

# NEWSLETTER #25

MARCH 2024



**ZOOM**

## **DIABETES MAKES EYES FRAGILE**

## 2 EDITORIAL



Insidious and painless, diabetes poses a threat to vision and is only worsening in France. The eyes of people with diabetes are particularly fragile. When diabetes gradually affects the vascular wall and the center of the eye, we then speak of diabetic retinopathy. Patients only become aware of visual symptoms in case of complications (hemorrhage, retinal detachment...), thus at a stage of development where the visual prognosis becomes very reserved, with a risk of blindness.

### **Early screening and management are therefore essential!**

Our challenge, as a research center, lies there: protecting the retina as early as possible in the pathology. That's why we wish to share with you two recent advances:

the first is led by Dr. Xavier Guillonnet to reduce the inflammatory response and the degeneration of micro-vessels. It opens **the prospect of studying new therapies.**

The second by Professor Michel Pâques. He has led to **the development of a specific laser** to treat lesions caused by diabetic macular oedema.

They both open the prospect of studying new therapies thanks to your support.

Thank you all for your help.

**Serge Picaud**

Director of the Institut de la Vision

### **SCIENTIFIC AWARD**

#### **Professor José-Alain Sahel is the winner of the EURORDIS 2024 Prize!**

Founder of the Institut de la Vision in Paris and Pittsburgh, President of the Foundation Voir et Entendre, Emeritus Professor, this prize highlights Professor Sahel's constant commitment. It rewards the excellence of his scientific research in the field of rare diseases, particularly retinal diseases. It is a great pride for the Institut de la Vision and its Foundation!

*EURORDIS is a unique non-profit alliance, bringing together over 1,000 patient associations for rare diseases in more than 70 countries.*



## DOSSIER

## DIABETES

Diabetes is defined as fasting hyperglycemia greater than 1.26 g measured on two occasions. There are two types of diabetes:

- **Type 1 diabetes** is an autoimmune disease that generally appears before the age of 30 and is characterized by almost total lack of insulin production. It requires lifelong insulin therapy. It is said to be insulin-dependent.
- **Type 2 diabetes** is the most common form of diabetes. For some people, insulin production is insufficient, while for others, the hormone does not work well or the cells are resistant to insulin (insulin resistance). In all cases, there is an abnormal increase in blood glucose.



Chronic hyperglycemia associated with diabetes leads to **changes in blood vessels that carry oxygen to tissues**. If this hyperglycemia is not sufficiently managed, it can have serious health consequences:

- **Cardiovascular diseases** (hypertension, dyslipidemia...).
- **Nerve damage** (diabetic neuropathy).
- **Kidney problems** (renal insufficiency).
- **Eye problems** (diabetic retinopathy).

## Prevalence



According to estimates by the International Diabetes Federation, the global population suffering from diabetes was **463 million people in 2019** and is expected to reach 700 million by 2045.



According to the Health Insurance, in France in 2020, more than **3.5 million people** are treated with medication for diabetes, representing **5.3% of the population**.

## Risk factors for diabetes

The aging of the population is leading to an increase in the number of diabetic patients, but it is mainly social and environmental factors (related to our lifestyles) that predispose to diabetes:

## Overweight and abdominal obesity

- Overweight or obesity with a body mass index (BMI) equal to or exceeding 25 kg/m<sup>2</sup>.
- Abdominal obesity with a waist circumference greater than or equal to 94 cm in men and 80 cm in women.

## Lack of physical activity and sedentary lifestyle

Another risk factor is low physical activity (less than 30 minutes a day).

Some diseases are associated with the onset of type 2 diabetes:

- High blood pressure.
- Abnormal blood fat levels such as cholesterol, for example.
- History of gestational diabetes, i.e., diabetes occurring during pregnancy.
- Having given birth to a baby weighing more than 4 kg.



## DOSSIER

DIABETIC  
RETINOPATHY

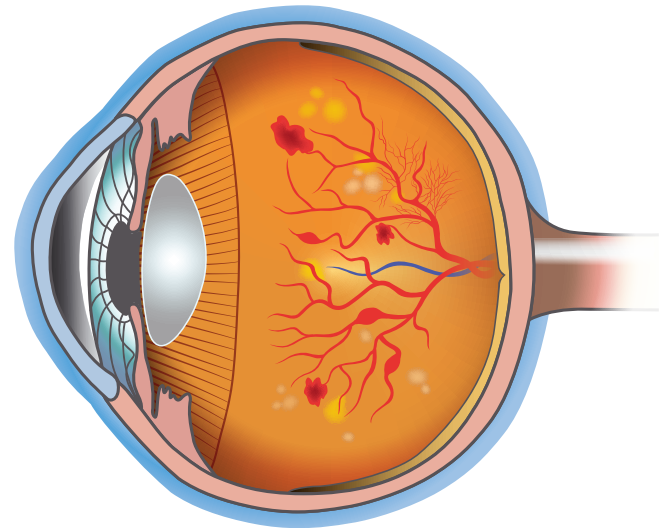
ONE THIRD OF PEOPLE  
WITH DIABETES DEVELOP  
DIABETIC RETINOPATHY\*

## Definition

An ocular complication of type 1 and type 2 diabetes, diabetic retinopathy is a **progressive disease** in which chronic hyperglycemia causes peripheral vascular lesions of the retina and/or macula (the center of the retina). It affects capillaries (small blood vessels) whose walls change because pericytes - cells surrounding capillaries - disappear. The blood network thus becomes hyper-permeable, leading to the accumulation of fluids in the retina and the formation of **macular oedema** responsible for vision loss.

Abnormalities in capillary walls can also lead to **occlusions**. The downstream retinal tissues are then deprived of oxygen: this is equivalent to a small retinal infarction. These so-called ischemic areas lead to the production of vascular growth factors (VEGF)

*Fundus with hemorrhage  
due to diabetic retinopathy.*



**Occlusion/  
Aneurysm**



**Mobile  
spots**



**Neovasculari-  
sation**



**Hemorrhage**

in order to produce new vessels that will provide compensation. Unfortunately, these “**neo-vessels**” are not effective in oxygenating the retina, they are fragile and will cause complications (**hemorrhage**, tractional retinal detachment, neovascular glaucoma, blindness) if left untreated. A small hemorrhage may manifest as simple **mobile spots** in vision, while a significant hemorrhage can cause complete vision loss in the affected eye.

The presence of these abnormalities allows determining the stage of development of diabetic retinopathy:

- Absent (no visible abnormalities).
- Non-proliferative (abnormalities reflecting retinal ischemia but without neovascularization).
- Proliferative (neo-vessels possibly accompanied by vitreous hemorrhage, retinal detachment, etc.)

Diabetic eye involvement can lead to bilateral damage to the eye with a decrease in visual acuity as well as complications that worsen the disease. **It is the leading cause of blindness before the age of 50.**



*A complication of diabetes, diabetic retinopathy impairs vision.*

## Screening and Monitoring

Screening and monitoring are done through a fundus examination performed by an ophthalmologist.

In case of doubt in the analysis of fundus photographs, two complementary examinations are used:

**Fluorescein angiography.** Blood vessels are colored intravenously, thus highlighting ischemic areas and neovascularization. It allows determining the extent of retinopathy, planning a therapeutic scheme, and monitoring its effects.

## EARLY SCREENING IS ESSENTIAL!

The french Health Insurance covers deferred reading retinography. This is a procedure performed by an orthoptist, a non-medical healthcare professional specialised in eye rehabilitation. It is then interpreted via telemedicine by an ophthalmologist. This screening method, validated by the French National Authority for Health, is aimed at diabetic patients under 70 years old and is designed to speed up screening without waiting for an appointment with an ophthalmologist.

*Source: AMELI.fr website*

**Optical coherence tomography (OCT)** is used to diagnose macular oedema. This examination provides cross-sectional images to assess the severity of oedema and the response to treatment.

## Treatments

Treatment is general to achieve **glycemic balance**:

- Glycated hemoglobin HbA1c <7%.
- Blood pressure less than or equal to 14/8.
- Smoking cessation, if applicable.
- Weight control and lipid profile.
- Regular physical exercise.

And specifically for the eyes:

- **Drug treatments** aimed at slowing the progression of the disease. Intraocular injections of anti-VEGF or corticosteroids help treat macular oedema and interrupt the overproduction of VEGF and thus the proliferation of neo-vessels.
- **Laser treatment or panretinal photocoagulation (PRP)** which coagulates blood and stops the proliferation of neo-vessels. It stabilises the evolution of peripheral lesions. It also helps treat certain forms of macular oedema by cauterising abnormal vascular lesions developed in the central region. Laser treatment helps prevent blindness but lost visual field areas cannot be restored.
- **Surgery by vitrectomy** which is used in cases of serious complications of retinopathy (retinal detachment, intraocular hemorrhage...) and involves cleaning the inside of the eye (vitreous). It notably allows removing blood preventing light from focusing correctly on the retina, or helping to reattach a detached retina to the eye wall.

*\* Source: HAS. Screening for diabetic retinopathy by delayed reading of fundus photographs. December 2010 (argument).*

## FOCUS ON RESEARCH

## ADVANCEMENTS IN RESEARCH AT THE INSTITUT DE LA VISION

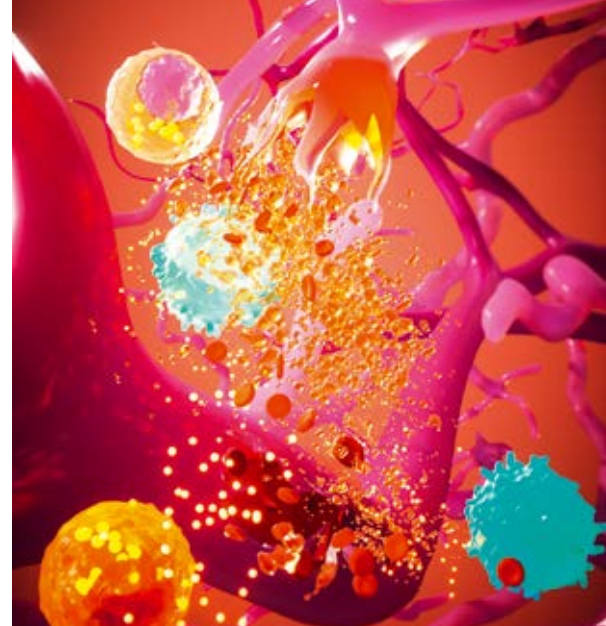
### Towards treatment in the early phase of diabetic retinopathy

The disease is characterized in its early stages by the loss of small retinal blood vessels and micro-hemorrhages for which no treatment is available. This early phase is accompanied by an inflammatory reaction, as evidenced by the presence of immune system cells (macrophages) and inflammatory proteins in the retina. However, the mechanisms linking diabetes to this early neuro-inflammation are still poorly understood. At the Institut de la Vision, researcher Xavier Guillonéau wondered if the abnormally high level of lipids (dyslipidemia) circulating in the blood could be a factor for patients with diabetic retinopathy. In a recent

*Dr. Xavier Guillonéau*



He leads a group of researchers studying the involvement of inflammatory mechanisms in retinal vascular diseases (diabetic retinopathy and retinopathy of prematurity) and in neurodegenerative processes associated with age-related macular degeneration (AMD).



issue of the Journal of Clinical Investigation, Xavier Guillonéau's group from the "Inflammation in Retinal Pathologies" team led by Florian Sennlaub, in collaboration with Lariboisière Hospital and the Conde de Valenciana Ophthalmological Foundation in Mexico, analyzed blood plasma and retinal tissue samples from patients with type 2 diabetes to study the role of inflammation and lipids in disease progression.

These works, supported by the UNADEV (Union of Blind and Visually Impaired), demonstrate for the first time that lipid-laden macrophages accumulate in regions of the retina with characteristic micro-hemorrhages of diabetic retinopathy. The team demonstrates that lipids present in the bloodstream, and to a lesser extent glucose, promote the formation of these pathogenic macrophages that contribute to vessel loss. The team found a way to pharmacologically reduce the inflammatory response and degeneration of micro-vessels.

**These original works highlight a new pathological process of diabetes independent of glucose. This major discovery could have very promising therapeutic implications for the treatment of early stages of diabetic retinopathy.**

#### Published article

> Perilipin 2-positive mononuclear phagocytes accumulate in the diabetic retina and promote PPAR.-dependent vasodegeneration.

<https://www.jci.org/articles/view/161348>





## Towards a simplified, non-invasive treatment for macular oedema

Professor Michel Paques, a physician-researcher at IHU FOReSIGHT (15-20 national hospital and Institut de la Vision), and his teams, have developed a means to treat lesions that lead some diabetic patients to blindness. **Targeted laser photocoagulation** is a treatment that uses the healing and coagulating effect of a laser to treat macular oedema. This treatment, called Indocyanine-green Guided Targeted Laser (IGTL), allows, in some cases, a single application and has beneficial effects for several years. Professor Paques' work has demonstrated that the combination of two common consultation techniques, indocyanine-green angiography (a precise imaging technique) and the impact of targeted laser on these vascular abnormalities (called macroaneurysms), **significantly lightens care procedures** by reducing or eliminating intraocular injections. During laser coagulation, a focused laser beam is directed onto the region of the retina with damaged blood vessels. Heat is generated, allowing the pathological regions of the retina to be destroyed. In this way, we can seal the porous blood vessels and prevent the onset of oedema. To understand the progression of this advancement, one must go back in time. In the 2000s, this team saw a patient in consultation with oedema resistant to standard treatments. Following a discussion with colleagues, including Dr. Severin Boni, then a resident at Hospital des 15-20, it was proposed to perform retinal angiography with a dye usually reserved for other pathologies, indocyanine green. This revealed a local anomaly, later called **TelCaps** (for capillary telangiectasias). These lesions often escape standard imaging. This first case was treated

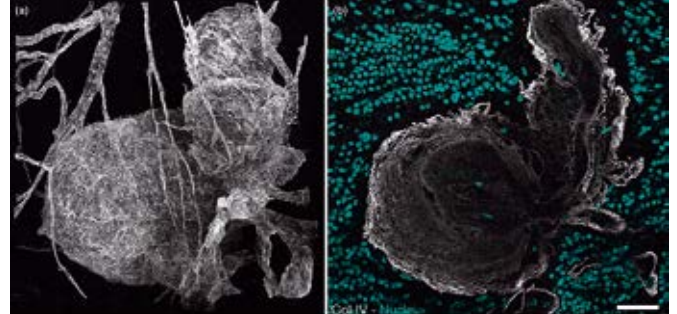
*“With this method, we can hope to reduce the number of injections patients receive, and even cure some oedemas resistant to conventional treatments. We now aim to better understand the mechanisms that lead to the appearance of these lesions and those that cause oedema. It is interesting to note that these TelCaps are associated with the presence of lipids in the retina, which aligns with Xavier Guillonneau's work.”*

– Prof. Michel Paques



Prof. Michel Paques

TelCaps responsible for chronic macular oedema following retinal vein occlusion. Its wall has a complex structure whose origin remains to be elucidated. The scale bar measures 100 microns. Published article: Confocal microscopy of telangiectatic capillaries (TelCaps) and other features of microvascular remodeling following branch retinal vein occlusion. J Anat 2023 <https://onlinelibrary.wiley.com/doi/10.1111/joa.13743>



with laser only on this lesion, and the oedema could heal. A long process of refining imaging and treatment procedures as well as identifying patients who could benefit from it was necessary. We were supported by funding from the CCAH (Comité national Coordination Action Handicap). As our research progressed, **the effectiveness of the treatment was confirmed**. The technique was presented at various congresses, indications were refined through exchanges and feedback from colleagues, a randomized study funded by the Ministry of Health was launched with 10 centers in France (to be completed in 2025) and discussions have been conducted with industrial partners regarding laser technique. An histological study of these lesions was conducted with the assistance of the Institut de la Vision. Some TelCaps are not accessible to laser, such as those too close to the center or affecting eyes with signs of AMD. Surgeons are considering surgically removing these lesions. Other laser modalities could help overcome this difficulty.

Today, **this treatment is used in many centers**. The next step is to integrate it into routine therapeutic practices. To achieve this, several groups of scientists, in France and worldwide, are coming together to establish recommendations for the ophthalmological community.

**He studies the mechanisms leading to vision loss in AMD and vascular diseases. In collaboration with physicists, biologists, and mathematicians, he also develops imaging procedures for studying retinal cellular dynamics *in vivo* in patients. He is an ophthalmologist at the 15-20 national hospital and the medical coordinator of the Clinical Investigation Center and the Retina Center.**



# DIABETES, IT'S ALWAYS WORTH KEEPING AN EYE ON!

Diabetic retinopathy remains a common complication of diabetes and one of the leading causes of preventable blindness in the working-age population. According to the most recent epidemiological data, the number of affected adults worldwide is estimated at 103 million, with an expected increase to 130 million by 2030 and over **160 million by 2045\***.

- LET'S NOT WAIT to be affected to take action!
- HELP US fight against vision diseases.
- TOGETHER, let's find new treatments today that will enable us to live better tomorrow.

\* Source: Global Prevalence of Diabetic Retinopathy and Projection of Burden through 2045: Systematic Review and Meta-analysis. Ophthalmology 2021.

## MAKING A DONATION IS SIMPLE!



**Online** at [institut-vision.org](http://institut-vision.org)

Secure site for credit card donations



**By mail**

Send your donation check to:  
Fondation Voir & Entendre  
17 rue Moreau 75012 PARIS

## FOR MORE INFORMATION

**Arnaud Bricout**

[relation-donateur@institut-vision.org](mailto:relation-donateur@institut-vision.org)  
Phone: 01 53 46 26 48

Seeing the world together is an opportunity.



F O N D A T I O N  
VOIR & ENTENDRE



[institut-vision.org](http://institut-vision.org)