

SLOWING THE GROWTH OF LIFESTYLE DISEASES IN CHINA

Diseases with an **ENDOCRINE AND METABOLIC COMPONENT** are a growing problem. In this Q&A, Jiajun Zhao, president of Shandong Provincial Hospital, talks about advances in research and treatment.

In the past decades, China has seen a significant increase in the incidence of non-communicable chronic diseases, such as heart attack, stroke, cancer, diabetes and chronic lung disease. In 1990, for example, cases of cardiovascular disease hovered

around 50 million; in 2019, they had increased to more than 120 million.

Most experts attribute the increase in these chronic diseases to lifestyle, mainly decreased physical activity and dietary changes. The diseases are closely related to metabolic and endocrine disorders, and together they account for around 89% of China's 10 million annual deaths, making them the greatest health concern in the country.

Jiajun Zhao, an endocrinologist and president of Shandong Provincial Hospital, which is affiliated to Shandong First Medical

University, has been researching endocrine and metabolic diseases and their clinical management since 1983. Here, he discusses his research on the links between obesity, metabolic disorders and non-communicable chronic diseases.

What distinguishes Shandong Provincial Hospital?

Shandong Provincial Hospital was founded in 1897 as Wanguo Union Charity Hospital. In the 125 years since, it has grown into a Class-A tertiary hospital, the highest rank in the national grading system in China. With approximately 6,700 staff and 3,890 beds, we provide

comprehensive clinical services. In 2021, we treated 4.38 million patients, discharged 216,000 in-patients, and performed 146,000 surgeries with an average stay of less than 7 days.

In addition to medical care, we are committed to medical research and talent development, which distinguishes our hospital from others. This is especially true for endocrinology, the study of conditions related to hormones. Over the past few decades, our team has been immersed in clinical demand-driven endocrine and metabolic disease research. Our work focuses specifically on the

fields of obesity, metabolic disorders and endocrine diseases, for which we have established platforms for basic research, clinical diagnosis and treatment, and translational and digital medicine.

Why are obesity and metabolic disorders of particular interest to you as an endocrinologist?

China has seen an increase in the incidence of many lifestyle diseases in the past 30 years. For example, the estimated prevalence of diabetes among adults has risen dramatically from less than 1% in 1980 to 12.8% by 2020. This upsurge warns us of the impact of obesity, a well-recognised risk factor for diabetes.

"OUR FINDINGS HIGHLIGHT ABNORMAL LIPID METABOLISM AND OBESITY AS THE KEY DRIVING FORCES BEHIND MANY DISEASES."

Obesity is also associated with an increased risk of macro- and microvascular complications — such as coronary artery disease, heart failure, stroke, as well as dysfunction in eyes, muscles and kidneys — in people with type 2 diabetes.

Obesity is also frequently linked to metabolic disorders such as problems with blood lipid levels, insulin resistance, and high blood pressure. Our studies found that these factors, alone or in combination, may promote the development of gastrointestinal polyps¹, malignancies and also lead to depression.

For early prevention and treatment of various diseases, it's critical to explore how they are associated with obesity and metabolic abnormality.

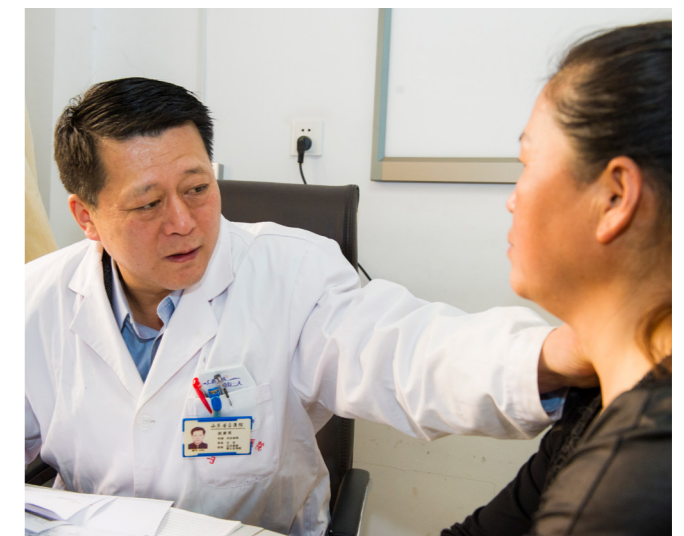
What is lipotoxicity and what are your major findings about it?

Free fatty acid levels are elevated in obesity, and when the adipose or fat tissues are overwhelmed, large amounts of free fatty acids can accumulate in non-adipose tissue cells and reach to toxic levels. Lipotoxicity thus describes lipid overload in non-adipose tissues, such as the heart, liver, and kidney. It can cause chronic damage to tissue cells, eventually leading to organ dysfunction.

Previous research focused primarily on lipotoxicity in pancreatic β cells, which produce, store, and release insulin, and its damaging effect on glucose metabolism in diabetes.

We have now expanded the scope and investigated its role in other endocrine disorders. For example, we observed that a high-fat diet significantly caused abnormal thyroid function and altered morphology in rats. Later in a population-based study, we found that elevated triglyceride levels were associated with a 35% increased risk of hypothyroidism — a condition where the thyroid gland doesn't produce sufficient levels of thyroid hormones — in both sexes². These findings point to lipotoxicity as a possible risk factor for thyroid dysfunction³.

We further explored the mechanisms underlying abnormal lipid metabolism. The pituitary, a tiny gland in the brain, synthesizes several essential hormones — including thyroid-stimulating hormone (TSH) and follicle-stimulating hormone (FSH) — that regulate growth and reproductive function. Through a series of studies, we found that elevated levels of TSH and FSH are associated with increased levels of cholesterol and triglycerides^{4,5}. This discovery provides new insights into the regulation of lipid metabolism through the pituitary axis.



▲ Jiajun Zhao has been exploring the links between obesity, metabolic disorders and non-communicable chronic diseases.

What clinical implications and applications do these findings have?

Our findings highlight abnormal lipid metabolism and obesity as key driving forces behind many diseases, including type 2 diabetes.

We advocate for the wide implementation of lipid screening for thyroid dysfunction in clinical settings. It may help with early diagnosis, prevention and treatment of endocrine diseases like mild thyroid dysfunction.

We hope that our findings will help raise public awareness of obesity and metabolic disorders as common causes of many chronic diseases, allowing us to better manage them.

What are the goals at Shandong Provincial Hospital?

Echoing the Healthy China Initiative 2019-2030, which aims to prevent disease and promote health, we will continue to conduct research on lipotoxicity, obesity and metabolic disorders, and develop more innovative and precise treatments in clinical practice.

We will also tap into innovative therapies such as gene therapy, aiming to grow Shandong Provincial

Hospital into an internationally renowned research centre. We are now building the Shandong Engineering Research Centre of Stem Cell and Gene Therapy for Endocrine and Metabolic Disease. There we will investigate different types of gene therapy vectors, and advance clinical translation and application of these technologies to better treat non-communicable diseases. ■

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