

Pig interorgan balance studies in health and disease

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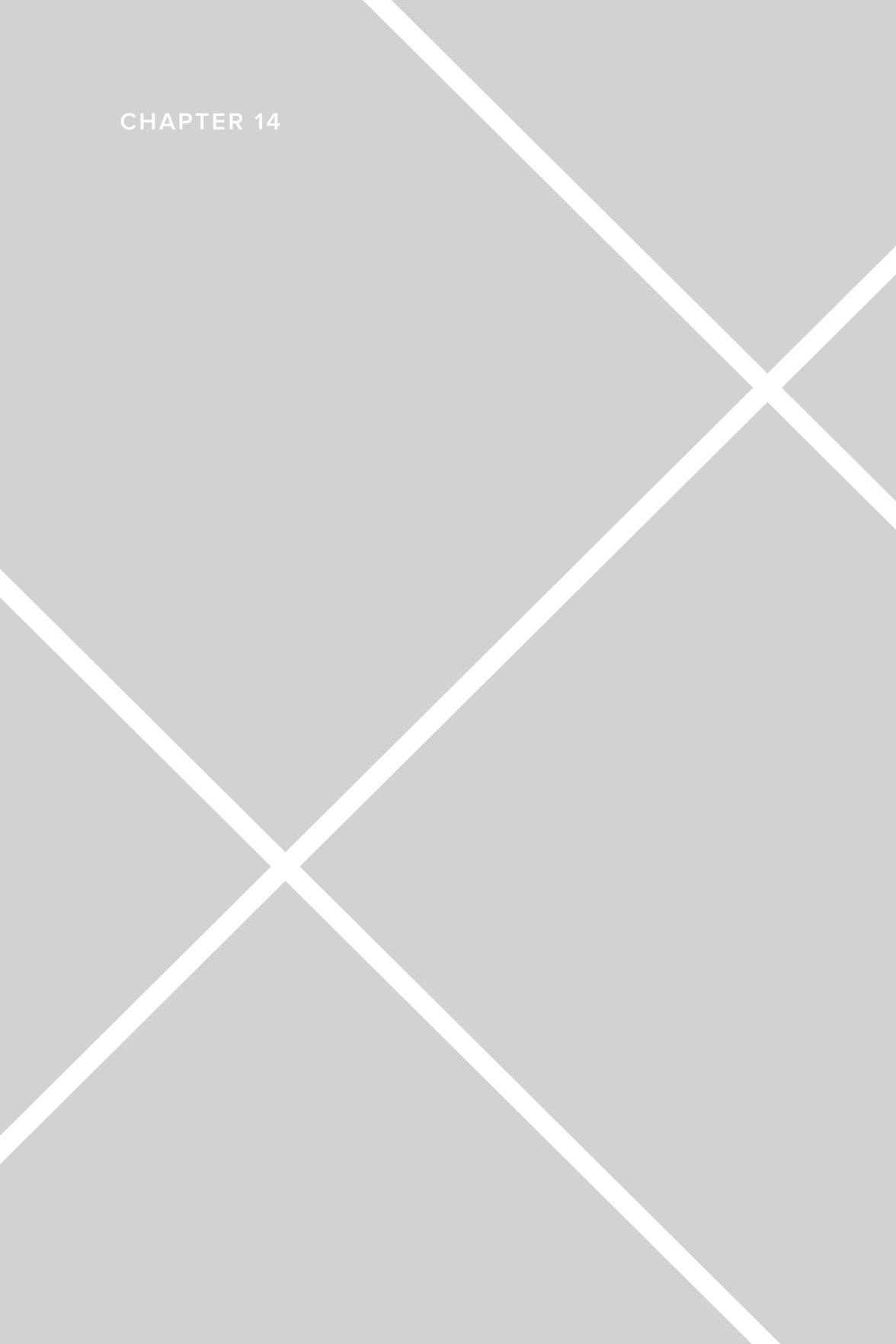
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CHAPTER 14

The image features a solid light gray background. Two thick, white diagonal lines intersect to form an 'X' shape. One line runs from the top-left towards the bottom-right, and the other runs from the top-right towards the bottom-left. The lines are positioned such that they cross each other in the center of the frame.

Valorization

A healthy human body needs nutrients to sustain its metabolic balance. To this end, complex interactions between specialized organs for transportation, digestion, absorption, redistribution, utilization, conversion, breakdown of nutritional substrates during post-prandial and/or post-absorptive stages must occur. These interactions are highly dynamic and subject to disturbances in many pathophysiological conditions (e.g. sepsis or liver failure) (1-10). To unravel (disturbed) complex nutritional substrate metabolism, quantitative and dynamic substrate flux measurements are needed. This knowledge will support the development of new nutritional strategies in health and disease, which are needed in light of many major worldwide nutritional problems:

World Health Organization (WHO) malnutrition factsheet (May 2017) (11):

Malnutrition, in all its forms, includes undernutrition (wasting, stunting, underweight), inadequate vitamins or minerals, overweight, obesity, and resulting diet-related non-communicable diseases.

- 1.9 billion adults are overweight or obese, while 462 million are underweight.
- 52 million children under 5 years of age are wasted, 17 million are severely wasted and 155 million are stunted, while 41 million are overweight or obese.
- Around 45% of deaths among children under 5 years of age are linked to undernutrition. These mostly occur in low- and middle-income countries. At the same time, in these same countries, rates of childhood overweight and obesity are rising.
- The developmental, economic, social, and medical impacts of the global burden of malnutrition are serious and lasting, for individuals and their families, for communities and for countries.

Malnutrition occurs in all countries and is considered one of the greatest global health challenges. Optimizing nutrition needs to start early in life to ensure long-term benefits. Poverty is considered a major risk factor for malnutrition and subsequently increases health care cost, reduces productivity and slows economic growth. Led by WHO and the Food and Agriculture Organization of the United Nations (FAO), the UN Decade of Action on Nutrition calls for policy action across several key areas. One of the areas is creating sustainable, resilient food systems for healthy diets. A healthy diet is a very generic term, and usually defined in terms

of the needs of the organism, i.e. metabolic demands, and the dietary amount which will satisfy those needs, i.e. efficiency of utilization, thus: dietary requirement = metabolic demand/efficiency of utilization (12). Therefore, an appropriate diet in health is different from that in disease. For instance, we recently published that appropriate clinical nutrition is lowering mortality in hospitalized adults (7). In critically ill patients, muscle wasting is a life-threatening organ dysfunction that can be treated with appropriate nutrition (13, 14). To determine the “metabolic demand” and “efficiency of utilization”, understanding of nutritional substrate metabolism, quantitative and dynamic substrate flux measurements in health and disease are needed and is the general focus of this dissertation.

Measuring complex fluxes and trafficking (amounts in time) of substrates in and between organs, is extremely difficult in humans due to the multitude of ethical issues and the limitations to perform invasive procedures, especially in pathophysiological conditions like in critically ill patients. Therefore, clinically relevant animal models are essential to study (patho) physiological metabolism in a controlled, repeatable way and to be able to use invasive techniques, providing multiple measurements and mechanistic data within the same animal in several nutritional and pathological stages. The pig, with its remarkable metabolic similarity to humans, is used often in biomedical research and more generally in the field of nutrition and associated metabolic disease states. Therefore the presented highly translational pig experiments generated important information that can be used for multiple purposes in the nutrition field.

We are aware that translational preclinical studies in the present dissertation are the “baby steps” in the journey to develop products and activities to solve worldwide nutritional health problems. However, the fact that eight of the ten described research projects in the present dissertation are published and received 184 citations (status 19th of July 2017) indicates the value for the scientific community (15). Besides the scientific recognition, the societal relevance of this research was also recognized by the food industry, the ministry of economic affairs (The Netherlands) and the National Institutes of Health (USA). The findings of this dissertation can be used and translated in multiple ways for the food industry (development new products, improve consumers information), agriculture and environmental field (better understanding dietary protein quality in relation to meat production and emissions of nitrogen), clinical field (new food strategies, improvement design of clinical trials, better understanding of disturbed metabolism in critically ill patients, new clinical food products) and policy makers for general public (improved healthy food definitions/ claims/ information, importance of a healthy gut).

Here an example:

In section 1 we presented research that shows the fate of amino acids (building blocks of protein) that are coming from dietary protein. We found that a high quality protein meal is healthy for your gut. In contrast with a low quality protein meal that breaks down the gut. Although these scientific findings were published a while ago, the discussion of dietary protein is currently a hot topic in the food social media. Online and on packages in the supermarket consumers are overwhelmed with beneficial health claims (“super foods”) of protein. This however is misinformation if the protein involved is of low quality. For instance a gelatin pudding with 10% of low quality protein has no health benefits, this in contrast with 10% of high quality protein in yogurt. The “nutrition facts” sheet of a food package contains information of different types of fat and carbohydrates but protein quality grades are still missing. Therefore, I strongly recommend policy makers (US Food & Drug Administration, European Food Safety Authority) to add the quality grade of the used food proteins to the “Nutrition Facts” sheet of a food package to ensure consumers are better informed and can make healthier choices.

In section 2 and 3 we presented with innovated techniques and preclinical models, new insights of how metabolic substrates are changed in critically ill pigs. The role of gut and liver metabolism on the disturbed whole body metabolism was studied in detail. This information gives physicians and (specialized) dieticians more knowledge how metabolic substrates behave in critically ill patients, which cannot be obtained with human research. These data are sound information for further design, planning and development of randomized controlled trials by physicians, specialized dieticians, scientists and the clinical nutrition industry, to improve nutritional interventions and strategies in critically ill humans.

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