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Protein intake and healthy aging : sooner rather than later?

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1 **TITLE PAGE**

2 **Title**

3 Protein intake and healthy aging: sooner rather than later?

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26 Protein is a ubiquitous nutrient. It can be found everywhere from almonds to zander, and its
27 biological actions are equally vast. Proteins are needed for bone calcification, liver activities,
28 and blood and muscle synthesis; they play a role in the immune system and peroxidative
29 protection mechanisms; participate in the coordination of motor cells; and are essential for
30 hormone regulation and immunological stimulation [1].

31 As these mechanisms suggest, protein is a key nutrient throughout the aging process.

32 Previous research has shown that protein deficit in older adults may cause impairments of
33 muscular, skeletal, and immune function [2, 3], while higher protein intake has been
34 associated with increased muscle mass and strength, slower rate of bone loss, lower risk of
35 frailty, and improved cardiovascular function and recovery from illness [2, 3].

36 Not all dietary proteins are created equal, however. Plant protein intake in older adults has
37 been linked to reduced muscle loss and lower risk of hip fracture, cognitive decline, and
38 frailty. In the same studies, animal protein intake only showed a beneficial association with
39 hip fracture in males and cognitive decline, and it was even associated with higher risk of
40 frailty [4].

41 But virtually all studies on protein intake and geriatric syndromes focused on old age. On the
42 one hand, because researchers may have an easier time demonstrating short-term associations
43 than those spanning decades [5]. On the other hand, because few had followed a big enough
44 cohort for long enough to assess if what people eats in their forties impacts their health in
45 their seventies.

46 The study published in this issue of the American Journal of Clinical Nutrition used dietary
47 data from the 1984 and 1986 waves of the Nurses' Health Study, and linked it to chronic
48 diseases, mental health, cognitive and physical function in 2014 and 2016 [4]. The authors

49 found that protein intake in midlife was associated with higher odds of healthy aging.
50 Analyses were extensively adjusted for sociodemographic, lifestyle, and dietary variables.
51 Although all protein sources showed a beneficial trend, plant protein intake was the clear
52 winner, with 35% higher odds of healthy aging associated with a ten gram/day increase in
53 midlife –roughly one serving of pasta or a small serving of beans.

54 When examining individual domains of healthy aging, the most consistent association of
55 plant protein was with absence of physical function limitations in old age. Substitution
56 analyses showed that the theoretical replacement of fats with proteins in midlife was
57 beneficial regardless of the protein source, same as that of carbohydrates with total, animal,
58 and plant protein. Monounsaturated fat replacement looked particularly favorable when
59 compared with other fatty acids, which is unexpected and may warrant further investigation.
60 In addition, replacing animal or dairy protein with plant protein in midlife resulted in higher
61 odds of healthy aging.

62 Potential mechanisms behind the differences between plant and animal proteins include not
63 only variations in amino acid composition, but the fact that plants provide phytochemicals
64 and fibers while animal foods do not [6]. One might also think that the beneficial associations
65 of plant protein in midlife could be due to the quantity and quality of other macronutrients.
66 Still, the theoretical replacement of carbohydrate from whole grains, monounsaturated fat,
67 and polyunsaturated fat with plant protein favored the latter, suggesting that the observed
68 beneficial associations could be attributed to plant protein itself.

69 As any other study, this one does not come without limitations. The role of changes in dietary
70 protein intake was not explored; on the contrary, the authors averaged dietary records to
71 reduce within-person variability. Nevertheless, previous investigations showed that increasing
72 plant protein intake in older adults may have benefits over aging, and evidence from the

73 Nurses' Health Study highlighted that increasing diet quality over time –which may entail an
74 increase in plant protein intake– is linked to lower risk of death [7, 8]. To our knowledge,
75 information on protein supplements was not recorded, although their use may have been less
76 prevalent among women at the time that data were collected [9]. As in any observational
77 study, it may not be possible to completely rule out residual confounding.

78 The main strength of this work lies in its large sample size paired with an extremely long
79 follow-up, so lengthy that it is hard to think of another dataset in which this hypothesis could
80 have been tested. Among other things, such design minimized reverse causation –health
81 status influencing nutrient intake– and allowed for a plausible induction period between the
82 assessment of protein intake and the development of age-related deficits. Furthermore, the
83 authors conducted a remarkable number of sensitivity analyses, in which they showed that
84 study associations were robust to choices in variable operationalization and model
85 specification.

86 One may wonder whether a more explicit use of life-course epidemiological models (i.e.,
87 latency, accumulation, or pathway/chains of risk) could have provided a better understanding
88 of the interplay between protein intake and healthy aging. In the authors' defense, modeling
89 30-year, 12-year, and 8-year lags between exposures and outcomes rendered equivalent
90 results, although protein intake was cumulatively averaged in the last two instances. Such
91 consistency was also observed in age-stratified analyses and is in line with previous
92 investigations in older adults, suggesting that protein intake is beneficial toward aging not
93 only in mid- or late life, but all the way through [7, 10]. Implications are important, as putting
94 a focus on protein earlier in life could help avoid later nutritional dilemmas (e.g., while
95 geriatric guidelines advocate for higher protein intake, some older adults may need protein
96 restriction to preserve kidney function).

97 Future studies could explore the external validity of these associations in males, ethnically
98 diverse populations, and settings where plants are the main protein source –despite the
99 consistent benefits found for plant protein intake, it comprised less than a quarter of total
100 protein. Public health policies targeting plant protein intake in midlife would seem better-
101 informed than ever, as they may not only result in lower mortality and chronic disease
102 incidence, but also healthier aging three decades later [4, 6]. As they say, it is never too early
103 to start planning.

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