values changes in death-rates, except M.CHD with obvious "tobacco delay". Effects of silicon and rcl/ft ratio are discussed.

ACKNOWLEDGEMENT

We are grateful to veterinary surgeon Seppo Haaranen for several discussions, as well as Mikko Lauronen, Purchasing Manager of Nordkalk Corporation, for his great work in analyzing the data concerning changes in Mg and Ca contents of liming agents in Finland.

ABBREVIATIONS

Ca – calcium; CHD – two purposes: 1) coronary heart disease or 2) CHD mortality (age adjusted by 35-64 y humans); CVD - cardiovascular disease; E - expected value, e.g. (Mg/Ca).sm.E.[(Mg/Ca).ft.(i-5)] - regression of soil (Mg/Ca) ratio by preceding (Mg/Ca) ratio of total fertilization 5 years earlier; Eq - equivalents; fm - mineral fertilizers, e.g. Mg.fm – Mg in mineral fertilizers; F - female; ft - total fertilizers (= fm + rcl) , e.g. Mg.ft; ha - hectare; ipol - interpolated; K - potassium; M - male; Mg – magnesium; M.i/M.1957 mortality in year i divided by mortality value in year 1957; N - nitrogen; non-CHD - mortality from other causes than CHD; nCHD = non-CHD in graphics and abbreviations; P - plasma (e.g. P-Mg – magnesium concentration in plasma); rcl - recycled fertilizers (e.g. manure); Se - selenium; sm – soil mean (e.g. Ca.sm - soluble Ca mEq in soil liter); sm.ipol - original soil values are rounded off by fixing their mean periodical values (e.g. 1963, 1968, ..) and linearly interpolated the intermediate annual values [e.g. "(Mg/Ca).sm.ipol"]; TOT - total mortality (age adjusted by 35-64 y men); T-Mg - tissue Mg.

REFERENCES

Amyard, N., Leyris, A., Monier, C., Frances, H., Boulu, R.G. and Henrotte, J.G. (1995). Brain catecholamines, serotonin and their metabolites in mice selected for low (MGL) and high (MGH) blood magnesium levels. *Magnesium Research*, 8(1):5-9.

Bloom, S. (1986). Effects of magnesium deficiency on the pathogenesis of myocardial infarction. *Magnesium*, 5(3-4):154-164.

Bourdon, E., Loreau, N., Lagrost, L., Davignon, J., Bernier, L. and Blanches, D. (2006). Differential effects of oxidized LDL on apolipoprotein AI and B synthesis in HepG2 cells. *Free Radical Biology & Medicine*, 41(5):786-796.

Charles, P., Mosekilde, L., Sondergard, K. and Jensen, F.T. (1984): Treatment with high-dose oral vitamin D2 in patients with jejunoileal bypass for morbid obesity. Effects on calcium and magnesium metabolism, vitamin D metabolites, and faecal lag time. *Scandinavian Journal of Gastroenterology*, 19(8):1031-1038.

Elin, R.J. (1994): Magnesium: the fifth but forgotten electrolyte. *American Journal of Clinical Pathology*,102(5):616-622.

Epstein, E. Silicon. (1999) Annual Review of Plant Physiology and Plant Molecular Biology, 50: 641- 664. DOI: 10.1146/annurev.arplant.50.1.641.

Esterbauer, H., Wäg, G. and Puhl, H. (1993): Lipid peroxidation and its role in atherosclerosis. *British Medical Bulletin*, 49(3):566-576.

Eurofins Viljavuuspalvelu Oy. Address: PL 500 FI-50101 Mikkeli, Finland. email: viljavuuspalvelu@eurofins.fi. (permission for publication given Jan 8, 2012).

FAOSTAT. (2017a). Fertilizers: http://www.fao.org/faostat/en/#data/RA. FAOSTAT. (2017b). Arable land: http://www.fao.org/faostat/en/#data/RL > DATA > Land.

Hsu, J.M., Rubenstein, B. and Paleker, A.G. (1982). Role of magnesium in glutathione metabolism of rat erythrocytes. *The Journal of Nutriton*, 112(3):488-496.

Gullestad, L., Dolva, L.O., Waage, A., Falch, D., Fagerthun, H. and Kjekshus, J. (1992). Magnesium deficiency diagnosed by an intravenous loading test. *Scandinavian Journal of Clinical and Laboratory Investigation*, 52(4):245-253.

Itallie, T.B. van. (1938). Cation equilibria in plants in relation to the soil. *Soil Science* 46(3): 175-186.

Jeppesen, B.B. (1986): Magnesium status in patients with acute myocardial infarction: a pilot study. *Magnesium*,5(2):95-100.

Jokinen, R. (1981): Requirements for Magnesium fertilization in Finland. *Journal of the Scientific Agricultural Society of Finland*, 53(4): 239-268.

Kemp, A. (1960). *Netherlands Journal of Agricultural Science*, 8:281-304

Koivistoinen, P., Ahlström, A., Nissinen, H., Pekkarinen, M. and Roine, P. (1970). Mineral Element Compositions of Finnish Diets Part I: Fe, Cu, Mn, Zn, Mg, Na, K, Ca and P. *Suomen Kemistilehti B43*:426-443.

Koivistoinen, P. (Editor). (1980). Mineral Element Composition of Finnish Foods: N, K, Ca, Mg, P, S, Fe, Cu, Mn, Zn, Mo, Co, Ni, Cr, F, Se, Si, Rb, Al, B, Br, Hg, As, Cd, Pb and Ash. *Acta Agriculturae Scandinavica*, Suppl 22:39-40. Stockholm.

Koivistoinen, P. and Huttunen, J.K. Selenium in food and nutrition in Finland. An overview on research and

action. *Annals of clinical research* 1986;18(1):13-17.

Kähäri, J. and Nissinen, H. The Mineral element Contents of Timothy (Phleum pratense L.) in Finland. *Acta Agriculturae Scandinavica*, Suppl 20 (1978):26- 39.Tabl.8.on pp 34–35, in Toysa. (2015). *Jacobs Journal of Agriculture.* 2015, 1(2): 006.

Laitinen, K., Tähtelä, R. and Välimäki, M. (1992). The dose-dependency of alcohol-induced hypoparathyroidism, hypercalciuria, and hypermagnesuria. *Bone and mineral*,19(1):75-83.

Lauronen, M. (2007). (as Purchasing Manager of) Nordkalk Oyj Abp, personal communications: emails Sept 16 - Dec 17, 2007.

Lin, X.Y., Xiao, L.Z., Gao, L.J. and Zhang, H.F. (2005). [Effects of carvedilol on neurohormone and magnesium metabolism in patients with chronic heart failure]. [Article in Chinese]. *Zhonghua Xin Xue Guan Bing Za Zhi*, 33(11):995-997.

Manju, L. and Nair, R.R. (2006): Magnesium deficiency augments myocardial response to reactive oxygen species. *Canadian journal of physiology and pharmacology*, 84(6):617-624.

Malpuech-Brugère, C., Nowacki, W., Daveau, M., Gueux, E., Linard, C., Rock, E., Lebreton, J., Mazur, A. and Rayssiguier, Y. (2000). Inflammatory response following acute magnesium deficiency in the rat. *Biochimica et biophysica acta*, 15;1501(2-3):91-98.

Masoudkabir, F., Karbalai, S., Vasheghani-Farahani, A., Aliabadi, L.L., Boroumand, M.A., Aiatollahzade-Esfahani, F., Pashing, M., Hakki, E., Goodarzynejad, H. and Saadat, S. (2011). The association of liver transaminase activity with presence and severity of premature coronary artery disease. *Angiology*, 62(8):614-619. doi: 10.1177/0003319711405312. Epub 2011 May 11.

Maehira, F., Motomura, K., Ishimine, N., Miyagi, I., Eguchi, Y. and Teruya, S. (2011). Soluble silica and coral sand suppress high blood pressure and improve the related aortic gene expressions in spontaneously hypertensive rats. *Nutrition research*, Feb;31(2):147-156. doi: 10.1016/j.nutres.2010.12.002.

McNair, P., Christensen, M.S., Christiansen, C., Madsbad, S. and Transbøl, I. (1982). Renal hypomagnesaemia in human diabetes mellitus: its relation to glucose homeostasis. *European journal of clinical investigation*,12(1):81-85.

Memon, R.A., Grunfeld, C., Moser, A.H. and Feingold, K.R. (1993): Tumor necrosis factor mediates the effects of endotoxin on cholesterol and triglyceride metabolism in mice. *Endocrinology*, 132(5):2246- 2253.

Niccoli, G., Della Bona, R., Cosentino, N., D'Amario, D., Belloni, F., Conti, M.G., Gustapane, M., Fracassi, F., Biasucci, L.M., Falcioni, E., Antonazzo Panico, R. and Crea, F. (2013). Serum levels of γ-glutamyltransferase and progression of coronary atherosclerosis. *Coronary artery disease*, 24(1):40-47. doi: 10.1097/MCA.0b013e32835bbe6e.

Nuoranne, P. (1978). On the effect of food magnesium level on the activity of BASP, ALAT, ASAT and LD in pig serum. *Nordisk veterinaermedicin*, 30(2):74-82.

Nuoranne, P.J., Raunio, P., Saukko, P. and Karppanen, H. (1980). Metabolic effects of a low-magnesium diet in pigs. *The British journal of nutrition*, Jul;44(1):53-60.

Pasternak, K., Sztanke, M., Borzecki, A. (2004). Magnesium concentration in rat tissues receiving sex hormones and vitamin E. *Annales Universitatis Mariae Curie-Skłodowska. Sectio D: Medicina,* 59(2):114-118.

Patja, K. Tobacco Free Finland Network (member of policy and scientific groups) http://www.ashscotland.org.uk/media/5716/Kristiina%20Patja%2040th%20Conf.pdf(pdf-page 6/27). (accessed Jul 7, 2016).

Rude, R.K., Gruber, H.E., Norton, H.J., Wei, L.Y., Frausto, A. and Kilburn, J. (2006). Reduction of dietary magnesium by only 50% in the rat disrupts bone and mineral metabolism. *Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*, 17(7):1022-1032.

Ryzen, E., Servis, K.L. and Rude, R.K. (1990). Effect of intravenous epinephrine on serum magnesium and free intracellular red blood cell magnesium concentrations measured by nuclear magnetic resonance. *Journal of the American College of Nutrition*, 9(2):114-119.

Shechter, M., Sharir, M., Labrador, M.J., Forrester, J., Silver, B. and Bairey Merz, C.N. (2000a). Oral magnesium therapy improves endothelial function in patients with coronary artery disease. *Circulation*, 102(19):2353-2358.

Shechter, M., Merz, C.N., Rude, R.K., Paul-Labrador, M.J., Meese, Shah PK and Kaul S. (2000b). Low intracellular magnesium levels promote platelet-dependent thrombosis in patients with coronary artery disease. *American heart journal*, 140(2):212-218.

Sippola, J. and Tares, T. (1978). The soluble Content of Mineral Elements in Cultivated Finnish Soils. *Acta Agriculturae Scandinavica*, Suppl 20:11-25, in Toysa. T. (2015). Agro-Geology and CHD in Finland. *Jacobs Journal of Agriculture.* 2015, 1(2): 006.

Statistics Finland (1991). Sales of fertilizers to farms. Official Statistics of Finland (Suomen Tilastollinen Vuosikirja)1981-90: https://www.doria.fi/handle/10024/67152 > 1991. OSF 1991, Table 81 on page 114 (pdf 100/546). Statistics Finland (2001). Sales of fertilizers to farms. Official Statistics of Finland (Suomen Tilastollinen Vuosikirja) 1991-2000:

https://www.doria.fi/handle/10024/67152 > 2001, OSF 2001, Table 105 on page 158 (pdf 138/645).

Statistics Finland (2014): Age adjusted total and coronary mortality (I20-I25) of men and women, 35-64 yrs, Finland 1969-2005. Source: © *Statistics Finland*, Causes of Death. (Permission given on Aug 14, 2014).

Tanabe, K., Yamamoto, A., Suzuki, N., Osada, N., Yokoyama, Y., Samejima, H., Seki, A., Oya, M., Murabayashi, T., Nakayama, M., Yamamoto, M., Omiya, K., Itoh, H. and Murayama, M. (1998). Efficacy of oral magnesium administration on decreased exercise tolerance in a state of chronic sleep deprivation. *Japanese circulation journal*, 62(5):341-346.

Toysa, T. (2015). Agro-Geology and CHD in Finland. *Jacobs Journal of Agriculture*, 2015, 1(2): 006.

Toysa, T. (2016 a). Time-related changes in magnesium content and magnesium/calcium ratio of Finnish agricultural soil associated inversely with human CHD in 1961-1990. *Jacobs Journal of Agriculture*, 2(1):011.

Toysa, T. (2016 b): Compliance of Finnish Male CHD and Total Mortality with Soil Fertilization in 1957-1990. *Jacobs Journal of Agriculture. 2016, 2(1): 013.*

Toysa, T. (2016 c). Soil Weathering, Silicon and CHD in Finland. *Jacobs Journal of Agriculture*, 2016, 2(1): 008.

Töysä, T. and Hänninen, O. (2014). Pale Europeans and Dark Africans share sun and common health problems: constancy in regional health differences and sunshine. *Journal of African Association of Physiological Sciences*, 2 (2): 87-94.

Valkonen, T. and Niemi, M.L. (1982): The development of cardiovascular mortality in Finland from 1951 to 1978. *Finnish Yearbook of Population Research (Väestöntutkimuksen vuosikirja)*, XX:32-44. The Family Federation of Finland. (Permission for publication given on June 6, 2014 by Valkonen T, the owner of the rights of the figures in this article).

Varo, P., Alfthan, G., Ekholm, P., Aro, A. and Koivistoinen, P. (1988): Selenium intake and serum selenium in Finland: effects of soil fertilization with selenium. *The American journal of clinical nutrition*, 48(2):324-329.

Witteman, J.C.M., Grobbee, D.E., Derkx, F.H., Bouillon, R., de Bruijn, A.M. and Hofman, A. (1994). Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *The American journal of clinical nutrition*, 60:129-135.

Yli-Savola, S. (2002). Guidebook for Liming (published) by Liming Society. [Article in Finnish]. 33 pages, Fig. 10 on p. 32. Helsinki. Kalkitusyhdistys, 2002.