VASCULI – TEST

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Vasculitis Overview:

- Vasculitis is a condition characterised by **inflammation of blood vessels.**
- It can affect **arteries, veins, and capillaries** throughout the body.
- The inflammation may result in **narrowing, weakening,** or **scarring of the blood vessels**, disrupting blood flow and potentially **leading to organ damage**.

Symptoms:

- Symptoms of vasculitis can vary widely depending on the size and location of the affected blood vessels.

Common symptoms:
- Fever
- Fatigue
- Weight loss
- Muscle and joint pain

Skin symptoms:
- Rashes
- Bruising
- Ulcers

Organ-specific symptoms:
- Headaches
- Vision changes
- Shortness of breath
- Cough
- Abdominal pain
- Kidney dysfunction

Neurological symptoms:
- Numbness
- Weakness
- Difficulty with coordination

What are the causes of vasculitis:

Vasculitis, characterised by **the immune system mistakenly attacking blood vessels**, stems from various triggers and risk factors:

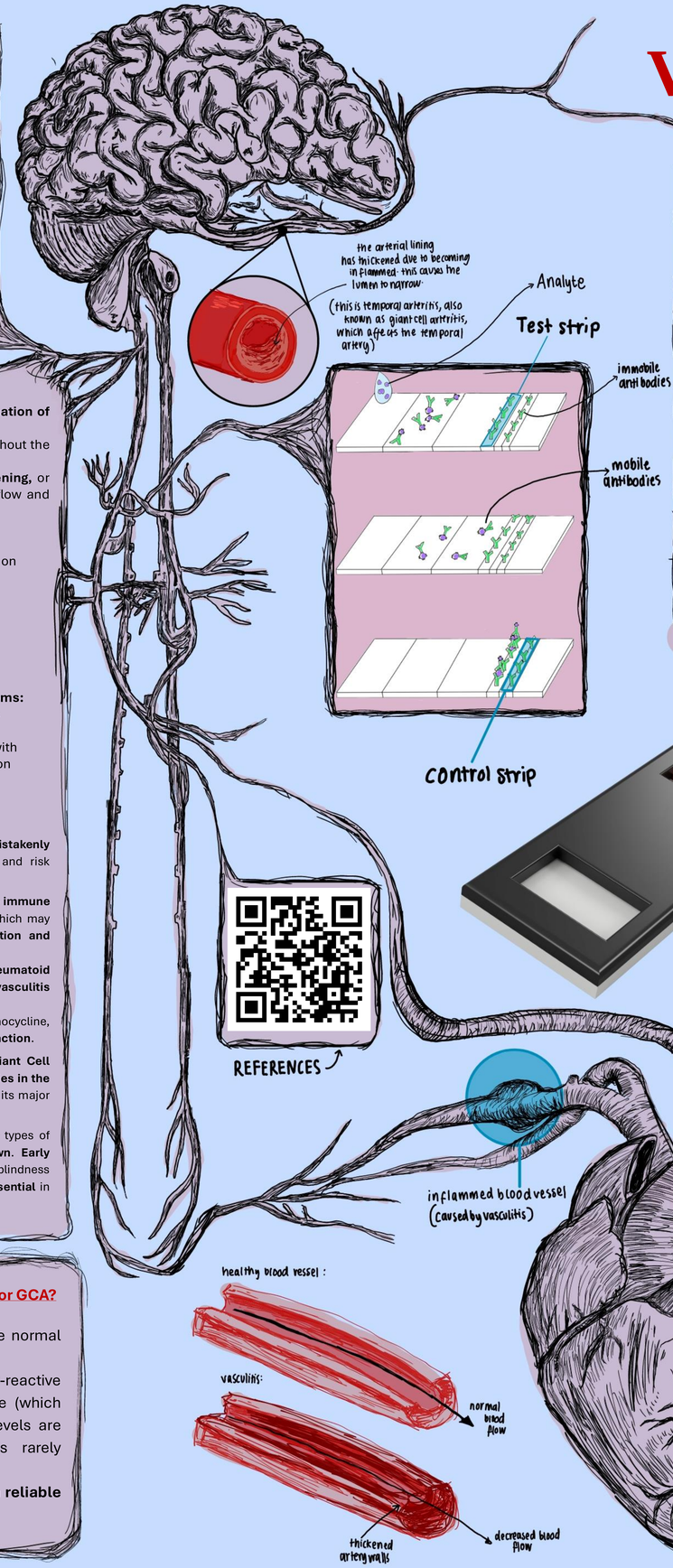
- **Infections,** such as Hepatitis B and C, can **provoke the immune system** to produce **excessive immune complexes**, which may **deposit in blood vessel walls**, **sparking inflammation and damage**.
- **Blood cancers** and **immune system** diseases like **rheumatoid arthritis, lupus, and scleroderma** can **contribute to vasculitis onset**.
- **Certain drugs**, including hydralazine, allopurinol, minocycline, and propylthiouracil, **can also induce vasculitis as a reaction**.

In people over **50**, **temporal arteritis**, also known as **Giant Cell Arteritis (GCA)**, is common. This condition **inflames arteries in the temples**, **neck, and scalp**, often **affecting the aorta** and its major branches to **the head, arms, and legs**.

Despite these known triggers, the **exact cause** of many types of vasculitis, including Giant Cell Arteritis, is still **unknown**. **Early treatment is crucial** to prevent severe complications like blindness or stroke, making **prompt diagnosis** and **intervention essential** in **managing vasculitis**.

Why use Serum Amyloid A as the biomarker for GCA?

- SAA levels can increase up to **83 times** the normal level in GCA patients.
- **Indicates inflammation** even when C-reactive protein and Erythrocyte sedimentation rate (which are two other inflammation biomarkers) levels are normal, a diagnostic advantage that is rarely reversed.
- **Rapid** and **significant rise** in SAA makes it a **reliable** and **specific indicator** of GCA.



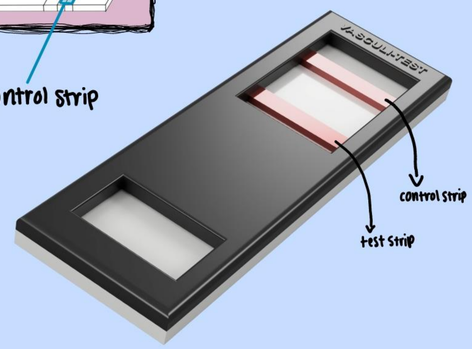
Our proposal:

Low cost, non-invasive, easy to use, efficacious.

Vasculi-test is a **one-use, early diagnosis tool** based on the principles of immunochromatography/ Lateral Flow Assay (LFA) testing. It uses **anti – Serum Amyloid A antibodies** which bind to Serum Amyloid A, a protein that increases in number in the early stages of the inflammatory process. Upon completion of the test, **the mobile phone app** can be used to capture an image of the test and control strip which will say the risk level based on the concentration of SAA in the blood, by looking at the strength of colour on the control strip using ImageJ software. It will inform a rheumatology specialist if the concentration is above expected.

The test kit comes with **sterile wipes**, **lancets**, **sample tube** (containing **Sodium Polyanethole Sulfonate**), **plasters** and the **LFA test**; everything would be **sanitised** and sealed in biodegradable packaging.

With future technology, better imaging can be developed to calculate a near-perfect numerical value for concentration. More research into GCA will allow for the **discovery of more specific biomarker**s which can be integrated into the same lateral flow test through **multiplexing capabilities** being developed by HDx.



Affordability and Availability

In the UK, Vasculi-test kits will be available through **GPs, hospitals, and pharmacies** with a doctor's recommendation, especially for **high-risk individuals**. Manufacturing these tests costs **$0.10** to **$3.00** each, not including development costs. **Monthly** testing is crucial for effective diagnosis. Only **0.01%** of people over 50 develop GCA. Assuming **0.1%** of over 50s will be screened, the **annual cost** of Vasculi-test, including packaging and sample tubes, is **approximately £900,000**.

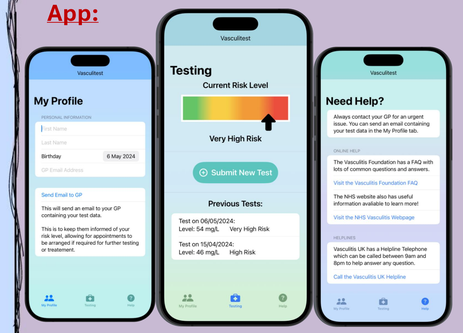
Given its affordability and potential for early diagnosis and treatment**, NICE approval for NHS coverage is likely**. This supports the NHS Long Term Plan's goal of 'helping people age well', ensuring **equitable access** and **improving outcomes for those at risk of vasculitis**. NHS coverage ensures **universal access to the test kits**, **reducing healthcare inequality**. The Vasculitest app makes it easy to diagnose GCA with lateral flow tests, and **community outreach extends access to populations with limited GCA awareness**, promoting early detection.

Target Audience

Regular LFA testing aims to **speed up diagnosis** and thus treatment, **increasing the chances of good recovery** for GCA patients as currently there is a median 7-month diagnosis delay.

This tool is aimed **towards older individuals** (the mean age of presentation is 71) who **bear the burden of multiple risk factors** including **smoking** and **past infections** like Hepatitis B and C, especially **those who have had GCA in the past year** as the chances of relapse are 83.9%.

App:



How does Vasculitest work?

1. **Clean finger** with **alcohol** and **prick** using **lancet**.
2. **Massage** drops of **blood** into **sample tube until it reaches black line**.
3. Turn sample tube **upside down 10 times**.
4. Add **drops to sample well** and **wait 10 minutes**.
5. Take **picture of test** and control strip on **Vasculi-test app** if **two strips appear** on test.
6. App tells you your **Vasculitis risk level**; a **green** result is **safe**, **yellow** is **slightly high** and **red** is **high**.

Dealing with Hook Effect

The app calculates **SAA concentration** by **comparing** test and control strip **intensities**. **High SAA levels** can cause a **decrease in control strip intensity**, often termed **the 'hook effect'**, leading to **inaccuracies**. **Diluting** the sample to **1% with saline** can resolve this, by aligning it with the analytical range. A **consistent dilution method** such as a **line marked on the sample tube,** similar to a volumetric flask**,** alongside clear patient instructions, **ensures accurate calculations by the app**.

Vasculitest trialling

- **Pre-clinical testing** evaluates the binding ability between SAA and its complementary antibody, by testing on cell and tissue cultures with SAA present. Additionally, these trials assess the optimal antibody concentration and ensure proper calibration of the accompanying phone app to accurately calculate concentration levels. Once approved by the MHRA for safety and efficacy, clinical trials can start.
- **Clinical trials**, in **Phase 1**, test the lateral flow test on healthy individuals to detect any potential false positives and any risk of infection. Subsequently in **Phase 2**, the test is administered to individuals at high risk of Giant Cell Arteritis (GCA) to evaluate its efficacy in diagnosis. Finally, in **Phase 3**, the test's efficacy is compared to existing alternatives to make sure the creation of this lateral flow isn't futile.
- **After licensing**, **trials** continue to monitor safety and efficacy. This includes regular patient check-ups in healthcare settings cross checked with the continuous assessment through the Vasculi-test app to ensure accurate and reliable results are being produced by the lateral flow test.