Release Notes 2022-12-28: : This does not seem to be coalescing but all the points seem important and relevant. So, I'm taking a break for now and releasing as-is. I guess it could make several small coherent notes or one opus. In places it may just need a few sentences to connect ideas but others need more reorganization of references. The release may use an experimental bibliography code that is not designed to achieve a particular format but to allow multiple links to reference works with modifications to the query string to allow identification of the citing work for tracking purposes. This may be useful for a bill-of-materials and purchases later.

This is a draft and has not been peer reviewed or completely proof read but released in some state where it seems worthwhile given time or other constraints. Typographical errors are quite likely particularly in manually entered numbers. This work may include output from software which has not been fully debugged. For information only, not for use for any particular purpose see fuller disclaimers in the text. Caveat Emptor.

Note that any item given to a non-human must be checked for safety alone and in combination with other ingredients or medicines for that animal. Animals including dogs and cats have decreased tolerance for many common ingredients in things meant for human consumption.

I am not a veterinarian or a doctor or health care professional and this is not particular advice for any given situation. Read the disclaimers in the appendicies or text, take them seriously and take prudent steps to evaluate this information.

This work addresses a controversial topic and likely advances one or more viewspoints that are not well accepted in an attempt to resolve confusion. The reader is assumed familiar with the related literature and controversial issues and in any case should seek additional input from sources the reader trusts likely with differing opinions. For information and thought only not intended for any particular purpose. Caveat Emptor

Recent Vitamin K Literature in the Conext of a non-Monotonic Response Curve : Local vs Global Optima and other Speculation

Mike Marchywka*
44 Crosscreek Trail Jasper GA 30143
marchywka@hotmail.com and
see bibtex in App E
(Dated: December 28, 2022)

This note reviews recent vitamin K literature in terms of a previously proposed conceptual non-monotonic relation between vitamin K activity and coagulability. The curve illustrates one sensitive optimum at "moderate" vitamin K activity but a much more tolerant optimum at very high activities. It then considers miscellaneous biochemical topics related to vitamin K and a concise relationship to clinical situation. While vitamin K is used for the addition of Gla domains to mutually moderating proteins , there may be a tendency to assume the vitamin K - coagulability relationship is monotonic preventing recognition of observations to the contrary. Moderation becomes even more significant when considering factors such as trigger density not strictly part of the coagulation "system." No overall curve relating vitamin K status to coagulability prior to my earlier work appears to exist and such a curve may be useful for understanding existing limitations and paradoxes with vitamin K control. Well known reasons for non-monotonicity include proteins C and S but others may exist over a broad range of genetics and conditions. Attempts to add only or of these proteins to correct hypercoagulability have had limited successes and a more complete solution may just involve more vitamin K. "Coagulability" and clots themselves are characterised by many parameters and a single curve will miss details but such a curve may inform vitamin K dosing concerns related to bleeding or occlusion. By non-fibrin effects such as controlling mineralization, vitamin K may also control nuclei or trigger density. The hemostatic response to a trigger may be most effective when it is "explosive" and can quickly shut itself off after isolating the trigger from circulation. In effect, this work suggests that an explosive response creates a more favorable quality-quantity tradeoff enabling the creation of more compact and effective clots at high vitamin K activity (which could be limited by the supply of reducing equivalents or other factors besides concentration of vitamin K). The complex regulatory network makes in vitro assessments of only indirect relevance to in vivo situation. This interpretation is considered in terms of selected literature and larger functions in calcium control. These results suggest that problems with anti-coagulation control and such isues as warfarin necrosis are more easily resovled with arbitrarily high levels of vitamin K supported with sufficient reducing equivalents and other forms of calcium control such as moderated vitamin D intake. Several other observations from the literature led to additional speculation that may be interesting for further investigation.

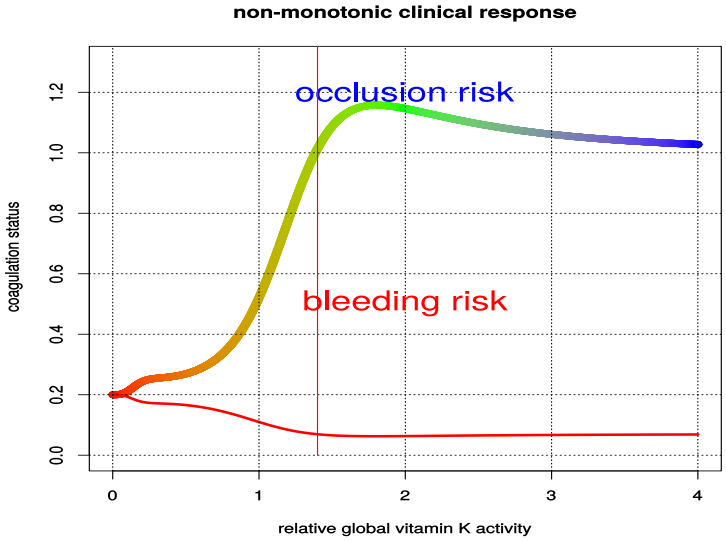

FIG. 1: Conceptual curve suggesting that pathological clotting occurs at intermediate vitamin K activity levels. In this case, triggers can not be effectively isolated by clots composed of cells and poorly organized non-fibrin. At very low activities solids may still form due to non-enzymatic or other poorly controlled processes involving fibrinogen etc. At high enough activity, fibrin clots quickly isolate offensive or damages nuclei and only a very thin impermeable clot is required. Vitamin K mediocrity does not need to precipitate thrombotic disease but it may if the nuclei are present. Red vertical line is the "warfarin optimum" which may be hard to control compared to the wider plateau at very high levels . Dynamic and static effects may be somewhat mingled but this may be useful to pick a vitamin K strategy. The rainbow color simply highlights the possibility that a lot of qualitative factors change along the path pointing to limitations of this graphic. Red curve suggests contribution of non-thrombin derived solids.

1. THE CURVE

In previous work [118] , a curve similar to Fig. 1 was described illustrating a non-monotonic relationship between coagulability state and vitamin K activity. This was based on a selection of the literture discovered at the time and some personal experience with giving vitamin K to heartworm positive dogs [119] [111] [115]. Consideration of additional literature tends to support the notion but the curve has been modified in Fig. 1 to include non-fibrin clotting by modified fibrinogen, NET's, and cellular components such as platelets and red blood cells. Central to vitamin K dependent coagulation is fibrinogen which is the precursor to fibrin clots although itself is not vitamin K dependent. It had unusual interfacial [157] and adhesion promoting [202] properties that can effect spontaneous chemistry. Fibrinogen has been observed to form solids near injured liver likely due to reactive species and FXIIIa crosslinking can still occur [147]. In cirrhosis, a known tendency for venous thromboembolism and portal vein thrombosis is made worse by vitamin K deficiency [77]. In other work, I described concerns about similar solid formation due to non-enzymatic FGN reactions that accumulate during its circulation lifetime when ROS sources are not well isolated [116] with high-quality fibrin and cellular clots.

Note that "coagulability" is not really a state that can be quantified by a single variable. Response to nuclei density, initiation, propagation, and termination as well as cellular contributions may all vary. This text attempts to describe the state of affairs as a decrease in quality with loss of vitamin K that can be compensated with larger quantity of solid deposition. If vitamin K activity improves endothelial quality then it may also help reduce trigger density independent of the response modulation. Also lacking is detail of the dynamics and those may be somewhat mingled to make this effective illustrative curve. Briefly, as elaborated later, the peak is largely due to reduced protein C or S availability as vitamin K activity is reduced. From an evolutionary standpoint, this makes some sense as a compensatory response and the dynamics may allow safe restoration as vitamin K is replenished.

Vitamin K is not purely coagulation producing and its important to appreciate the larger evolutionary and regulatory contexts. The importance of coagulation is difficult to overestimate for survival in the "wild" prior to

*Electronic address: marchywka@hotmail.com; to cite or credit this work, see bibtex in Appendix E

modern lifestyles. The textbook process involves conversion of fibrinogen to fibrin and subsequent crosslinking. Fibrinogen deficient mice can survive except for pregnancy [172] while prothrombin KO in mice is uniformly fatal , largely due to brain and heart bleeding, aside from decreased resistance to bacterial infection [138] in the short time before death. When interpreting results like this however its important to question broader applicability due to species differences and experimental conditions such as overall diet. Still, the difference in outcomes may be considered for possible implications of thrombin inhibitors. A response to injury or pathogens ideally is fast but self-regulating. The fast response can be aided by maintaining a high concentration of circulating inactive coagulation proteins such as zymogens of fibrinogen and then rapid cleavage in a self-amplifying cascade as is observed. Indeed, the required response has been described as an "explosive" thrombin burst [109] which is facilitated by the membrane interactions made possible by the vitamin K dependent Gla domains.

Thinking outloud
This arrangement itself is quite unusual as the Gla plus calcium allows sequestering of themselves to force exposure of hydrophobic residues Phe, Leu, and Val [174] with dynamics on unusual time scales [137].

The Gla domains also influence interactions such as prothrombin with Factor Va [18],

Positive feedback is great, an important part of an "explosive" response, as long as it is well regulated and self-limiting or exhausting. Earlier, no control loops were considered although an idling current due to constitutive tissue factor expression was known as was the thrombin activation of platelets [76]. Consumption of clotting factors is often assumed to be pathological leading to the term "consumptive coagulopathy" but that need not be the case if they are depleted with the right dynamics. If coagulation is ever going to work well, it has to shut off once the threat has been contained but that may not show up in incomplete simulations. One work found a self-propagating thrombin wave could form that would terminate with protein C [38]. Other simulations produced a propagating coagulation wave that is contrary to an exponentially decaying experimental result [87],

The currently elucidated schemes do not appear to explain observations and additional details need to be considered or hypothesized. This work advances the quality-quantity idea without elaborating details of its implementation. Many signals to nucleate a clot would be better covered up than left exposed if they can not be immediately removed. However, if a high quality clot can not be created, the source continues to signal that it needs to be covered by emitting noxious compounds. Quantity can compensate for quality but any barrier may remain permeable to both clotting factors and noxious substances. Thin cell based barriers like platelets may not stop even "large" molecules from diffusing if they result in gaps. Ironically, it may turn out that anti-platelet therapies simply improve the cell to fibrin ratio in a clot reducing its permeability. A similar result may be obtained with more fibrin. This notion is, however, contrary to one work on clot permeability in vitro. A 2013 study compared the hydraulic permeability of platelet rich and poor clots formed with only thrombin,calcium chloride, and fibrinogen finding that under pressure the permeability decreased with increasing platelet fraction with pore sizes from 4 to 250 nm [192]. However, losses include fluid parameters like viscosity which may not similarly effect diffusion at zero pressure differential across clots between circulation and damaged but intact vessel walls. Lack of any process to densify or crosslink the fibrin ,such as FXIIIa, makes results overestimate fibrin permeability in in vivo real physiological clots. Indeed, loss of FXIIIa crosslinking increased embolic events, decreased time to event, and more eratic but similar clot size in a ferric chloride model in mice [45] suggesting quality matters and low quality creates more overall solid deposition and occlusive disease. Although another work with ferric chloride induced stroke in mice suggested that FXIIIa inhibition could be protective [74] In the clinic, stoke patients showed increased mortality after thrombolytic therapy if they had low FXIII levels [175]. In thinner inhomogeneous physiological clots the distribution of the fibers holding the platelets together may vary substantially as the platelet fraction and thrombin distribution change. Differential pressure may push platelets together making a better seal than would occur at low pressure. In the case of very thin clots, it is unlikely a few layers of thin plates (platelets) could be as impermeable as well crosslinked continuous fibrin. Pressure pulses transiently compressing layers of platelets may even act as pumps.

Consumption of protein C may contribute to consumptive coagulopathy [36]. which presumably could be mitigated with faster protein C production and activation. Even platelets express a protein C receptor [53].

Thinking outloud
none of what?

None of this matters though if failure to make a high quality "wall" allows nuclei and clotting factors to inter diffuse. This allows the process to make a larger lower quality wall. If coagulation does not work, the organism faces a dilemma of uncontained pathogen spread, blood loss, or a larger pathological occlusion formation. The strategy may not always make sense with modern lifestyles however. It also did not evolve to make laboratory analysis particularly easy as assays have many artifacts including from the new DOAC's even when these are known prior to analysis.

Thinking outloud
failure to distinguich FGN from fibrin may make a good central point

Analysis of vitamin K impact even on clotting is complicated by the limited laboratory approaches to measuring

the state of the coagulation system in a patient relevant way. Positive feedback and large gradients create a lot of opportunities for modelling difficulties. This work recognizes lab values as being ambiguous and tries to consider ways in which a robust coagulation system may be able to work and then consider if in vitro work is generally consistent with these ideas. Even the DOAC's, introduced in a controlled intentional way, may not always be considered in clinical sample interpretation. With many triggers, steep spatial gradients, and positive feedback loops, definition and measurement of useful parameters is itself a challenge. In fact, not until about 2015 were fibrinogen and fibrin even distinguished but making that distinction points to an important role for fibrin in clotting and infection [99] [152] . Further, fibrinogen is sufficient for aggregation of human platelets although not mouse unless transfected with human glycoprotein VI [107] . Clearer understanding likely will show the limited utility of thrombin inhbition and important species differences. By 2013 the regulatory and moderating role of protein C was well known [21]. Protein S binds to phosphotidylserine on apoptotic cells and regulates C4BP and consequently C4b regulating complement response [189] and it inhbits prothrombinase in a coordinated way [96]. But still the original functions of vitamin K were largely associated with increasing clotting in nebulous terms.

The introduction of DOAC's directly inhibiting thrombin or factor Xa, further demonstrated the problems with lab characterisation of the coagulation system. Even when the DOAC's were dosed in known amounts, the interferences with lab tests, in particular functional tests, were not appreciated. While this can be corrected, it does illustrate the problems interpreting functional assays, specifically an in vitro clotting time, to measure concentration of fibrinogen. Several interferences and work -arounds are now known [52] [135] but the larger problem is interpreting one or two functional tests as the concentration of some specific component, such as fibrinogen or protein C, remains. As fibrinogen may "age" or become modified, a functional assay would be more useful than a total concentration but the right function needs to be measured and a detailed subtype concentration may be more useful. Alternatively, all possible variants could be quantified individually but the practicality is questionable and then open to functional interpretation.

Vitamin K dependent calcium binding sites provide a variety of functions . Vitamin K is often introduced in popular press or other superficial coverage as an important part of pathological coagulation and occlusive disease. However, it is important to note that the actual coagulant precursor, fibrinogen, is not even vitamin K dependent. Recent reviews [16] [131] [130] list currently known vitamin K dependent proteins, the functions of vitamin K ,and consequences of incomplete vitamin K activity. More precisely, then, instead of just promoting coagulation an important function of vitmain K is producing calcium binding sites known as Gla domains.

The human coagulation system mostly descended from other proteins [43]. Vitamin K dependent calcium binding Gla domain is more evolutionarily diverse than earlier thought, appearing even in marine organisms [67] with γ-carboxylation occurring in molluscs [11] and chordates [86] with functions including modulation of ion channels [10]. Interaction with calcium (and other calcium modulators like citrate and vitamin D) then is important context for understanding the clinical impact of vitamin K. The Gla domains are important for interaction with phosphatidylserine and activity enhancement of several coagulation related proteins [17]. Mutations effecting the protein S Gla domain may cause thrombotic disease [158] highlighting the control aspect of vitamin K dependent modifications.

For these and likely other reasons, vitamin K, among others [57] , is associated with diverse outcomes such as optimal brain health [31]. [149] and menaquinone-7 may even reduce natural age related cognitive impairment in rats [50]. As if vitamin K was not counterintuitive enough, thrombrin or mutant thrombrins has also been proposed as an anti-coagulant if its only action is to activate protein C [26]. Although prothrombin cleaved to meizothrombin which is anti-coagulant [108] but labelled as "paradoxical." Apparently it is much better at activating protein C than alpha thrombin [65].

One damage associated signal that may illustrate the "covering up" issue is Von Willebrand Factor(vWF). vWF is released from and then binds to endothelial cells or platelets [62]. High serum levels may be associated with increased risk of venous thromboemolism [48] and major adverse cardiac events [56]. A 2022 result suggests that vWF reacts only with fibrin rather than fibrinogen to make clots quickly [153]. A thin impermeable barrier could keep vWF out of circulation and hopefully become passive. A study of mice with diet induced obesity (high fat diet) developed enhanced secretion and impaired clearance of vWF along with less fibrin in clots [126]. Its difficult to rule out fibrin deficiency due to vitamin K deciciency related to the high fat diet. In fact lipophillic vitamins are a likely issue with high-fat diets [46] and in mice vitamin K supplementation can correct some bone [83] and mitochondria or muscle [171] problems. However, there is no obvious indication that vitamin K supplementation reduces red thrombus although red thrombus may be NET dependent [23] and therefore indirectly controlled by vitamin K.

Personal experience giving vitamin K to dogs in cases often considered for anti-thrombotics has been good. In one case, a pregnant pit bull with heartworm and later diganosed fibroids (unpublished personal communication from vet who removed them) did well with vitamin K among other things [119]. An earlier heartworm positive dog did well too [111] [115]. Note that all dogs received a broard range of nutrients rotated in a way to avoid some competitions. All that can really be said about the vitamin K is that it did not appear unsafe under these conditions. Note that significant citrate was typically included.

Hopefully this introduction explained the origin of the proposed curve, explained some of the problems with prior art, but created several more quesitons. The rest of this work covers some topics that should further support the curve but organized as plausibility considerations. At issue is interpretation of specific observations and the validity of various conclusions that need to be re-examined. Miscellaneous observations that could be a basis for further resolution are listed in the conclusion.

Thinking outloud
part of the organization issue is it is mostly a collection of stuff I thought was interesting, the proverbial "darlings".

2. VITAMIN K STEREOTYPE

Concerns about vitamin K may derive from its association with pathological coagulation and over-generalization of theoretical or ex vivo works. Vitamin K antagonists such as warfarin are well known and produce measurable benefits which may make it seem counterintuitive to find a better solution in the opposite direction

Thinking outloud
x avoid rat poison comment as if a hitler analogy lol

. There may be a presumption that if vitamin K antagonism fixes some problems, then more must be bad. Indeed, some limited work suggests that more circulating vitamin K is associated with higher stroke risk [89] but that is exactly what is predicted of the low vitamin K part of the proposed curve. Confusing results of vitamin K intake and outcomes may be considered in terms of the non-monotonic curve presented here. The expectations may be so great, that when supplementation fails to create a hypercoagulable state it seems to be a noteworthy result [69] but this too makes sense if the supplementation is great enough to get to the plateau of Fig. 1. An inverse association was found between blood phylloquinone and risk of ischemic stroke among Chinese with hypertension and high BMI [190].

Due to the complex nature of the coagulation system, "hypercoagulability" takes on many forms. In 2000, several forms were recognized including defects in protein C and S with treatment consisting of warfarin sometimes leading to "warfarin necrosis" [177]. The existence of "warfarin necrosis", likely due to faster decay of protein C than procoagulant proteins [84], points to the consideration of "safe passage" from the narrow warfarin optimin to the more tolerant high-vitamin K region. While unfavorable dynamics in one direction do not assure a safer route in the other direction, there is some indication that exists [118] . One case report illustrates some issues with managing an INR about 10 and necrotic lesions [151] that finally led to consideration of vitamin K before returning to anticoagulants leading to amputation and eventually hospice care . While not intuitive, its worth speculating on which genetic conditions may even be better treated with vitamin K supplements instead of antagonists. Note too that a fast fall in vitamin K cycling activity ,which may occur from limited reducing equivalents, could presumably produce effects similar to warfarin necrosis or paradoxical "hypercoagulabilit" either locally or systemically.

Ironically, as opposed to vitamin D [120] (see historical controveries on fortification limits [60] [187]) , I was unable to locate a single case report of vitamin K overdose other than concerns about INR in warfarin patients. This excludes, of course, the non-natural vitamin K3 [130].

In healthy people anyway the consensus seems to be that supplementation, particularly of MK-7, does not to create a coagulation or any other problem [156]. Currently there is even consideration of recommending more vitamin K intake for stroke patients [191] although this is based on food association studies.

A 2021 review suggested K2 supplementation for improved cardiovascular outcomes and suggested it failed to create a hypercoagulable state [69].

It is recognized that anticoagulation in the elderly is difficult due to narrow window [34]. However, supplementation or increased vitamin K status correlates with various favorable clinical results [167] including cognitive function [19] and cardiovascular health [69].

Thinking outloud
why no bone health here? lead with CVD as that was the point

Proteins C and S are well known vitamin K dependent coagulation moderators but their relative response to vitamin K supplementation may be unclear. Prothrombin and protein C carboxylation status in response to warfarin were explored as early as 1989 [32] . Neonatal vitamin K deficiency is a well known problem and some literature exists although it may not be applicable to mature people. A 1993 investigation into vitamin K deficiency and replenishment of neonates suggested proteins C and S gamma-carboxylate in parallel with coagulant proteins minimizes chance of vitamin K related coagulopathies [121]. A study comparing des-carboxy prothrombin and protein C in term and premature babies found correlations between the two and suggested hepatic cycling rates may be limited while cautioning that lab results were sensitive to methods [22] but no scatter plots to look for various trends. It is also worth noting though that they quote 4-60 hour half life for protein C. This may make it effected by short term loss

of reducing equivalents that can occur under "stress." Indeed, cytosolic NADPH limitation may be a big driver of pathology [9].

Another study of protein C in mice suggested that extra-hepatic mRNA could be reduced in response to LPS exposure [195] suggesting that more vitamin K may not help. However, while some relative reduction in protein C may be adaptive it is not clear how this relates to other factors like prothrombin.

3. WORD GAMES : BLOOD THICKNESS

Anti-coagulants may be colloquially described as "blood thinners" and indeed blood viscosity does appear to correlate with cardiovascular disease [35] [181] [100] [25] [20] . The association was described at lest since the 1980's [29] [41] and recently recognized with covid-19 mortality [30]. While the details remain to be worked out [42] , protein content and notably fibrinogen content as well as RBC physical properties are thought to dominate viscosity measures [15]. RBC flexibility or deformability is thought to be an important component of blood function [47].

Vitamin K antagonists do reduce blood viscosity in many studies [92] but that is not always the case [98]. By eliminating on sink for fibrinogen, fibrinogen and blood viscosity would be expected to increase after warfarin dosing. When reductions in blood viscosity in response to warfarin do occur, it may not have anything to do with the coagulation cascade directly. As early as 1985, A small rat study suggested that RBC deformability and low hematocrit were more important than fibrinogen levels [63]. Accidental modification can occur when attempting to achieve some other goal. Blood rheology cam be modified by calcium channel blockers [85] and blood calcium also may correlate with viscosity [185]. Warfarin usage is also associated with calcium deposition in arteries which may suggest important calcium redistribution.

Early on, erythrocyte flexibility was observed in ponies along with a blood viscosity fall in response to warfarin treatment [5]. It is entirely possible that clinical benefits for warfarin relate to RBC rheology as much as vitamin K antagonism or reduced coagulation. Literature on other thrombin inhibitors or DOAC's may be interesting for comparison in a later work. Similarly, heparin may have clinical impact due to effects other than anti-coagulation which are preparation specific [102]. Accidental or unappreciated effects of details or formulation are likely to be a common issue. Literature fragmentation may be common and has been seen before in related topics with vitamin D [112] and may occur in benzoate for brain disease effects other than d-amino acid oxidase activity do not appear to be considered [110].

4. PARTIAL CARBOXYLATION AND REDUCED PH

Probably the oldest indication of a relationship between vitamin K and pH is a study on the response of phytoplankton Emiliania huxleyi to acidification. The authors found increased synthesis of proteins likely to be involved in vitamin K synthesis [81] merging ancient issues with mineralization, pH, and energy usage.

Today, one enigma that may offer important context and perspective on vitamin K is osteocalcin which oddly seems most effective in an undercarboxylated state. It is secreted mostly from osteoblasts and is evolutionarily ancient appearing first with "bony structures" apparently derived from the MGP (and also called BGP) that appeared coincident with "cartilaginous structures" but today interacts with insulin, fertility, and cognition [201]. Essentially sufficient for a stress response, serum levels increase after exercise and decline after midlife (reversible by osteocalcin injection) with known functions relating too pancreas, memory and exercise capacity Undercarboxylation occurs due to removal in the low pH lacunae but it may also occur during PTM by glutamate signalling [14] . It is interesting to speculate that OCN may also decarboxylate in the lactate rich low pH environments around oxygen deficits. Further, excess glutamate may be suspected of depressing gamma carboxylation more generally leading to undercarboxylated vitamin K dependent proteins. Interestingly, some decreases were observed at lower chronic doses although MSG is known to provoke clotting acutely [144] presumably through other mechanisms (although maybe including protein C inhibition) and is not a clean test. Interestingly, Gas6 was found to reduce apoptosis during CO2 induced acidification [37] although its carboxylation state was not examined.

It may be expected then that levels of partially carboxylated proteins could mediate mood by various means. Indeed, there is some evidence relating vitamin K status and presumably then carboxylation rate to various mental states. A small rat study suggested improvement in anxiety and depression in rats fed a high fat/fructose diet [59] . And indeed "perceived stress" appeared to correlate with the intake of many nutrients including vitamins A,C,B-X, and K as well as essential amino acids [90].

pH or acidosis related coagulopathy may be interesting to investigate. Currently there do seem to be acidosis related coagulopahies that remain incompletely understood [61] even in specific settings such as trauma [129] or transplantation [39].

5. CLINICAL IMPACT IN VARIOUS CONDITIONS

For children and young adults without specific conditions, vitamin K appears to be recognized as safe in unlimited amounts but there is generally not a compelling need for supplements. Vitamin K usage for neonates is well known and is quickly evolving for older populations. Neonatal supplementation has been cited here in passing as results were relevant to dynamics of vitamin K dependent proteins in response to vitamin K activity changes. More recent indications for the elderly will be the main focus here however as these illustrate some functions that are not explicitly coagulation related and thoughts on cryptic deficiencies in other populations. Less familiar targets include brain and bone and endothelial cells in general with wide ranging implications for health. Explicit consideration of vitamin K supplements would likely impact larger overall treatment plans that may include other coagulation modifiers such as aspirin. Therefore, recent results related to these entities are also shown

Vitamin K is increasingly recognized as a mediator of conditions of old age [167]. [123]. As of 2019 its general role in aging was recognized and a consensus developing that increased intake reduced CVD incidence [166]. Its important to remember though that no single vitamin is likely to be deficient in isolation. Dietary or digestive defects may impact many vitamins even with a "single point of failure." In general, digestive incompetence may be a correlate of old age [114].

A variety of observations link vitamin K cycling to calcium fate. However, consistent results with either vitamin K or vitamin K antagonists are not always obtained. Clinical trials for osteoporosis in post menopausal women have been conducted with some successes [58] . $MGP^{-/-}$ or MGP-KO mice exhibit osteopenia and MGP depletion increases bone resorption and osteoclast production [200] apparently contrary to other functions. Besides being vitamin K depedent, MGP expression is regulated by vitamin D, retinoic acid, calcium, and various growth factors [88]. It is thought to improve osteoporosis/osteopenia and muscle mass while being susceptible to pancreatic insufficiency [2] making it an ideal candidate for diseases of old age and requiring care for absorption if GI problems are present. While being chemically much different, it may share uptake issues with other suspects like tryptophan or vitamin D. A trial on osteopenic postmenopausal women with 5mg/day of K1 demonstrated possible protection against fracture and cancer without changing bone mineral density [103]. A 2022 review of the trials suggests significant fracture risk reduction but only questionable BMD improvement [162] motivating the importance of clinical endpoints. Mineral density may not be as important as architecture- bone is not chalk.

However, other vitamins may have to be considered or even limited to get an effective overall nutrient profile. 500 micrograms of K1 added to 600mg of Ca and 400IU cholecalciferol could not improve coronary artery calcifucation (CAC) although it did decrease ucMGP (uncarboxylated matrix Gla Protein) in 60-80 year olds in generally good health [165]. However, mineralization may be regulated locally rather than by serum levels [139] and coronary artery calcification may depend on general malnutrition as determined from serum albumin and BMI[7] or some combination of several nutrients. At least one report suggested MK-4 in a high phosphate environment could lead to calcification via PXR [198].

Most recently, a role in brain sulfatide production was elucidated. In 2007, sulfatide depletion was identified as a very early sign of Alzheimer's disease and modulated by apoE [66]. Vitamin K has been linked to sulfatides in the brain in several settings including remyelination [150] and in young mice and rats since 1996 [173]. Low intake from a 2015 observational study associated with worse MMSE scores in people 65 years or older [31]. At least as early as 2001, vitamin K deficiency was suspected of contributing to Alzheimer's and CVD. Reduced blood levels associated with AD risk factor APOE4 [1] in one study although the opposite genotype-phenotype association was found in a study of Chinese and British people [196]. Interestingly, the opposite association appears to hold for vitamin D [105] although this may be non-monotonic. Inconsistent results may point to a genotype modulating the vitamin D dose-response curve as I had earlier suggested with possible concerns about lifestyle factors [113]. A very recent study suggested brain and plasma vitamin K associated with less cognitive decline [19].

Endothelial function's relationship to vitamin K is most directly described by Gas6 although that may incidentally impact coagulation too. For example, Gas6 is thought to help uptake of pro-coagulant platelet secreted microparticles [68] . The literature is somewhat mixed and some results suggest it could be pathological. It has been reported to increase inflammation [178] and induce tissue factor expression [91] as well as promote venous thrombosis [155] . However, it appears to protect the brain from inflammation after hemorrhage [176], improve pulmonary arterial hypertension along with a role for BMPR2 [142] [180] and it may also preserve barrier function and reduce permeability during sepsis [141]. One small study found associations between low levels of Gas6 and type 2 diabetes and carotid atherosclerosis [55] . It has a well known anti-apoptotic effect on endothelial cells [71] and vascular smooth muscle cells [125] as well as reducing inflammation in response to silicosis [194]. Its difficult to immediately dismiss the conflicting results but overall it is likely that deficiency may contribute to disease.

Unfortunately , a of clinical experience with vitamin K function has been gained by antagonism or inhibition of vitamin K dependent proteins or coagulation and is relevant to understanding overall cause and effect. Significant clinical experience has been gained with new "DOAC's" that typically are selective for reducing thrombin activity

either by inhibiting thrombin directly or factor Xa [164] of prothrombinase. In theory then these are cleaner ways to slow down fibrin generation. As they have much wider therapeutic windows than warfarin, presumably the fibrin reduction level is not critical but off target effects would have to be considered such as RBC rheology as described earlier. Comparisons to antiplatelet and aspirin protocols appear to be a learning experience as bleeding can offset any benefits in occlusive disease [161]. Some successes were with combination therapy versus aspirin alone as in COMPASS [145]. With other anti-platelets only being superior to aspirin by a small but statistically significant amount in some trials although at that time in 2019 aspirin had a "strong track record" [64],

Many possible concerns exist with clotting inhibition ranging from purely hypothetical to having been realized in various ways. The risks largely depend on the pathological entity which is no longer covered up. Certainly blood loss is one class but another important one is pathogens. Failure to clear infection can occur. This was recently shown in zebrafish for warfarin, aspirin, or ticagrelor [179] and the organism is accepted as a decent model for human coagulation [163]. Frequent infections may motivate an interest in vitamin K [12]. One recent work observed a well known relation between thrombosis and bacterial infection and found an affinity for fibrinogen and ability to modify clot properties by Staphylococcus epidermidis [184]. An overwhelming fast response may be needed to avoid a proliferation of pathological clots and stop spread. A review of the protein C pathway suggested benefits in e coli challenge [51].

Various specific indications have produced unsatisfactory results. For example, "More specifically, the REALIGN (Dabigatran Versus Warfarin in Patients With Mechanical Heart Valves) trial established the use of DOACs as contraindicated in patients with mechanical heart valves.26 The study was terminated early, as patients with mechanical prosthetic heart valves experienced excess thromboembolic and bleeding events." [28] The same article suggested bleeding offset some of the benefits in COMPASS adding DOAC to aspirin. Trials stopped early for excess morality include AFIRE when adding antiplatelet to rivaroxaban. Use against VTE in cancer seems robust however.

The ASPREE and ANTISEPSIS results were interesting too. With ASPREE showing excess mortality with low dose aspirin in those older than 65 or 70 largely due to cancer and some bleeding but thought to be less than post hoc general population controls even though stopped early for futility [80]. Analysis for ANTISEPSIS did not find a benefit for spesis although interaction with cancer may be one limitation [49]. A cohort study including the US "stroke belt" showed sepsis more common in aspirin users but that evaporated on correction and there were differences among the user and non-user groups [79]. Additional concerns exist when used to delay antibiotic usage in UTI's and increase infection persistence despite aspirin having some anti-biotic properties as well as anti-inflammatory [143] . A mortality-delay relation has also been explored in relation to coagulation factors in mouse sepsis [72]. Reduced platelet function may alow infection to spread easier but use of aspirin may also delay prescription of effective antibiotics [93].

Response to damage and invaders is often more effective if it is fast but regulated. If sufficient resources do not exist, a long battle may play out. Clotting employs positive feedback using many zymogens to achieve fast and decisive response but that strategy will be a problem if it does not achieve a victory and shut itself off. A trigger needs to be quickly buried with a barrier impermeable to diffusion by clot forming reactants. If that does not happen, a long futile clotting process may continue creating clots that may only be effective in stopping red blood cells.

6. GREATER RESILIENCY

The coagulation pathways certainly make organisms more resilient to injuries in the "real world" but that improved fitness extends beyond coagulation. Some forms of improved fitness do indeed relate to coagulation. For example, vitamin K appears to facilitate better responses to hypoxia as may occur with ischemia due to coagulation errors among other cuases. In general, vitamin K coagulation pathways are largely self moderating over many states and genetics. Another level of moderation may come from greater resilience to transient occlusive disease. Although it is also interesting to note that 'ischemic preconditioning" is protective against future ischemiai [199], Vitamin K appears to be neuroprotective to rats when given after experimental ischemia [132]. Menaquinone improved rat astrocyte response to hypoxia likely through Gas6 [197]. Vitamin K is a robust protector against ferroptosis and in this role can use warfarin insensitive FSP1 and NAD(P)H for reduction to VKH2 [128]. Gas6 is a locally produced vitamin K dependent protein [154]. Rather than solely being produced in the liver, it is now thought that, "Virtually every tissue expresses at least 1 of the 16 known VKD proteins, which have functions that include hemostasis, calcium homeostasis, signal transduction, growth control, and apoptosis.1 " [159].

It functions through non-gamma carboxylation means to reduce inflammation and oxidative stress [166]although these words tend to be a bit general.

At very high doses in rats, it had varying effects on coagulation similar to phytol and geranylgeraniol suggesting an effect of the side chain rather than gamma carboxylation [160]. This suggests however that at these does K1 may encourage clotting as opposed to K2.

Many of these benefits may be due to interactions within the mitochondria although direct evidence for this in

humans is lacking. For example, it appears important for muscle and nerve health via mitochondria [124] and it is thought to improve mitochondrial function in mice fed a high-fat diet [171].

The overall structure of a quninone and side chain makes it attractive to consider as a part of electron transport. This may be the case in Drosophila [186] but despite entering the mitochondria, no evidence has been found to support the idea that, in human cells, it can replace ubiquinone [27] . In any case, the range of benefits appear to coincide well with many concerns.

7. SUPPLEMENT INSTEAD OF ANTAGONIZE

Generally vitamin K is considered in terms of coagulation and there is a tendency to antagonize it even as regulatory proteins like C and S may be the first victims of insufficient reduced vitamin K. While this response may be adaptive, making clotting easier if there is less vitamin K, it does not always have a beneficial result. It is becoming apparent that vitamin K antagonism may not be the optimal solution or may even be counter productive and consideration of supplementation occurs. Many attempts have been made to supplement only with specific vitamin K dependent proteins such as activated protein C. Generally these run into control and bleeding problems again motivating vitamin K as a better controlled solution over a range of genetics and conditions. . For example, this was considered in 2019 with idiopathic pulmonary fibrosis [24] and it now appears that vitamin K dependent periostin is involved in other remodelling activities including cardiac fibrosis [193] Given the link between cardiac fibrosis and atrial fibrillation [95], you have to suspect that vitamin K supplements rather than antagonists may be beneficial in this case too. That is, additional vitamin K would actually improve clot quality and be disease modifying.

At least one case report involving covid-19 replaced aspirin and clopidogrel on presentation with vitamin K on discharge [8] even as anticoagulant strategies continue to get a lot of attention.

Even in sepsis, the errors in models have been recognized and the futility of blanket anti-coagulation has yielded to the need for compartmentalization of pathogens [168] although strategies tend to continue to focus on particular anti-coagulant components such as activated protein C.

Protein C comes up in cancers [146] as they are often considered hypercoagulable states and vitamin K itself has been explored too. Some literature has suggests other concerns with breast [188] and liver cancer [182]. Yet, vitamin K may inhibit some cancer [101] . While a trial in hepatocellular carcinoma did not show a benefit [78], it may synergize significantly with sorafenib [70]. The test of vitamin K were done in spite of coagulation issues, notably portal vein thrombosis, associated with HCC [106],

Even in occlusive disease such as ischemic stroke, activated protein C is being explored due to failure of thrombolytics [3]. While not vitamin K per se, the fast response of protein C and S to supplementation point to possible utility and "safe passage" from the narrow warfarin optimum to the wider latitude high-K state. Prior use of activated protein C appears to have mixed results and the warfarin necrosis associated with inhibition points to additional vitamin K dependent factors in resolving the circulatory issues.

Figures 2 for K1 and to a lesser extent Figure 3 for K2 intake in [13] demonstrate increasing various CVD risks at lower vitamin K intakes mostly reproducing the higher dose part of the curve in [118]. The intakes were estimated from self reported food frequency questionnaires. These data limit the quality of the result and the intake levels covered are quite moderate around 30-100μgrams/day .

8. OF COURSE, COVID-19

covid-19 is a good example of the evolution of treatment approaches to new conditions that may respond to vitamin K. Coagulopathy has been a persistent component of covid-19 with a lot of attention to anti-coagulants [33] although a correlation between vitamin K deficiency and severe disease has been recgonized too [104] [75]. In another work, uncarboxylated MGP (dp-ucMGP) correlated with IL-6 which correlated with poor outcomes compared to marginal significance for vitamin D [183]. Previously, I had suggested vitamin K, along with other ideas such as citrate, as an covid-19 intervention [114]. The 2022 review of covid-19 coagulopathy cites NET's and protein C [33] as important factors regnozied early on issues that may be addressed with vitmain K [114] [117] . Vitamin K correlated with covid-19 severity as measured by dephosphorylated uncarboxylated matrix Gla protein (dp-ucMGP) after correcting for other factors [40]. In another small study, it was also found to be higher in controls than covid-19 patients [133]. While not much has been done with high-dose vitamin K supplementation, attempts have been made to consider just one vitamin K protein at a time such as C and S. Low protein C has been observed in patients and considered [122] while Protein S depletion [54] blamed for the cytokine storm and other covid-19 complications [94] perhaps related to complement. Neither may work well alone due to being an incomplete solution without the other vitamin K dependent proteins.

Other work more generally considers vitamin K for older people (> 50) while pointing to a reduced activation of protein S and consequent thrombogenecity in covid-19 patients due to vitamin K depletion as well as Gas6 in brain function [148]. One small study from early 2021 found clear patterns in MGP carboxylation among healthy and covid-19 survivors or non survivors [97]. A small study from 2021 found about a fctor of 2 reduced blood levels of vitamin K in covid-19 patients compared to healthy controls and an insignificant increase with severity with an opposite situation of vWF [133].

The "hypercoagulability" associated with covid-19 includes high d-dimers and higher fibrinogen levels [134]. Elevated FGN could enable faster production (perhaps unbalanced low quality clots), reduced hepatic clearance, or actually reduced clot formation rates. D-dimers could reflect clot velocity but also liver damage. Elevated D-dimers with measured hypofibinolysis could reflect a lung-specific fibrinolysis [73] which points to the limitations of another coagulation related assay. Note also that phagocytic fibrin clearance may be an unappreciated factor [127] [136] . Generally it seems phagocytosis of apoptotic cells iw regulated by protein S [82] [6] which may make it important for this pathway suggesting high d-dimers are related to protein S deficiency. Work from the 1990's found some significant attributes of the non-plasmin fibinrolytic pathway involving monocytes not effected by serine protease inhibitors but inhibited by Fastor X and thought to be lysosomal [4]. A lytic role for monocytes and Mac-I within their larger clotting role has been described [170]. Cathepsin-D appears to degrade fibrinogen and fibrin [169] while other secreted cathepsins have been considered as causes of disease with signature fragment patterns [44]. It is possible that the real harm related to elevated d-dimers is the increased usage of the promiscuous plasmin instead of alternatives such as lysosomal degradation.

Vitamin K blood levels may not reflect adequacy of internal stores or cycling rate but may correlate somewhat.

9. CONCLUSIONS

Vitamin K excess may create a pathological mix of dependent proteins in some limited combinations of genetics and conditions such as with limitations in protein S or C but in most known cases likely does not cause pathological clotting at arbitrarily high activities or concentrations. For coagulation to ever work, it is likely to be "explosive" and self limiting. A high quality clot can isolate the trigger and prevent the diffusion of danger signals allowing for reasonably silent removal. A low quality clot may not be able to sequester clotting signals and a futile coagulation prcess can occur until some factors are depleted and then continue in a possibly worse state. Laboratory attempts to recreate a subset of this intricate system may produce misleading results. In most cases, vitamin K supplementation with adequate supply of reducing equivalents is probably more beneficial than limitation. Attempts to simply supply activated protein C have not been fully successful probably because other vitamin K dependent products such as protein S are also required for good outcomes.

At least four observations from the literature that may not be appreciated include significance of non-plasmin clot removal, the likely need for reducing equivalents over hour time scales to maintain protein C levels, and the ability of free glutamate to impact gamma carboxylation of vitamin K dependent proteins, and finally the clinical relevance of low pH on gamma carboxylation. The first was incidental o the work but correlations of high d-dimers and clinical outcome along with other observations suggest reconsideration of phagocytosis and monocytes as healthy clot removal approaches. It may be intersting to determine if IDH1 needs support during "hypercoaguable" stress or if chronic high Glu intake causes clinical symptoms by this interference independent of any acute effects of MSG or glutamate. In either case, there is plenty of suggestion that idiopathic coagulopathies may be due to nutrient derangements beyond any single nutrient but vitamin K activity could be a central issue. NADPH may be regenerated from cytosolic citrate [140] and a role in clot control by this mechanism may not have been considered.

10. SUPPLEMENTAL INFORMATION

10.1. Computer Code

11. BIBLIOGRAPHY

[1] **M.J. Marchywka**. A Proposed Qualitative Non-monotonic Paradox Resolving Actvitiy-Coagulability Curve for Vitamin K (June 1, 2021) src:www.researchgate.net.

[2] **M.J. Marchywka**. Supplement Usage Including Vitamin K by a Heartworm Positive Pregnant Pit Bull and Her Puppies (September 29, 2021) src:www.researchgate.net.

[3] **Mike J Marchywka**. Happy Again : Possible Canine Riboflavin Deficiency (March 27, 2022) src:www.researchgate.net.

[4] **M.J. Marchywka**. Canine Heartworm Treated with Doxycycline, Ivermectin and Various Supplements (March 27 2021) src:www.researchgate.net.

[5] **Retzinger , Gregory S. and DeAnglis , Ashley P. and Patuto , Samantha J.**. Adsorption of Fibrinogen to Droplets of Liquid Hydrophobic Phases Arteriosclerosis, Thrombosis, and Vascular Biology (1998) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[6] **Zuliani-Alvarez , Lorena and Midwood , Kim S.**. Fibrinogen-Related Proteins in Tissue Repair: How a Unique Domain with a Common Structure Controls Diverse Aspects of Wound Healing. Advances in Wound Care (2015-May-01) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[7] **Poole , Lauren G. and Kopec , Anna K. and Groeneveld , Dafna J. and Pant , Asmita and Baker , Kevin S. and Cline-Fedewa , Holly M. and Flick , Matthew J. and Luyendyk , James P.**. Factor XIII cross-links fibrin(ogen) independent of fibrin polymerization in experimental acute liver injury. Blood (2021-May-6) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[8] **Jin , Stephanie and Hong , Lisa and FakhriRavari , Alireza**. The Role of Vitamin K in Cirrhosis: Do Pharmaco-K-Netics Matter? Gastrointestinal Disorders 15-21 (2022) src:dx.doi.org. src:mdpi-res.com.

[9] **M.J. Marchywka**. Considering Alternative Fibrinogen Fates in Diseased States (July 17, 2021) src:www.researchgate.net.

[10] **Suh , T T and Holmback , K and Jensen , N J and Daugherty , C C and Small , K and Simon , D I and Potter , S and Degen , J L**. Resolution of spontaneous bleeding events but failure of pregnancy in fibrinogen-deficient mice. Genes & development (1995-Aug-15) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[11] **Mullins , Eric S and Kombrinck , Keith W and Talmage , Kathryn E and Shaw , Maureen A and Witte , David P and Ullman , Joni M and Degen , Sandra J and Sun , William and Flick , Matthew J and Degen , Jay L**. Genetic elimination of prothrombin in adult mice is not compatible with survival and results in spontaneous hemorrhagic events in both heart and brain. Blood (20081016) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[12] **Mann , K.G. and Kalafatis , M.**. The Coagulation Explosion Cerebrovasc Dis (1995) src:dx.doi.org. src:www.karger.com. src:www.karger.com.

[13] **Sunnerhagen , M and Forsen , S and Hoffren , A M and Drakenberg , T and Teleman , O and Stenflo , J**. Structure of the Ca(2+)-free Gla domain sheds light on membrane binding of blood coagulation proteins. Nature structural biology (1995-Jun) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[14] **Muller , Melanie P. and Wang , Yan and Morrissey , James H. and Tajkhorshid , Emad**. Lipid Specificity of the Membrane Binding Domain of Coagulation Factor X. Journal of thrombosis and haemostasis : JTH (20170901) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[15] **Blostein , Mark D. and Rigby , Alan C. and Jacobs , Margaret and Furie , Bruce and Furie , Barbara C.**. The Gla Domain of Human Prothrombin Has a Binding Site for Factor Va Journal of Biological Chemistry 38120-38126 (2000) src:dx.doi.org. src:www.jbc.org.

[16] **Jesty , Jolyon and Beltrami , Edward**. Positive Feedbacks of Coagulation Arteriosclerosis, Thrombosis, and Vascular Biology 2463-2469 (2005) src:dx.doi.org. src:www.ahajournals.org.

[17] **Dashkevich , N.M. and Ovanesov , M.V. and Balandina , A.N. and Karamzin , S.S. and Shestakov , P.I. and Soshitova , N.P. and Tokarev , A.A. and Panteleev , M.A. and Ataullakhanov , F.I.**. Thrombin Activity Propagates in Space During Blood Coagulation as an Excitation Wave Biophysical Journal 2233-2240 (2012) src:dx.doi.org. src:core.ac.uk.

[18] **Kuprash , Anna D. and Shibeko , Alexey M. and Vijay , Ramya and Nair , Sukesh C. and Srivastava , Alok and Ataullakhanov , Fazoil I. and Panteleev , Mikhail A. and Balandina , Anna N.**. Sensitivity and Robustness of Spatially Dependent Thrombin Generation and Fibrin Clot Propagation Biophysical Journal 2461-2473 (2018) src:dx.doi.org. src:www.cell.com.

[19] **Wufsus , A.R. and Macera , N.E. and Neeves , K.B.**. The Hydraulic Permeability of Blood Clots as a Function of Fibrin and Platelet Density Biophysical Journal 1812-1823 (2013) src:dx.doi.org. src:www.cell.com.

[20] **Duval , Cédric and Baranauskas , Adomas and Feller , Tímea and Ali , Majid and Cheah , Lih T. and Yuldasheva , Nadira Y. and Baker , Stephen R. and McPherson , Helen R. and Raslan , Zaher and Bailey , Marc A. and Cubbon , Richard M. and Connell , Simon D. and Ajjan , Ramzi A. and Philippou , Helen and Naseem , Khalid M. and Ridger , Victoria C. and Ariëns , Robert A. S.**. Elimination of fibrin upgamma-chain cross-linking by FXIIIa increases pulmonary embolism arising from murine inferior vena cava thrombi

Proceedings of the National Academy of Sciences (07/06/2021) src:dx.doi.org. src:www.pnas.org.

[21] **Increases Cerebral Infarct Size by Promoting Thrombus Stabilization , Factor XIII and Revascularization Treatments in Ischemic Stroke - ISTH Congress Abstracts , Resistance to and Abstracts , ISTH Congress and Abstracts , ISTH Congress**. Factor XIII Increases Cerebral Infarct Size by Promoting Thrombus Stabilization and Resistance to Revascularization Treatments in Ischemic Stroke - ISTH Congress Abstracts (06/19/2021) src:abstracts.isth.org.

[22] **Szkely , Edina Gabriella and Czuriga-Kovcs , Katalin Rka and Bereczky , Zsuzsanna and Katona , va and Mezei , Zoltn Andrs and Nagy , Attila and Tth , Nomi Klra and Bernyi , Ervin and Muszbek , Lszl and Csiba , Lszl and Bagoly , Zsuzsa**. Low factor XIII levels after intravenous thrombolysis predict short-term mortality in ischemic stroke patients. Scientific Reports (20180516) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[23] **Dahlbäck , Björn and Villoutreix , Bruno O.**. Regulation of Blood Coagulation by the Protein C Anticoagulant Pathway Arteriosclerosis, Thrombosis, and Vascular Biology (2005) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[24] **Fager , A. M. and Machlus , K. R. and Ezban , M. and Hoffman , M.**. Human platelets express endothelial protein C receptor, which can be utilized to enhance localization of factor VIIa activity Journal of Thrombosis and Haemostasis 1817-1829 (2018) src:dx.doi.org. src:onlinelibrary.wiley.com.

[25] **Litvinov , Rustem I. and Weisel , John W.**. Not fibrin(ogen), but fibrinogen or fibrin. Blood (2015-Oct-22) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[26] **Prasad , Joni M. and Gorkun , Oleg V. and Raghu , Harini and Thornton , Sherry and Mullins , Eric S. and Palumbo , Joseph S. and Ko , Ya-Ping and Höök , Magnus and David , Tovo and Coughlin , Shaun R. and Degen , Jay L. and Flick , Matthew J.**. Mice expressing a mutant form of fibrinogen that cannot support fibrin formation exhibit compromised antimicrobial host defense Blood 2047-2058 (10/22/2015) src:dx.doi.org. src:ashpublications.org.

[27] **Mangin , Pierre H and Onselaer , Marie-Blanche and Receveur , Nicolas and Le Lay , Nicolas and Hardy , Alexander T and Wilson , Clare and Sanchez , Ximena and Loyau , Stphane and Dupuis , Arnaud and Babar , Amir K and Miller , Jeanette LC and Philippou , Helen and Hughes , Craig E and Herr , Andrew B and Arins , Robert AS and Mezzano , Diego and Jandrot-Perrus , Martine and Gachet , Christian and Watson , Steve P.**. Immobilized fibrinogen activates human platelets through glycoprotein VI. Haematologica (2018-May) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[28] **Bouwens , E. A. M. and Stavenuiter , F. and Mosnier , L. O.**. Mechanisms of anticoagulant and cytoprotective actions of the protein C pathway Journal of Thrombosis and Haemostasis 242-253 (06/30/2013) src:dx.doi.org. src:onlinelibrary.wiley.com.

[29] **Webb , Joanna H. and Blom , Anna M. and Dahlbäck , Björn**. Vitamin K-Dependent Protein S Localizing Complement Regulator C4b-Binding Protein to the Surface of Apoptotic Cells The Journal of Immunology (2002) src:dx.doi.org. src:www.jimmunol.org.

[30] **Li , Xian and Bidarian , Sara J and Sim , Martha and Song , Xiaohong and Wood , Jeremy P.**. Protein S Coordinates the Inhibition of Prothrombinase By Tfpiupalpha and Activated Protein C Blood (2019) src:dx.doi.org. src:www.sciencedirect.com.

[31] **Exner , Thomas and Rigano , Joseph and Favaloro , Emmanuel J.**. The effect of DOACs on laboratory tests and their removal by activated carbon to limit interference in functional assays International Journal of Laboratory Hematology 41-48 (2020) src:dx.doi.org. src:onlinelibrary.wiley.com.

[32] **Moser , Karen A. and Smock , Kristi J.**. Direct oral anticoagulant (DOAC) interference in hemostasis assays. Hematology: the American Society of Hematology Education Program (20211210) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[33] **Berkner , Kathleen L. and Runge , Kurt W.**. Vitamin K-Dependent Protein Activation: Normal Gamma-Glutamyl Carboxylation and Disruption in Disease International Journal of Molecular Sciences 5759 (2022) src:dx.doi.org. src:mdpi-res.com.

[34] **MladUx011b[bad char vv=283]nka , PUx0159[bad vv=345]emysl and Macáková , KateUx0159[bad vv=345]ina and Kujovská KrUx010d[bad char vv=269]mová , Lenka and Javorská , Lenka and MrUx0161[bad char vv=353]tná , Kristýna and Carazo , Alejandro and Protti , Michele and Remião , Fernando and Nováková , Lucie and researchers , the OEMONOM and collaborators**. Vitamin K - sources, physiological role, kinetics, deficiency, detection, therapeutic use, and toxicity Nutrition Reviews (2021-09) src:dx.doi.org. src:doi.org. src:academic.oup.com.

[35] **Mladnka , Pemysl and Mackov , Kateina and Kujovsk Krmov , Lenka and Javorsk , Lenka and Mrtn , Kristna and Carazo , Alejandro and Protti , Michele and Remio , Fernando and Novkov , Lucie**. Vitamin K sources, physiological role, kinetics, deficiency, detection, therapeutic use, and toxicity. Nutrition Reviews (20210902) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[36] **Doolittle , R. F.**. Step-by-Step Evolution of Vertebrate Blood Coagulation Cold Spring Harbor Symposia on Quantitative Biology 35-40 (2010-06-21-2009-01-01) src:dx.doi.org. src:symposium.cshlp.org.

[37] **Hansson , Karin and Ma , Xiaosong and Eliasson , Lena and Czerwiec , Eva and Furie , Bruce and Furie , Barbara C. and Rorsman , Patrik and Stenflo , Johan**. The First upgamma-Carboxyglutamic Acid-containing Contryphan Journal of Biological Chemistry 32453-32463 (2004) src:dx.doi.org. src:www.jbc.org.

[38] **Bandyopadhyay , Pradip K. and Garrett , James E. and Shetty , Reshma P. and Keate , Tyler and Walker , Craig S. and Olivera , Baldomero M.**. upgamma-Glutamyl carboxylation: An extracellular posttranslational

modification that antedates the divergence of molluscs, arthropods, and chordates Proceedings of the National Academy of Sciences 1264-1269 (02/05/2002) src:dx.doi.org. src:www.pnas.org.

[39] **Kulman , John D. and Harris , Jeff E. and Nakazawa , Noriko and Ogasawara , Michio and Satake , Masanobu and Davie , Earl W.**. Vitamin K-dependent proteins in ¡i¿Ciona intestinalis¡/i¿ , a basal chordate lacking a blood coagulation cascade Proceedings of the National Academy of Sciences 15794-15799 (10/24/2006) src:dx.doi.org. src:www.pnas.org.

[40] **Bandyopadhyay , Pradip K.**. Vitamin KDependent upgammaGlutamylcarboxylation: An Ancient Posttranslational Modification Academic Press (2008) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[41] **Bevers , Edouard M. and Williamson , Patrick L.**. Getting to the Outer Leaflet: Physiology of Phosphatidylserine Exposure at the Plasma Membrane Physiological Reviews 605-645 (2016) src:dx.doi.org. src:journals.physiology.org.

[42] **Rezende , Suely M. and Lane , David A. and Mille-Baker , Blandine and Samama , Michel M. and Conard , Jacqueline and Simmonds , Rachel E.**. Protein S Gla-domain mutations causing impaired Ca2+-induced phospholipid binding and severe functional protein S deficiency Blood 2812-2819 (10/15/2002) src:dx.doi.org. src:ashpublications.org.

[43] **Fenech , Michael**. Vitamins Associated with Brain Aging, Mild Cognitive Impairment, and Alzheimer Disease: Biomarkers, Epidemiological and Experimental Evidence, Plausible Mechanisms, and Knowledge Gaps Advances in Nutrition (2017-11) src:dx.doi.org. src:doi.org. src:academic.oup.com.

[44] **Chouet , Justine and Ferland , Guylaine and Féart , Catherine and Rolland , Yves and Presse , Nancy and Boucher , Kariane and Barberger-Gateau , Pascale and Beauchet , Olivier and Annweiler , Cedric**. Dietary Vitamin K Intake Is Associated with Cognition and Behaviour among Geriatric Patients: The CLIP Study Nutrients 6739-6750 (2015) src:dx.doi.org. src:www.mdpi.com.

[45] **Popescu , Alexander and German , Monica**. Vitamin K2 Holds Promise for Alzheimers Prevention and Treatment. Nutrients (20210627) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[46] **Elkattawy , Hany A. and Ghoneim , Fatma M. and Eladl , Mohamed Ahmed and Said , Eman and Ebrahim , Hasnaa Ali and El-Shafey , Mohamed and Asseri , Saad Mohamed and El-Sherbiny , Mohamed and Alsalamah , Reem Hamoud and Elsherbiny , Nehal M. and Hadhod , Shimaa**. Vitamin K2 (Menaquinone-7) Reverses Age-Related Structural and Cognitive Deterioration in Naturally Aging Rats. Antioxidants (20220308) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[47] **Cera , Enrico Di**. Thrombin as an Anticoagulant Proteases in Health and Disease 145-184 (2011) src:dx.doi.org. src:biochem.slu.edu.

[48] **Mann , Kenneth G.**. Thrombin Generation in Hemorrhage Control and Vascular Occlusion Circulation 225-235 (07/12/2011) src:dx.doi.org. src:europepmc.org.

[49] **Hackeng , T M and Tans , G and Koppelman , S J and de Groot , P G and Rosing , J and Bouma , B N**. Protein C activation on endothelial cells by prothrombin activation products generated in situ: meizothrombin is a better protein C activator than alpha-thrombin. The Biochemical journal (1996-Oct-15) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[50] **Grobler , Corlia and Maphumulo , Siphosethu C. and Grobbelaar , L. Mireille and Bredenkamp , Jhade C. and Laubscher , Gert J. and Lourens , Petrus J. and Steenkamp , Janami and Kell , Douglas B. and Pretorius , Etheresia**. Covid-19: The Rollercoaster of Fibrin(Ogen), D-Dimer, Von Willebrand Factor, P-Selectin and Their Interactions with Endothelial Cells, Platelets and Erythrocytes. International Journal of Molecular Sciences (20200721) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[51] **Edvardsen , Magnus S. and Hindberg , Kristian and Hansen , Ellen-Sofie and Morelli , Vânia M. and Ueland , Thor and Aukrust , Paal and Braekkan , Sigrid K. and Evensen , Line H. and Hansen , John-Bjarne**. Plasma levels of von Willebrand factor and future risk of incident venous thromboembolism Blood Advances 224-232 (01/12/2021) src:dx.doi.org. src:ashpublications.org.

[52] **Fan , Mengge and Wang , Xia and Peng , Xun and Feng , Shuo and Zhao , Junyu and Liao , Lin and Zhang , Yong and Hou , Yinglong and Liu , Ju**. Prognostic value of plasma von Willebrand factor levels in major adverse cardiovascular events: a systematic review and meta-analysis BMC Cardiovascular Disorders (2020) src:dx.doi.org. src:bmccardiovascdisord.biomedcentral.com.

[53] **Rayner , Samuel G. and Scholl , Zackary and Mandrycky , Christian J. and Chen , Junmei and LaValley , Karina N. and Leary , Peter J. and Altemeier , William A. and Liles , W. Conrad and Chung , Dominic W. and López , José A. and Fu , Hongxia and Zheng , Ying**. Endothelialderived von Willebrand factor accelerates fibrin clotting within engineered microvessels Journal of Thrombosis and Haemostasis 1627-1637 (04/11/2022) src:dx.doi.org. src:onlinelibrary.wiley.com.

[54] **Michels , Alison and Dwyer , Courtney N. and Mewburn , Jeffrey and Nesbitt , Kate and Kawecki , Charlotte and Lenting , Peter and Swystun , Laura L. and Lillicrap , David**. von Willebrand Factor Is a Critical Mediator of Deep Vein Thrombosis in a Mouse Model of Diet-Induced Obesity Arteriosclerosis, Thrombosis, and Vascular Biology (2020) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[55] **Eastep , Jennifer and Chen , Guoxun**. The relationships of high-fat diet and metabolism of lipophilic vitamins Integrative Food, Nutrition and Metabolism (2015) src:dx.doi.org. src:www.oatext.com.

[56] **Kim , Misung and Na , Woori and Sohn , Cheongmin**. Vitamin K1 (phylloquinone) and K2 (menaquinone-4) supplementation improves bone formation in a high-fat diet-induced obese mice. Journal of clinical biochemistry and nutrition (20130724) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[57] **Su , Xiangni and Zhou , Jian and Wang , Wenchen and Yin , Caocao and Wang , Feng**. VK2 regulates slow-twitch muscle fibers expression and mitochondrial function via SIRT1/SIRT3 signaling Nutrition (2022) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[58] **BRILL , A. and FUCHS , T. A. and SAVCHENKO , A. S. and THOMAS , G. M. and MARTINOD , K. and DE MEYER , S. F. and BHANDARI , A. A. and WAGNER , D. D.**. Neutrophil extracellular traps promote deep vein thrombosis in mice Journal of Thrombosis and Haemostasis 136-144 (2012) src:dx.doi.org. src:onlinelibrary.wiley.com.

[59] **Larsson , Susanna and Traylor , Matthew and Markus , Hugh**. Circulating Vitamin K1 Levels in Relation to Ischemic Stroke and Its Subtypes: A Mendelian Randomization Study Nutrients 1575 (10/25/2018) src:dx.doi.org. src:www.mdpi.com.

[60] **Hariri , Essa and Kassis , Nicholas and Iskandar , Jean-Pierre and Schurgers , Leon J and Saad , Anas and Abdelfattah , Omar and Bansal , Agam and Isogai , Toshiaki and Harb , Serge C and Kapadia , Samir**. Vitamin K2—a neglected player in cardiovascular health: a narrative review Open Heart (2021) src:dx.doi.org. src:openheart.bmj.com. src:openheart.bmj.com.

[61] **Wei , Yaping and Wang , Zhuo and He , Qiangqiang and Siddiqi , Sultan mehmood and Zhou , Ziyi and Liu , Lishun and Song , Yun and Chen , Ping and Li , Jianping and Zhang , Yan and Mao , Guangyun and Wang , Binyan and Tang , Genfu and Qin , Xianhui and Xu , Xiping and Huo , Yong and Guo , Huiyuan and Zhang , Hao**. Inverse Association between Plasma Phylloquinone and Risk of Ischemic Stroke in Chinese Adults with Hypertension and High BMI: A Nested Case-Control Study The Journal of Nutrition (2022-06) src:dx.doi.org. src:doi.org. src:academic.oup.com.

[62] **Thomas , R. H.**. Hypercoagulability Syndromes Archives of Internal Medicine 2433-2439 (11/12/2001) src:dx.doi.org. src:jamanetwork.com.

[63] **Kitchens , Craig S.**. 11 - Purpura and Other Hematovascular Disorders W.B. Saunders (2013) src:dx.doi.org. src:www.sciencedirect.com.

[64] **Pourdeyhimi , Neda and Bullard , Zackery**. Warfarin-Induced Skin Necrosis. Hospital Pharmacy (20141211) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[65] **Marins , Tatiana Aporta and Fátima Gonçalves Galvão , Tatiana de and Korkes , Fernando and Cherino Malerbi , Domingos Augusto and Ganc , Arnaldo José and Korn , Davi and Wagner , Jairo and de Campos Guerra , João Carlos and Borges Filho , Wladimir Mendes and Ferracini , Fábio Teixeira and Korkes , Hélio**. Vitamin D intoxication: case report Einstein (São Paulo) 242-244 (2014) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[66] **Gilaberte , Y. and Aguilera , J. and Carrascosa , J.M. and Figueroa , F.L. and Romaní de Gabriel , J. and Nagore , E.**. Vitamin D: Evidence and Controversies Actas Dermo-Sifiliográficas (English Edition) (2011) src:dx.doi.org. src:www.sciencedirect.com.

[67] **Wacker , Matthias and Holick , Michael F.**. Sunlight and Vitamin D: A global perspective for health. Dermato-endocrinology (20130101) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[68] **Ren , Ruijun and Liu , Jia and Cheng , Guo and Tan , Jing**. Vitamin K2 (Menaquinone-7) supplementation does not affect vitamin K-dependent coagulation factors activity in healthy individuals. Medicine (20210611) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[69] **Wessinger , Chad and Hafer-Macko , Charlene and Ryan , Alice S.**. Vitamin K Intake in Chronic Stroke: Implications for Dietary Recommendations Nutrients 3059 (10/06/2020) src:dx.doi.org. src:www.mdpi.com.

[70] **Coutrot , Maxime and Delrue , Maxime and Joly , Bérangère S and Siguret , Virginie**. Unexpected acute pulmonary embolism in an old COVID-19 patient with warfarin overdose: a case report European Heart Journal - Case Reports (2021-06) src:dx.doi.org. src:doi.org. src:academic.oup.com.

[71] **Simes , Dina C. and Viegas , Carla S. B. and Araújo , Nuna and Marreiros , Catarina**. Vitamin K as a Diet Supplement with Impact in Human Health: Current Evidence in Age-Related Diseases Nutrients 138 (01/03/2020) src:dx.doi.org. src:www.mdpi.com.

[72] **Booth , Sarah L. and Shea , M. Kyla and Barger , Kathryn and Leurgans , Sue E. and James , Bryan D. and Holland , Thomas M. and Agarwal , Puja and Fu , Xueyan and Wang , Jifan and Matuszek , Gregory and Schneider , Julie A.**. Association of vitamin K with cognitive decline and neuropathology in communitydwelling older persons Alzheimer's & Dementia: Translational Research & Clinical Interventions (04/20/2022) src:dx.doi.org. src:alz-journals.onlinelibrary.wiley.com.

[73] **Church , William R. and Bhushan , Frances H. and Mann , Kenneth G. and Bovill , Edwin G.**. Discrimination of Normal and Abnormal Prothrombin and Protein C in Plasma Using a Calcium Ion-Inhibited Monoclonal Antibody to a Common Epitope on Several Vitamin K-Dependent Proteins Blood (1989) src:dx.doi.org. src:www.sciencedirect.com.

[74] **Matsuzaka , T and Tanaka , H and Fukuda , M and Aoki , M and Tsuji , Y and Kondoh , H**. Relationship between vitamin K dependent coagulation factors and anticoagulants (protein C and protein S) in neonatal vitamin K deficiency. Archives of Disease in Childhood (1993-Mar) src:www.ncbi.nlm.nih.gov.

[75] **Bovill , EG and Soll , RF and Lynch , M and Bhushan , F and Landesman , M and Freije , M and Church , W and McAuliffe , T and Davidson , K and Sadowski , J**. Vitamin K1 metabolism and the production of des-carboxy prothrombin and protein C in the term and premature neonate Blood 77-83 (01/01/1993) src:dx.doi.org. src:www.sciencedirect.com.

[76] **Balsa , Eduardo and Perry , Elizabeth A. and Bennett , Christopher F. and Jedrychowski , Mark and**

Gygi , Steven P. and Doench , John G. and Puigserver , Pere. Defective NADPH production in mitochondrial disease complex I causes inflammation and cell death Nature Communications (06/01/2020) src:dx.doi.org. src:www.nature.com.

[77] **Yamamoto , Koji and Loskutoff , David J.**. Extrahepatic Expression and Regulation of Protein C in the Mouse. The American Journal of Pathology (1998-Aug) src:www.ncbi.nlm.nih.gov.

[78] **Cowan , Aimee Q. and Cho , Daniel J. and Rosenson , Robert S.**. Importance of Blood Rheology in the Pathophysiology of Atherothrombosis Cardiovascular Drugs and Therapy (2012-Aug-01) src:dx.doi.org. src:doi.org. src:link.springer.com.

[79] **Uzunget , Sezen Baglan and Sahin , Kader Eliz**. Another possible determinant for ischemic stroke with nonvalvular atrial fibrillation other than conventional oral anticoagulant treatment: The relationship between whole blood viscosity and strokebigwhitestar Journal of Stroke and Cerebrovascular Diseases (2022) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[80] **Lowe , Gordon O**. Measurement of thrombosis and its prevention. British Journal of Clinical Pharmacology (2002-Jul) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[81] **Cakmak , Gulfidan and Alkan , Fatma Ates and Korkmaz , Kazim and Saglam , Zuhal Aydan and Karis , Denizhan and Yenigun , Mustafa and Ercan , Meltem**. Blood viscosity as a forgotten factor and its effect on pulmonary flow. Translational Respiratory Medicine (20130222) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[82] **Booth , Stephanie and Chohan , Saima and Curran , James C. and Karrison , Theodore and Schmitz , Amanda and Utset , Tammy O.**. Whole blood viscosity and arterial thrombotic events in patients with systemic lupus erythematosus Arthritis & Rheumatism 845-850 (06/15/2007) src:dx.doi.org. src:onlinelibrary.wiley.com.

[83] **Chien , Shu**. Blood rheology in myocardial infarction and hypertension Biorheology 633-653 (12/01/1986) src:dx.doi.org. src:content.iospress.com.

[84] **Dintenfass , Leopold**. The Clinical Impact of the Newer Research in Blood Rheology: An Overview Angiology 217-229 (1981) src:dx.doi.org. src:journals.sagepub.com.

[85] **Choi , Daein and Waksman , Ori and Shaik , Aleesha and Mar , Phyu and Chen , Qinzhong and Cho , Daniel J. and Kim , HyoungSup and Smith , Robin L. and Goonewardena , Sascha N. and Rosenson , Robert S.**. Association of Blood Viscosity With Mortality Among Patients Hospitalized With COVID-19. Journal of the American College of Cardiology (20220718) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[86] **Domingues , Marco M. and Carvalho , Filomena A. and Santos , Nuno C.**. Nanomechanics of Blood Clot and Thrombus Formation Annual Review of Biophysics 201-221 (05/09/2022) src:dx.doi.org. src:www.annualreviews.org.

[87] **Beris, Antony N. and Horner, Jeffrey S. and Jariwala, Soham and Armstrong, Matthew J. and Wagner, Norman J.**. Recent advances in blood rheology: a review Soft Matter (2021-dec) src:dx.doi.org. src:arxiv.org.

[88] **Ebrahimi , Saman and Bagchi , Prosenjit**. A computational study of red blood cell deformability effect on hemodynamic alteration in capillary vessel networks Scientific Reports (03/11/2022) src:dx.doi.org. src:www.nature.com.

[89] **Lee , Chan-Hyuk and Jung , Keun-Hwa and Cho , Daniel J. and Jeong , Seul-Ki**. Effect of warfarin versus aspirin on blood viscosity in cardioembolic stroke with atrial fibrillation: a prospective clinical trial BMC Neurology (2019-May-01) src:dx.doi.org. src:doi.org. src:link.springer.com.

[90] **Lip , Gregory Y.H. and Lip , Peck Lin and Zarifis , John and Watson , Robert D.S. and Bareford , David and Lowe , Gordon D.O. and Beevers , D. Gareth**. Fibrin ¡span class=smallcaps smallerCapital¿d¡/span¿-Dimer and β-Thromboglobulin as Markers of Thrombogenesis and Platelet Activation in Atrial Fibrillation Circulation (1996) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[91] **Grotta , J and Ostrow , P and Fraifeld , E and Hartman , D and Gary , H**. Fibrinogen, blood viscosity, and cerebral ischemia. Stroke (1985) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[92] **Koenig , W and Ernst , E**. The effects of calcium channel blockers on blood fluidity. Journal of cardiovascular pharmacology (1990) src:pubmed.ncbi.nlm.nih.gov.

[93] **Vizza , Patrizia and Tradigo , Giuseppe and Parrilla , Marianna and Guzzi , Pietro Hiram and Gnasso , Agostino and Veltri , Pierangelo**. On Blood Viscosity and Its Correlation with Biological Parameters Computational Science - ICCS 2018 347-353 (2018) src:dx.doi.org. src:www.iccs-meeting.org.

[94] **AMIN , T.M. and SIRS , J.A. and ALLEN , B.V. and COLLES , C.M.**. Effects of warfarin on blood rheology in navicular disease Research in Veterinary Science (1986) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[95] **Ludwig , Ralf**. Therapeutic Use of Heparin beyond Anticoagulation Current Drug Discovery Technologies 281-289 (12/01/2009) src:dx.doi.org. src:www.ingentaconnect.com.

[96] **Mike J Marchywka**. Live and Let Dye: A Confounding Factor in Vitamin D Data, Covid-19 Treatments and Everything Else ? (August 1, 2022) src:dx.doi.org. src:www.researchgate.net.

[97] **Mike J Marchywka**. Clinical and microbiological improvement in dog after metal and benzoate containing supplement mix (November 4, 2022) src:dx.doi.org. src:zenodo.org.

[98] **Jones , Bethan M. and Iglesias-Rodriguez , M. Debora and Skipp , Paul J. and Edwards , Richard J. and Greaves , Mervyn J. and Young , Jeremy R. and Elderfield , Henry and O'Connor , C. David**. Responses of the Emiliania huxleyi Proteome to Ocean Acidification. PLoS ONE (20130412) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[99] **Zoch, ML and Clemens, TL and Riddle, RC**. New Insights into the Biology of Osteocalcin. Bone (2016) src:www.ncbi.nlm.nih.gov.

[100] **Berger , Julian Meyer and Karsenty , Gerard**. Osteocalcin and the physiology of danger FEBS Letters 665-680

(2022) src:dx.doi.org. src:febs.onlinelibrary.wiley.com.

[101] **P;Asdamongkol K; , Varavithya W;Phuapradit**. Control of intractable gastric hemorrhage by monosodium glutamate The Southeast Asian journal of tropical medicine and public health (1994) src:pubmed.ncbi.nlm.nih.gov.

[102] **D'Arcangelo , Daniela and Gaetano , Carlo and Capogrossi , Maurizio C.**. Acidification Prevents Endothelial Cell Apoptosis by Axl Activation Circulation Research (2002) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[103] **Gancheva , Silvia M. and Zhelyazkova-Savova , Maria D.**. Vitamin K2 Improves Anxiety and Depression but not Cognition in Rats with Metabolic Syndrome: a Role of Blood Glucose? Folia Medica 264-272 (12/01/2016) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[104] **Laugero , Kevin D. and Falcon , Luis M. and Tucker , Katherine L.**. Relationship between perceived stress and dietary and activity patterns in older adults participating in the Boston Puerto Rican Health Study,. Appetite (20101109) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[105] **Gissel , M. and BrummelZiedins , K. E. and Butenas , S. and Pusateri , A. E. and Mann , K. G. and Orfeo , T.**. Effects of an acidic environment on coagulation dynamics Journal of Thrombosis and Haemostasis 2001-2010 (2016) src:dx.doi.org. src:onlinelibrary.wiley.com.

[106] **Mitrophanov , Alexander Y. and Vandyck , Kofi and Tanaka , Kenichi A.**. Thrombin Generation in Trauma Patients: How Do we Navigate Through Scylla and Charybdis? Current Anesthesiology Reports (2022-Jun-01) src:dx.doi.org. src:doi.org. src:link.springer.com.

[107] **de Souza , Júlia Ruete and Yokoyama , Ana Paula and Magnus , Mariana Munari and Boin , Ilka and de Ataide , Elaine Cristina and Munhoz , Derli Conceição and Pereira , Fabrício Bíscaro and Luzo , Angela and Orsi , Fernanda Andrade**. Association of acidosis with coagulopathy and transfusion requirements in liver transplantation Journal of Thrombosis and Thrombolysis (2022-May-01) src:dx.doi.org. src:doi.org. src:link.springer.com.

[108] **McCann , Joyce C and Ames , Bruce N**. Vitamin K, an example of triage theory: is micronutrient inadequacy linked to diseases of aging? The American Journal of Clinical Nutrition (2009-08) src:dx.doi.org. src:doi.org. src:academic.oup.com.

[109] **Simes , Dina C. and Viegas , Carla S. B. and Araújo , Nuna and Marreiros , Catarina**. Vitamin K as a Powerful Micronutrient in Aging and Age-Related Diseases: Pros and Cons from Clinical Studies International Journal of Molecular Sciences 4150 (2019) src:dx.doi.org. src:www.mdpi.com.

[110] **M.J. Marchywka**. On the age distribution of SARS-Cov-2 Patients (July 1, 2020) src:www.linkedin.com.

[111] **Fusaro , Maria and Cianciolo , Giuseppe and Brandi , Maria Luisa and Ferrari , Serge and Nickolas , Thomas L. and Tripepi , Giovanni and Plebani , Mario and Zaninotto , Martina and Iervasi , Giorgio and La Manna , Gaetano and Gallieni , Maurizio and Vettor , Roberto and Aghi , Andrea and Gasperoni , Lorenzo and Giannini , Sandro and Sella , Stefania and M. Cheung , Angela**. Vitamin K and Osteoporosis. Nutrients (20201125) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[112] **Zhang , Yan and Zhao , Liting and Wang , Naining and Li , Jing and He , Fang and Li , Xu and Wu , Shufang**. Unexpected Role of Matrix Gla Protein in Osteoclasts: Inhibiting Osteoclast Differentiation and Bone Resorption Molecular and Cellular Biology (06/15/2019) src:dx.doi.org. src:journals.asm.org.

[113] **Laizé , Vincent and Martel , Paulo and Viegas , Carla S.B. and Price , Paul A. and Cancela , M. Leonor**. Evolution of Matrix and Bone upgamma-Carboxyglutamic Acid Proteins in Vertebrates Journal of Biological Chemistry 26659-26668 (2005) src:dx.doi.org. src:www.jbc.org.

[114] **Alonso , N. and Meinitzer , A. and Fritz-Petrin , E. and Enko , D. and Herrmann , M.**. Role of Vitamin K in Bone and Muscle Metabolism Calcified Tissue International (2022-Feb-12) src:dx.doi.org. src:doi.org. src:link.springer.com.

[115] **Cheung Angela M AND Tile Lianne AND Lee Yuna AND Tomlinson George AND Hawker Gillian AND Scher Judy AND Hu Hanxian AND Vieth Reinhold AND Thompson Lilian AND Jamal Sophie AND Josse , Robert**. Vitamin K Supplementation in Postmenopausal Women with Osteopenia (ECKO Trial): A Randomized Controlled Trial PLOS Medicine (2008-10) src:dx.doi.org. src:doi.org. src:journals.plos.org.

[116] **Salma and Ahmad , Syed Sufian and Karim , Shahid and Ibrahim , Ibrahim M. and Alkreathy , Huda M. and Alsieni , Mohammed and Khan , Mohammad Ahmed**. Effect of Vitamin K on Bone Mineral Density and Fracture Risk in Adults: Systematic Review and Meta-Analysis Biomedicines 1048 (2022) src:dx.doi.org. src:www.mdpi.com.

[117] **Shea , M. Kyla and ODonnell , Christopher J. and Vermeer , Cees and Magdeleyns , Elke P. and Crosier , Michael D. and Gundberg , Caren M. and Ordovas , Jos M. and Kritchevsky , Stephen B. and Booth , Sarah L.**. Circulating Uncarboxylated Matrix Gla Protein Is Associated with Vitamin K Nutritional Status, but Not Coronary Artery Calcium, in Older Adults1234. The Journal of Nutrition (20110531) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[118] **Murshed , Monzur and Schinke , Thorsten and McKee , Marc D. and Karsenty , Gerard**. Extracellular matrix mineralization is regulated locally; different roles of two gla-containing proteins Journal of Cell Biology 625-630 (06/07/2004) src:dx.doi.org. src:rupress.org.

[119] **Anzaki , Kazuhiro and Kanda , Daisuke and Ikeda , Yoshiyuki and Takumi , Takuro and Tokushige , Akihiro and Ohmure , Kenta and Sonoda , Takeshi and Arikawa , Ryo and Ohishi , Mitsuru**. Impact of Malnutrition on Prognosis and Coronary Artery Calcification in Patients with Stable Coronary Artery Disease Current Problems in Cardiology (2022) src:dx.doi.org. src:www.sciencedirect.com.

[120] **Yang , wei and Yu , Zaiqiang and Chiyoya , Mari and Liu , Xu and Daitoku , Kazuyuki and Motomura , Shigeru and Imaizumi , Tadaatsu and Fukuda , Ikuo and Furukawa , Ken-Ichi and Tsuji , Motonori and Seya , Kazuhiko**. Menaquinone-4 accelerates calcification of human aortic valve interstitial cells in high-phosphate medium through PXR Journal of Pharmacology and Experimental Therapeutics (2019) src:dx.doi.org. src:jpet.aspetjournals.org.

[121] **Han , Xianlin**. Potential mechanisms contributing to sulfatide depletion at the earliest clinically recognizable stage of Alzheimer's disease: a tale of shotgun lipidomics Journal of Neurochemistry 171-179 (-) src:dx.doi.org. src:onlinelibrary.wiley.com.

[122] **Popescu , Daniela C. and Huang , He and Singhal , Naveen K. and Shriver , Leah and McDonough , Jennifer and Clements , Robert J. and Freeman , Ernest J.**. Vitamin K enhances the production of brain sulfatides during remyelination. PLoS ONE (20180827) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[123] **Sundaram , K S and Fan , J H and Engelke , J A and Foley , A L and Suttie , J W and Lev , M**. Vitamin K status influences brain sulfatide metabolism in young mice and rats. The Journal of nutrition (1996-Nov) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[124] **Allison , A C**. The possible role of vitamin K deficiency in the pathogenesis of Alzheimer's disease and in augmenting brain damage associated with cardiovascular disease. Medical hypotheses (2001-Aug) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[125] **Yan , Liya and Zhou , Bo and Nigdikar , Shailja and Wang , Xiaohong and Bennett , Janet and Prentice , Ann**. Effect of apolipoprotein E genotype on vitamin K status in healthy older adults from China and the UK. The British journal of nutrition (2005-Dec) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[126] **Maddock , J and Cavadino , A and Power , C and Hyppönen , E**. 25-Hydroxyvitamin D, APOE Ux025b[bad char vv=603]4 genotype and cognitive function: findings from the 1958 British birth cohort European Journal of Clinical Nutrition (10/08/2014) src:dx.doi.org. src:www.nature.com.

[127] **Mike J Marchywka**. Vitamin D: Towards A Conflict Resolving Hypothesis (July 28, 2022) src:dx.doi.org. src:www.researchgate.net.

[128] **Happonen , Kaisa E. and Tran , Sinh and Mrgelin , Matthias and Prince , Raja and Calzavarini , Sara and Angelillo-Scherrer , Anne and Dahlbck , Bjrn**. The Gas6-Axl Protein Interaction Mediates Endothelial Uptake of Platelet Microparticles*. The Journal of Biological Chemistry (20160322) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[129] **Tjwa , Marc and Bellido-Martin , Lola and Lin , Yuan and Lutgens , Esther and Plaisance , Stéphane and Bono , Françoise and Delesque-Touchard , Nathalie and Hervé , Caroline and Moura , Rute and Billiau , An D. and Aparicio , Cristina and Levi , Marcel and Daemen , Mat and Dewerchin , Mieke and Lupu , Florea and Arnout , Jef and Herbert , Jean-Marc and Waer , Mark and de Frutos , Pablo García and Dahlbäck , Björn and Carmeliet , Peter and Hoylaerts , Marc F. and Moons , Lieve**. Gas6 promotes inflammation by enhancing interactions between endothelial cells, platelets, and leukocytes Blood 4096-4105 (04/15/2008) src:dx.doi.org. src:ashpublications.org.

[130] **Laurance , S. and Aghourian , M. N. and Lila , Z. Jiva and Lemarié , C. A. and Blostein , M. D.**. Gas6-induced tissue factor expression in endothelial cells is mediated through caveolin-1-enriched microdomains Journal of Thrombosis and Haemostasis 395-408 (2014) src:dx.doi.org. src:onlinelibrary.wiley.com.

[131] **Reinhardt , Christoph**. GAS6 Arteriosclerosis, Thrombosis, and Vascular Biology (2017) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[132] **Tang , Junjia and Jin , Yichao and Jia , Feng and Lv , Tao and Manaenko , Anatol and Zhang , Lin-Feng and Zhang , Zeyu and Qi , Xin and Xue , Yajun and Zhao , Bin and Zhang , Xiaohua and Zhang , John H. and Lu , Jianfei and Hu , Qin**. Gas6 Promotes Microglia Efferocytosis and Suppresses Inflammation Through Activating Axl/Rac1 Signaling in Subarachnoid Hemorrhage Mice Translational Stroke Research (2022-Nov-03) src:dx.doi.org. src:doi.org. src:link.springer.com.

[133] **Novoyatleva , Tatyana and Rai , Nabham and Kojonazarov , Baktybek and Veeroju , Swathi and Ben-Batalla , Isabel and Caruso , Paola and Shihan , Mazen and Presser , Nadine and Götz , Elsa and Lepper , Carina and Herpel , Sebastian and Manaud , Grégoire and Perros , Frédéric and Gall , Henning and Ghofrani , Hossein Ardeschir and Weissmann , Norbert and Grimminger , Friedrich and Wharton , John and Wilkins , Martin and Upton , Paul D. and Loges , Sonja and Morrell , Nicholas W. and Seeger , Werner and Schermuly , Ralph T.**. Deficiency of Axl aggravates pulmonary arterial hypertension via BMPR2 Communications Biology (08/24/2021) src:dx.doi.org. src:www.nature.com.

[134] **Upton , Paul and Novoyatleva , Tatyana and Rai , Nabham and Kojonazarov , Baktybek and Veeroju , Swathi and Ben-Batalla , Isabel and Caruso , Paola and Shihan , Mazen and Presser , Nadine and Gotz , Elsa and Lepper , Carina and Herpel , Sebastian and Manaud , Gregoire and Perros , Frederic and Gall , Henning and Ghofrani , Hossein Ardeschir and Weissman , Norbert and Grimminger , Friedrich and Wharton , John and Wilkins , Martin and Loges , Sonja and Morrell , Nicholas and Seeger , Werner and Schermuly , Ralph**. Axl is a Novel Modulator of Bone Morphogenetic Protein Receptor 2 in pulmonary arterial hypertension Apollo - University of Cambridge Repository (2021-10-04 and 2021-10-04) src:dx.doi.org. src:www.repository.cam.ac.uk.

[135] **Ni , Jingjing and Lin , Miaotong and Jin , Yangjie and Li , Jiajia and Guo , Yayong and Zhou , Jindong and Hong , Guangliang and Zhao , Guangju and Lu , Zhongqiu**. Gas6 Attenuates Sepsis-Induced Tight Junction Injury and Vascular Endothelial Hyperpermeability via the Axl/NF-upkappaB Signaling Pathway Frontiers in Pharmacology (2019) src:dx.doi.org. src:www.frontiersin.org. src:www.frontiersin.org.

[136] **Fan , Huaying and Han , Junxia and Chen , Ling and Feng , Bin and Sun , Xin and Shi , Bimin**. Association between plasma growth arrest-specific protein 6 and carotid atherosclerosis in type 2 diabetes mellitus Nutrition, Metabolism and Cardiovascular Diseases 1917-1923 (2022) src:dx.doi.org. src:pdf.sciencedirectassets.com.

[137] **HASANBASIC , I. and RAJOTTE , I. and BLOSTEIN , M.**. The role of gamma-carboxylation in the anti-apoptotic function of gas6 Journal of Thrombosis and Haemostasis 2790-2797 (2005) src:dx.doi.org. src:onlinelibrary.wiley.com.

[138] **Melaragno , Matthew G. and Cavet , Megan E. and Yan , Chen and Tai , Lung-Kuo and Jin , Zheng-Gen and Haendeler , Judith and Berk , Bradford C.**. Gas6 inhibits apoptosis in vascular smooth muscle: role of Axl kinase and Akt Journal of Molecular and Cellular Cardiology (2004) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[139] **Xie , Yujia and Ma , Jixuan and Xie , Li and Li , Wei and Yang , Meng and Gu , Pei and Zhang , Yingdie and Fan , Lieyang and Wang , Dongming and Chen , Weihong**. Inhibition of Gas6 promotes crystalline silicainduced inflammatory response of macrophages via blocking autophagy flux Environmental Toxicology 1925-1933 (2022) src:dx.doi.org. src:onlinelibrary.wiley.com.

[140] **Schwarb , Heike and Tsakiris , Dimitrios A.**. New Direct Oral Anticoagulants (DOAC) and Their Use Today. Dentistry Journal (20160311) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[141] **Sagris , Dimitrios and Ntaios , George**. Anticoagulation for stroke prevention after embolic stroke of undetermined source of presumably cardiac source: The sail to Ithaca European Journal of Internal Medicine 42-43 (-) src:dx.doi.org. src:www.ejinme.com.

[142] **Perera , Kanjana S. and Ng , Kelvin K. H. and Nayar , Sumiti and Catanese , Luciana and Dyal , Leanne and Sharma , Mukul and Connolly , Stuart J. and Yusuf , Salim and Bosch , Jackie and Eikelboom , John W. and Hart , Robert G.**. Association Between Low-Dose Rivaroxaban With or Without Aspirin and Ischemic Stroke Subtypes JAMA Neurology 43 (01/01/2020) src:dx.doi.org. src:jamanetwork.com.

[143] **Hackam , Daniel G. and Spence , J. David**. Antiplatelet Therapy in Ischemic Stroke and Transient Ischemic Attack Stroke (2019) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[144] **Tran , Vi L.T. and Hortle , Elinor and Britton , Warwick J. and Oehlers , Stefan H.**. Common anti-haemostatic medications increase the severity of systemic infection by uropathogenic Escherichia coli Microbiological Research (2022) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[145] **Schurgers , Evelien and Moorlag , Martijn and Hemker , Coenraad and Lindhout , Theo and Kelchtermans , Hilde and de Laat , Bas**. Thrombin Generation in Zebrafish Blood. PLoS ONE (20160212) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[146] **Bast , Aalt and Drent , Marjolein**. The role of vitamin K in the etiology of diffuse alveolar hemorrhage. Sarcoidosis, Vasculitis, and Diffuse Lung Diseases (20190501) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[147] **Vitale , Carolyn and Ma , Tianhui Maria and Sim , Janice and Altheim , Christopher and Martinez-Nieves , Erika and Kadiyala , Usha and Solomon , Michael J. and VanEpps , J. Scott**. Staphylococcus epidermidis Has Growth Phase Dependent Affinity for Fibrinogen and Resulting Fibrin Clot Elasticity Frontiers in Microbiology (2021) src:dx.doi.org. src:www.frontiersin.org. src:www.frontiersin.org.

[148] **Esmon , C T**. The protein C anticoagulant pathway. Arteriosclerosis and Thrombosis: A Journal of Vascular Biology (1992) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[149] **Chen , Ashley and Stecker , Eric and Warden , Bruce A.**. Direct Oral Anticoagulant Use: A Practical Guide to Common Clinical Challenges Journal of the American Heart Association (2020) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[150] **Johnston , Colin I. and Radziszewska , Barbara and Grimm , Richard and Murray , Anne M. and McNeil , John J. and Nelson , Mark R. and Woods , Robyn L. and Lockery , Jessica E. and Wolfe , Rory and Reid , Christopher M. and Kirpach , Brenda and Shah , Raj C. and Ives , Diane G. and Storey , Elsdon and Ryan , Joanne and Tonkin , Andrew M. and Newman , Anne B. and Williamson , Jeff D. and Margolis , Karen L. and Ernst , Michael E. and Abhayaratna , Walter P. and Stocks , Nigel and Fitzgerald , Sharyn M. and Orchard , Suzanne G. and Trevaks , Ruth E. and Beilin , Lawrence J. and Donnan , Geoffrey A. and Gibbs , Peter**. Effect of Aspirin on All-Cause Mortality in the Healthy Elderly New England Journal of Medicine 1519-1528 (10/18/2018) src:dx.doi.org. src:www.nejm.org.

[151] **Eisen , Damon P and Leder , Karin and Woods , Robyn L and Lockery , Jessica E and McGuinness , Sarah L and Wolfe , Rory and Pilcher , David and Moore , Elizabeth M and Shastry , Adithya and Nelson , Mark R and Reid , Christopher M and McNeil , John J and McBryde , Emma S**. Effect of aspirin on deaths associated with sepsis in healthy older people (ANTISEPSIS): a randomised, double-blind, placebo-controlled primary prevention trial. The Lancet. Respiratory medicine (20200917) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[152] **Hsu Joann AND Donnelly John P. AND Chaudhary Ninad S. AND Moore Justin X. AND Safford Monika M. AND Kim Junghyun AND Wang , Henry E.**. Aspirin use and long-term rates of sepsis: A population-based cohort study PLOS ONE (2018-04) src:dx.doi.org. src:doi.org. src:journals.plos.org.

[153] **Ong Lopez , Albert Macaire C. and Tan , Charles Jeffrey L. and Yabon , Antonio S. and Masbang , Armin N.**. Symptomatic treatment (using NSAIDS) versus antibiotics in uncomplicated lower urinary tract infection: a meta-analysis and systematic review of randomized controlled trials BMC Infectious Diseases (2021) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[154] **Heithoff , Douglas M. and Pimienta , Genaro and Mahan , Scott P. and Yang , Won Ho and Le , Dzung T. and House , John K. and Marth , Jamey D. and Smith , Jeffrey W. and Mahan , Michael J.**. Coagulation

factor protein abundance in the pre-septic state predicts coagulopathic activities that arise during late-stage murine sepsis eBioMedicine 103965 (2022) src:dx.doi.org. src:doi.org.

[155] **Legras , Annick and Giraudeau , Bruno and Jonville-Bera , Annie-Pierre and Camus , Christophe and François , Bruno and Runge , Isabelle and Kouatchet , Achille and Veinstein , Anne and Tayoro , Jérome and Villers , Daniel and Autret-Leca , Elisabeth**. A multicentre case-control study of nonsteroidal anti-inflammatory drugs as a risk factor for severe sepsis and septic shock Critical Care R43 (2009) src:dx.doi.org. src:ccforum.biomedcentral.com.

[156] **Yue , Y and Krenz , M and Cohen , M V and Downey , J M and Critz , S D**. Menadione mimics the infarct-limiting effect of preconditioning in isolated rat hearts. American journal of physiology. Heart and circulatory physiology (2001-Aug) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[157] **Moghadam , Bahram Farhadi and Fereidoni , Masoud**. Neuroprotective effect of menaquinone-4 (MK-4) on transient global cerebral ischemia/reperfusion injury in rat PLOS ONE e0229769 (03/09/2020) src:dx.doi.org. src:journals.plos.org.

[158] **Yang , R-Y and Pan , J-Y and Chen , Y and Li , Y and Wu , J and Wang , X-D**. Menaquinone-7 protects astrocytes by regulating mitochondrial function and inflammatory response under hypoxic conditions. European review for medical and pharmacological sciences (2020-Oct) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[159] **Mishima , Eikan and Ito , Junya and Wu , Zijun and Nakamura , Toshitaka and Wahida , Adam and Doll , Sebastian and Tonnus , Wulf and Nepachalovich , Palina and Eggenhofer , Elke and Aldrovandi , Maceler and Henkelmann , Bernhard and Yamada , Ken-ichi and Wanninger , Jonas and Zilka , Omkar and Sato , Emiko and Feederle , Regina and Hass , Daniela and Maida , Adriano and Mourão , André Dias and Linkermann , Andreas and Geissler , Edward K. and Nakagawa , Kiyotaka and Abe , Takaaki and Fedorova , Maria and Proneth , Bettina and Pratt , Derek A. and Conrad , Marcus**. A non-canonical vitamin K cycle is a potent ferroptosis suppressor Nature (2022) src:dx.doi.org. src:www.nature.com.

[160] **Recarte-Pelz , Pedro and Tàssies , Dolors and Espinosa , Gerard and Hurtado , Begoña and Sala , Núria and Cervera , Ricard and Reverter , Joan and Frutos , Pablo de**. Vitamin K-dependent proteins GAS6 and Protein S and TAM receptors in patients of systemic lupus erythematosus: correlation with common genetic variants and disease activity Arthritis Research & Therapy R41 (2013) src:dx.doi.org. src:arthritis-research.biomedcentral.com.

[161] **Rishavy , Mark A. and Hallgren , Kevin W. and Wilson , Lee and Singh , Savita and Runge , Kurt W. and Berkner , Kathleen L.**. Warfarin alters vitamin K metabolism: a surprising mechanism of VKORC1 uncoupling necessitates an additional reductase. Blood (2018-Jun-21) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[162] **Ronden , J.E and Groenen-van Dooren , M.M.C.L and Hornstra , G and Vermeer , C**. Modulation of arterial thrombosis tendency in rats by vitamin K and its side chains Atherosclerosis (1997) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[163] **Mehta , Dilip and Souza , Anselm de and Jadhav , Shashank S.**. Menaquinone-7: Wide Ranging Physiological Relevance in Muscle and Nerve Health Biochemistry (03/23/2022) src:dx.doi.org. src:www.intechopen.com.

[164] **Vos , Melissa and Esposito , Giovanni and Edirisinghe , Janaka N. and Vilain , Sven and Haddad , Dominik M. and Slabbaert , Jan R. and Meensel , Stefanie Van and Schaap , Onno and Strooper , Bart De and Meganathan , R. and Morais , Vanessa A. and Verstreken , Patrik**. Vitamin K $_2$ Is a Mitochondrial Electron Carrier That Rescues Pink1 Deficiency Science 1306-1310 (06/08/2012) src:dx.doi.org. src:www.science.org.

[165] **Cerqua , Cristina and Casarin , Alberto and Pierrel , Fabien and Vazquez Fonseca , Luis and Viola , Giampiero and Salviati , Leonardo and Trevisson , Eva**. Vitamin K2 cannot substitute Coenzyme Q10 as electron carrier in the mitochondrial respiratory chain of mammalian cells Scientific Reports (04/25/2019) src:dx.doi.org. src:www.nature.com.

[166] **Brouwer , Bart De and Piscaer , Ianthe and Von Der Thusen , Jan H. and Grutters , Jan C and Schutgens , Roger EG. and Wouters , Emiel FM. and Janssen , Rob**. Should vitamin K be supplemented instead of antagonised in patients with idiopathic pulmonary fibrosis? Expert Review of Respiratory Medicine 169-175 (2018-01-22-2018-03-04) src:dx.doi.org. src:www.tandfonline.com.

[167] **Xiao , Huiyu and Chen , Jiepeng and Duan , Lili and Li , Shuzhuang**. Role of emerging vitamin KUx2011[bad char vv=8209]dependent proteins: Growth arrestUx2011[bad char vv=8209]specific protein 6, GlaUx2011[bad char vv=8209]rich protein and periostin (Review) International Journal of Molecular Medicine (12/29/2020) src:dx.doi.org. src:www.spandidos-publications.com.

[168] **Li , Chang and Zhang , Jing and Hu , Wan and Li , Song**. Atrial fibrosis underlying atrial fibrillation (Review) International Journal of Molecular Medicine (12/31/2020) src:dx.doi.org. src:www.spandidos-publications.com.

[169] **Ayesh , Hazem and Beran , Azizullah and Mhanna , Mohammed and Hejeebu , Srini**. Secondary Immune Thrombocytopenia Associated With Asymptomatic COVID-19 Successfully Managed With Intravenous Immunoglobulin and Glucocorticoids. Cureus (-) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[170] **Simmons , Jeff and Pittet , Jean-Francois**. The Coagulopathy of Acute Sepsis. Current opinion in anaesthesiology (2015-Apr) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[171] **Pontarollo , Giulia and Melzow , Florentina and Reinhardt , Christoph**. Comment on : Endothelial Protein C Receptor (EPCR), Protease Activated Receptor-1 (PAR-1) and Their Interplay in Cancer Growth and Metastatic Dissemination , Cancers 2019, 11, 51 Cancers 374 (2019) src:dx.doi.org. src:www.mdpi.com.

[172] **Wang , Kang and Wu , Qianxue and Li , Zhuyue and Reger , Michael K. and Xiong , Yongfu and Zhong , Guochao and Li , Qing and Zhang , Xiang and Li , Hongyuan and Foukakis , Theodoros and**

Xiang , Tingxiu and Zhang , Jianjun and Ren , Guosheng. Vitamin K intake and breast cancer incidence and death: results from a prospective cohort study Clinical Nutrition (2021) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[173] **Vera , Marina C. and Lorenzetti , Florencia and Lucci , Alvaro and Comanzo , Carla G. and Ceballos , María P. and Pisani , Gerardo B. and Alvarez , María de L. and Quiroga , Ariel D. and Carrillo , María C.**. Vitamin K2 supplementation blocks the beneficial effects of IFN-upalpha-2b administered on the early stages of liver cancer development in rats Nutrition (2019) src:dx.doi.org. src:www.sciencedirect.com. src:www.sciencedirect.com.

[174] **Lu , Xin and Ma , Panpan and Kong , Lingyu and Wang , Xi and Wang , Yaqi and Jiang , Lingling**. Vitamin K2 Inhibits Hepatocellular Carcinoma Cell Proliferation by Binding to 17upbeta-Hydroxysteroid Dehydrogenase 4 Frontiers in Oncology (2021) src:dx.doi.org. src:www.frontiersin.org. src:www.frontiersin.org.

[175] **Jinghe , Xia and Mizuta , Toshihiko and Ozaki , Iwata**. Vitamin K and hepatocellular carcinoma: The basic and clinic. World Journal of Clinical Cases : WJCC (20150916) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[176] **Haruna , Yoshimichi and Hasegawa , Noriko and Imanaka , Kazuho and Inoue , Atsuo and Kudo , Masatoshi**. Impact of vitamin K dosing during sorafenib treatment for hepatocellular carcinoma: Effect on ischemic tumor cell damage caused by sorafenib. Journal of Clinical Oncology e15585-e15585 (05/20/2016) src:dx.doi.org. src:ascopubs.org.

[177] **Malaguarnera , Giulia and Catania , Vito Emanuele and Latteri , Saverio and Borzì , Antonio Maria and Bertino , Gaetano and Madeddu , Roberto and Drago , Filippo and Malaguarnera , Michele**. Folate levels in hepatocellular carcinoma patients with portal vein thrombosis BMC Gastroenterology (2020) src:dx.doi.org. src:bmcgastroenterol.biomedcentral.com.

[178] **Amar , Arun Paul and Sagare , Abhay P. and Zhao , Zhen and Wang , Yaoming and Nelson , Amy R. and Griffin , John H. and Zlokovic , Berislav V.**. Can adjunctive therapies augment the efficacy of endovascular thrombolysis? A potential role for activated protein C. Neuropharmacology (20170918) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[179] **Bellinge , Jamie W. and Dalgaard , Frederik and Murray , Kevin and Connolly , Emma and Blekkenhorst , Lauren C. and Bondonno , Catherine P. and Lewis , Joshua R. and Sim , Marc and Croft , Kevin D. and Gislason , Gunnar and TorpPedersen , Christian and Tjonneland , Anne and Overvad , Kim and Hodgson , Jonathan M. and Schultz , Carl and Bondonno , Nicola P.**. Vitamin K Intake and Atherosclerotic Cardiovascular Disease in the Danish Diet Cancer and Health Study Journal of the American Heart Association (2021) src:dx.doi.org. src:www.ahajournals.org. src:www.ahajournals.org.

[180] **Conway , Edward M. and Mackman , Nigel and Warren , Ronald Q. and Wolberg , Alisa S. and Mosnier , Laurent O. and Campbell , Robert A. and Gralinski , Lisa E. and Rondina , Matthew T. and van de Veerdonk , Frank L. and Hoffmeister , Karin M. and Griffin , John H. and Nugent , Diane and Moon , Kyung and Morrissey , James H.**. Understanding COVID-19-associated coagulopathy Nature Reviews Immunology (2022) src:dx.doi.org. src:www.nature.com.

[181] **M Dofferhoff , Anton S and Piscaer , Ianthe and Schurgers , Leon J and J Visser , Margot P and W van den Ouweland , Jody M and de Jong , Pim A and Gosens , Reinoud and Hackeng , Tilman M and Daal , Henny van and Lux , Petra and Maassen , Cecile and A Karssemeijer , Esther G and Vermeer , Cees and M Wouters , Emiel F and M Kistemaker , Loes E and Walk , Jona and Janssen , Rob**. Reduced Vitamin K Status as a Potentially Modifiable Risk Factor of Severe Coronavirus Disease 2019 Clinical Infectious Diseases e4039-e4046 (2020-08-27-2021-12-06) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[182] **Janssen , Rob and Visser , Margot P. J. and Dofferhoff , Anton S. M. and Vermeer , Cees and Janssens , Wim and Walk , Jona**. Vitamin K metabolism as the potential missing link between lung damage and thromboembolism in Coronavirus disease 2019 British Journal of Nutrition 191-198 (07/28/2021) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[183] **Visser , Margot J. and Dofferhoff , Anton M. and van den Ouweland , Jody W. and van Daal , Henny and Kramers , Cornelis and Schurgers , Leon J. and Janssen , Rob and Walk , Jona**. Effects of Vitamin D and K on Interleukin-6 in COVID-19 Frontiers in Nutrition (2022) src:dx.doi.org. src:www.frontiersin.org. src:www.frontiersin.org.

[184] **M.J. Marchywka**. On the age distribution of SARS-Cov-2 Patients (March 12, 2021) src:www.researchgate.net.

[185] **Desai , Ankita P and Dirajlal-Fargo , Sahera and Durieux , Jared C and Tribout , Heather and Labbato , Danielle and McComsey , Grace A**. Vitamin K & D Deficiencies Are Independently Associated With COVID-19 Disease Severity Open Forum Infectious Diseases (2021-07) src:dx.doi.org. src:doi.org. src:academic.oup.com.

[186] **Mohsin , Haneen Saeed and Ali , Hanaa Addai and Al-Tu'ma , Fadhil Jawad**. Assessment of von Willebrand Factor/ADAMTS13 Ratio and Vitamin K Levels as Predictor Markers for Severity of COVID-19 Patients Journal of Contemporary Medical Sciences (10/26/2021) src:dx.doi.org. src:www.jocms.org.

[187] **Mazzeffi , Michael and Chow , Jonathan H. and Amoroso , Anthony and Tanaka , Kenichi**. Revisiting the Protein C Pathway: An Opportunity for Adjunctive Intervention in COVID-19? Anesthesia and Analgesia (20200610) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[188] **Faiez , Amouri**. Role of S protein in thromboembolic complications during COVID19 and activated protein C as a serious therapeutic avenue in severe forms of patients Journal of Applied and Natural Science 88-90 (06/15/2020) src:dx.doi.org. src:journals.ansfoundation.org.

[189] **Lemke , Greg and Silverman , Gregg J.**. Blood clots and TAM receptor signalling in COVID-19 pathogenesis. Nature Reviews. Immunology (20200602) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[190] **Popa , Daniela-Saveta and Bigman , Galya and Rusu , Marius Emil**. The Role of Vitamin K in Humans: Implication in Aging and Age-Associated Diseases Antioxidants 566 (04/06/2021) src:dx.doi.org. src:www.mdpi.com.

[191] **Linneberg , Allan and Kampmann , Freja Bach and Israelsen , Simone Bastrup and Andersen , Liv Rabol and Jorgensen , Henrik Lovendahl and Sandholt , Haakon and Jorgensen , Niklas Rye and Thysen , Sanne Marie and Benfield , Thomas**. The Association of Low Vitamin K Status with Mortality in a Cohort of 138 Hospitalized Patients with COVID-19 Nutrients 1985 (2021) src:dx.doi.org. src:www.mdpi.com.

[192] **Mortus , Jared Robert and Manek , Stephen E. and Brubaker , Lisa Suzanne and Loor , Michele and Cruz , Miguel Angel and Trautner , Barbara W. and Rosengart , Todd K.**. Thromboelastographic Results and Hypercoagulability Syndrome in Patients With Coronavirus Disease 2019 Who Are Critically Ill JAMA Network Open e2011192 (06/01/2020) src:dx.doi.org. src:jamanetwork.com.

[193] **Ibañez , C. and Perdomo , J. and Calvo , A. and Ferrando , C. and Reverter , J. C. and Tassies , D. and Blasi , A.**. High D dimers and low global fibrinolysis coexist in COVID19 patients: what is going on in there? Journal of Thrombosis and Thrombolysis (2021-Feb-01) src:dx.doi.org. src:doi.org. src:link.springer.com.

[194] **Miles , Lindsey A. and Parmer , Robert J.**. Angry macrophages patrol for fibrin. Blood (2016-Mar-3) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[195] **Motley , Michael P. and Madsen , Daniel H. and Jürgensen , Henrik J. and Spencer , David E. and Szabo , Roman and Holmbeck , Kenn and Flick , Matthew J. and Lawrence , Daniel A. and Castellino , Francis J. and Weigert , Roberto and Bugge , Thomas H.**. A CCR2 macrophage endocytic pathway mediates extravascular fibrin clearance in vivo Blood 1085-1096 (03/03/2016) src:dx.doi.org. src:ashpublications.org.

[196] **Kask , Lena and Trouw , Leendert A. and Dahlbäck , Björn and Blom , Anna M.**. The C4b-binding Protein-Protein S Complex Inhibits the Phagocytosis of Apoptotic Cells Journal of Biological Chemistry 23869-23873 (2004) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[197] **Anderson , Howard A. and Maylock , Caroline A. and Williams , Joy A. and Paweletz , Cloud P. and Shu , Hongjun and Shacter , Emily**. Serum-derived protein S binds to phosphatidylserine and stimulates the phagocytosis of apoptotic cells Nature Immunology (2003) src:dx.doi.org. src:www.nature.com.

[198] **AM;Francis SA;Rennke H;Loscalzo J; , Simon DI;Ezratty**. Fibrin(ogen) is internalized and degraded by activated human monocytoid cells via Mac-1 (CD11b/CD18): a nonplasmin fibrinolytic pathway Blood (10/15/1993) src:pubmed.ncbi.nlm.nih.gov.

[199] **Simon , DI and Ezratty , AM and Francis , SA and Rennke , H and Loscalzo , J**. Fibrin(ogen) is internalized and degraded by activated human monocytoid cells via Mac-1 (CD11b/CD18): a nonplasmin fibrinolytic pathway Blood 2414-2422 (10/15/1993) src:dx.doi.org. src:www.sciencedirect.com.

[200] **Simon , Daniel I. and Ezratty , Ari M. and Loscalzo , Joseph**. The Fibrin(ogen)olytic Properties of Cathepsin D Biochemistry 6555-6563 (05/01/1994) src:dx.doi.org. src:pubmed.ncbi.nlm.nih.gov.

[201] **Douglas , Simone A. and Lamothe , Sarah E. and Singleton , Tatiyanna S. and Averett , Rodney D. and Platt , Manu O.**. Human cathepsins K, L, and S: related proteases, but unique fibrinolytic activity. Biochimica et biophysica acta. General subjects (20180623) src:dx.doi.org. src:www.ncbi.nlm.nih.gov.

[202] **Mycielska , Maria E. and Patel , Ameet and Rizaner , Nahit and Mazurek , Maciej P. and Keun , Hector and Patel , Anup and Ganapathy , Vadivel and Djamgoz , Mustafa B. A.**. Citrate transport and metabolism in mammalian cells BioEssays 10-20 (2009) src:dx.doi.org. src:mri-q.com.

Acknowledgments

1. Pubmed eutils facilities and the basic research it provides.

2. Free software including Linux, R, LaTex etc.

3. Thanks everyone who contributed incidental support.

Appendix A: Statement of Conflicts

No specific funding was used in this effort and there are no relationships with others that could create a conflict of interest. I would like to develop these ideas further and have obvious bias towards making them appear successful. Barbara Cade, the dog owner, has worked in the pet food industry but this does not likely create a conflict. We have no interest in the makers of any of the products named in this work.

Appendix B: About the Authors and Facility

This work was performed at a dog rescue run by Barbara Cade and housed in rural Georgia. The author of this report ,Mike Marchywka, has a background in electrical engineering and has done extensive research using free online literature sources. I hope to find additional people interested in critically examining the results and verify that they can be reproduced effectively to treat other dogs.

Appendix C: Symbols, Abbreviations and Colloquialisms

TERM definition and meaning

Appendix D: General caveats and disclaimer

This document was created in the hope it will be interesting to someone including me by providing information about some topic that may include personal experience or a literature review or description of a speculative theory or idea. There is no assurance that the content of this work will be useful for any paricular purpose.

All statements in this document were true to the best of my knowledge at the time they were made and every attempt is made to assure they are not misleading or confusing. However, information provided by others and observations that can be manipulated by unknown causes ("gaslighting") may be misleading. Any use of this information should be preceded by validation including replication where feasible. Errors may enter into the final work at every step from conception and research to final editing.

Documents labelled "NOTES" or "not public" contain substantial informal or speculative content that may be terse and poorly edited or even sarcastic or profane. Documents labelled as "public" have generally been edited to be more coherent but probably have not been reviewed or proof read.

Generally non-public documents are labelled as such to avoid confusion and embarassment and should be read with that understanding.

Appendix E: Citing this as a tech report or white paper

Note: This is mostly manually entered and not assured to be error free.
This is tech report MJM-2022-015.

Version	Date	Comments
0.01	2022-11-02	Create from empty.tex template
-	December 28, 2022	version 0.10 MJM-2022-015
0.10	2022-12-28	Note version, stalled
1.0	20xx-xx-xx	First revision for distribution

Released versions,
build script needs to include empty releases.tex

Version	Date	URL
0.10	2022-12-28	https://www.researchgate.net/publication/366642398_Recent_Vitamin_K_Literature_in_the_Conext_of_a_non

@techreport{marchywka-MJM-2022-015-0.10 ,
filename =”klotz” ,
run-date =”December 28, 2022” ,
title =” Recent Vitamin K Literature in the Conext of a non-Monotonic Response Curve : Local vs Global Optima and other Speculation ” ,
author =”Mike J Marchywka ” ,
type =”techreport” ,
name =”marchywka-MJM-2022-015-0.10 ” ,
number =”MJM-2022-015” ,
doi =”10.13140/RG.2.2.34218.29124” ,
version =”0.10 ” ,
institution =”not institutionalized, independent ” ,
address =” 44 Crosscreek Trail Jasper GA 30143” ,
date =”December 28, 2022” ,
startdate =”2022-11-02” ,
day =”28” ,
month =”12” ,
year =”2022” ,
author1email =”marchywka@hotmail.com” ,
contact =”marchywka@hotmail.com” ,
author1id =”orcid.org/0000-0001-9237-455X” ,
pages =” 25”
}

Supporting files. Note that some dates,sizes, and md5's will change as this is rebuilt.

This really needs to include the data analysis code but right now it is auto generated picking up things from prior build in many cases

```
3471 Dec 28 09:33 comment.cut d72314ca3e59e6b7b7503750d96ef35b
34436 Dec 14 09:35 /home/documents/latex/bib/mjm_tr.bib f9cfedd86bb54989681a539ef5e32280
39827 Dec 28 09:16 /home/documents/latex/bib/releases.bib 6b67470c5300aa29e23b9e4c4a906d5b
7331 Jan 24 2019 /home/documents/latex/pkg/fltpage.sty 73b3a2493ca297ef0d59d6c1b921684b
7434 Oct 21 1999 /home/documents/latex/pkg/lgrind.sty ea74beead1aa2b711ec2669ba60562c3
7162 Nov 13 2015 /home/documents/latex/pkg/mol2chemfig.sty f5a8b1719cee30a4df0739275ac75f8a
1069 Oct 15 2021 /home/documents/latex/share/includes/disclaimer-gaslight.tex 94142
    bbe063984d082bff3b400abe0fb
425 Oct 11 2020 /home/documents/latex/share/includes/disclaimer-status.tex b276f09e06a3a9114f927e4199f379f7
1478 May 14 2022 /home/documents/latex/share/includes/mjmaddbib.tex cb57cbf8cd5c5ac8f44c98b34ba9227a
122 Jun 27 2022 /home/documents/latex/share/includes/mjmlistings.tex 439aab9f9b760c03d4278a11e1a03079
4225 Oct 25 06:03 /home/documents/latex/share/includes/mycommands.tex 4c9a19e4d486f05addf05b60f79c3192
2901 Jun 17 2020 /home/documents/latex/share/includes/myskeletonpackages.tex
    fcfcd2e3c8d69d533932edaaa47f53a1
1538 Aug 14 2021 /home/documents/latex/share/includes/recent_template.tex 49763d2c29f74e4b54fa53b25c2cc439
940 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/cmextra/cmex7.tfm
    f9e66c0105a30e64e3a0f5c4f79efb8d
852 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/symbols/msam10.tfm
    b4a46d2c220ee4ffaaf87c608f8593cd
860 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/symbols/msam5.tfm
    c4142ffef6136ff95621fbe99efb7cec
864 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/symbols/msam7.tfm 2998
    d813a00ebf21070684f214a50f7e
844 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/symbols/msbm10.tfm
    f7721eee07bdc9e743e6c5f3f7e3d06d
876 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/symbols/msbm5.tfm 9
    e3df3efef7afc4b0381e88a6402f777
876 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/amsfonts/symbols/msbm7.tfm 374365713297
    d597717720c5786882e5
1260 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmbx12.tfm 41596a2c763cf972bbdd853b378ec55a
1264 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmbx9.tfm c3f8c3f0292777e1e9153581c59f8506
928 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmex10.tfm 0086317ff95b96ceb2bce0f96985e044
```

```
1464 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmmi10.tfm 9178465cbc6627ccd42a065dd4f917b7
1444 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmmi5.tfm db43b8082a0d9caedc6aeca524ed2faf
1448 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmmi6.tfm be0f1d444547257aeb3f042af14f3e47
1464 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmmi7.tfm 2b1ed046f0a24d705b439f2ed4b18786
1456 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmmi8.tfm e7bb485e28fc530112b40f5c89496200
1232 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr10.tfm a358ecd9b8cdb1834c30ae3213ec1dbc
1224 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr12.tfm 48d5728dc6473917c0e45f34e6a0e9cd
1156 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr5.tfm 19157dffae90ad9aaaed44f08b843218
1236 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr6.tfm 63e3c1344d1e22a058a5cb87731337e0
1236 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr7.tfm a2fb4ba2746c3da17e6135d75cc13090
1228 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr8.tfm 29a15bf51bfb16348a5cabb3215cf3fd
1228 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmr9.tfm b0280c40050dc3527dafc7c425060d31
1060 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmsy10.tfm 9408bd198fd19244e63e33fd776f17f4
1048 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmsy5.tfm b9935dfec2c2d4ccfda776f1749f536b
1052 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmsy6.tfm 00c03700e0e2f29cde6c0b50a5c56df5
1056 Jul 23 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmsy7.tfm fc9ac3acaa80c036582e6636bbac4655
1056 Jul 24 2019 /home/marchywka/.texmf-var/fonts/tfm/public/cm/cmsy8.tfm 7ef80e56d3b9e223d3bce5a9065b95ad
92378 Nov 20 03:56 keep/klotz1.pdf 0fc29cdb6bcc2d6c1c120c68e5cc092c
26558 Dec 28 09:33 klotz.aux c98ace5db55ea94c18c77593f6a36520
120768 Dec 28 09:32 klotz.bbl 238def5e4047c9cbf618905ffec20a29
702285 Dec 28 09:32 klotz.bib e7a1a6d98c437e006439b5164e436d1f
2353 Dec 28 09:32 klotz.blg 6b4cc084bd01dae84c03e1eaaa310b78
4096 Dec 28 09:33 klotz.bundle_checksums 1fd5cded1956e9391c2c4573ce1f7e03
30134 Dec 28 09:32 klotz.fls 36d74eb9dd449629505cc05140d82324
3 Dec 28 09:32 klotz.last_page 2a52a5e65fc3c43f409550dfad1f904f
63298 Dec 28 09:33 klotz.log 5841f64a9071ed9aea3b6d24f00c2103
1182 Dec 28 09:33 klotz.out 085fa71e0a1f7ca124435b7180f70f3e
455812 Dec 28 09:33 klotz.pdf 747ed5b62a293182ad8a8e3ec1f5e836
83618 Dec 28 09:31 klotz.tex 190c66f4357549c1650c923ae1ee0b4c
555410 Dec 22 13:52 non_pmc_klotz.bib fc402a72b40ea13645b39c621d828a12
146482 Dec 22 13:38 pmc_klotz.bib efb1c2cb6b54691d2d6cc7789f85595e
617 Dec 28 09:32 releases.tex ac7224c1a45d463763b7d72d5bb8cfed
31050 Jul 21 2011 /usr/share/texlive/texmf-dist/bibtex/bst/urlbst/plainurl.bst
    ffdaefb09013f5fd4b31e485c13933c1
1293990 Jul 23 2019 /var/lib/texmf/web2c/luatex/lualatex.fmt 0fdf3dce2c9cd956e421c2c52037b3cc
455812 Dec 28 09:33 klotz.pdf 747ed5b62a293182ad8a8e3ec1f5e836
```