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Continuous Temperature Monitoring – Use in Fever Detection and Other Areas

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Body Temperature - Background

- A person's body temperature says a lot about their health!
- Several diseases including **COVID-19** are characterised by fever (an increase in body temperature) meaning that temperature monitoring is a vital tool in detection / diagnosis and consequently in preventing the spread of such diseases.
- Measuring body temperature can also be used track the course of a disease and so allow doctors to analyse the effectiveness of treatments and thus proactively adapt to improve outcomes.
- It's not all about diseases either – monitoring body temperature can assist in other areas such as helping a woman track her ovulation cycle and hence can be a powerful ally in helping couples understand the fertility cycle and so give them the best chance of conception.

Body Temperature - Background

- The temperature of the human body can vary depending on a number of factors including the age of the person, their level of (recent) physical activity, the time the measurement is taken and importantly where on the body the measurement is taken from.

- As such and contrary to popular opinion, there is no standard ‘normal’ temperature. Generally accepted temperature ranges for adults are presented in the table below:

Site of Measurement	Normal Temperature Range
Forehead (Temporal)	35.8 - 37.8°C (96.4 - 100.0°F)
Ear (Tympanic)	35.8 - 38.0°C (96.4 - 100.4°F)
Mouth (Oral)	35.5 - 37.5°C (95.9 - 99.5°F)
Armpit (Axillary)	34.7 - 37.3°C (94.5 - 99.1°F)
Anus (Rectal)	36.6 - 38.0°C (97.9 - 100.4°F)

Current ways to measure body temperature

- There are number of relatively simple ways to monitor temperature at a ‘point in time’ and these are outlined below with some of their advantages / disadvantages[1]:

Site of Measurement	Advantages	Disadvantages
Forehead (Temporal)	Easy of use	Highly inaccurate
Ear (Tympanic)	Ease and speed of use More closely estimates core temperature than oral Reasonable accuracy in children and adults	Accuracy limited by air or cerumen in ear canal
Mouth (Oral)	Ease of use Inexpensive	Hazard of broken glass / mercury Underestimates core temperature due to air / beverage exposure or probe placement
Armpit (Axillary)	Ease of use Inexpensive	Inaccurate in children and adults due to air exposure / sweat
Anus (Rectal)	Accurate core temperature at steady state	Uncomfortable Lags change in core temperature Potential transmission of stool borne pathogens

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Temperature changes in response to a fever

- Thermoregulation is a vital function of the autonomic nervous system in response to cold and heat stress. Thermoregulatory physiology sustains health by keeping body core temperature within a degree or two of 37°C [1].

- Our bodies have evolved to function at a body temperature of around 37°C as this enables normal cellular function while being hot enough to make us resistant to most fungal infections but not hot enough to increase our metabolic rate such that we need to eat all the time.

- Fever results from the release of inflammatory cytokines that act on the hypothalamus to elevate body temperature. It can be seen with any infection and is a sign of the body's immune system fighting the invading organisms.

- Viruses thrive at a temperature of around 37.5°C. As the immune system attempts to kill the virus and prevent it from multiplying, it raises the normal body temperature to place the virus outside of optimal conditions. This makes it easier for the immune system to rid the body of infection.

Temperature changes in response to a fever

- For practical clinical purposes a person is considered febrile or pyrexical if their body temperature rises above the following values:

Site of Measurement	Temperature (°C)	Temperature (°F)
Forehead (Temporal)	37.8	100.0
Ear (Tympanic)	35.8	100.4
Mouth (Oral)	37.5	99.5
Armpit (Axillary)	37.3	99.1
Anus (Rectal)	38.0	100.4

Current Diagnosis of COVID-19 (Corona)

- Currently there are two main ways to initially detect or screen people for the contagious virus COVID-19 without performing a formal test:
  - Elevated temperature due to fever i.e. temperature above the values provided in previous table.
  - Persistent dry cough
- We already know that there are a number of disadvantages with the current methods for temperature monitoring especially those that are quick and easy to use such as the infrared forehead thermometer[2]
- These include inaccurate readings due to recent physical activity, drinking or eating foods and the taking of concomitant medications. In addition each of them gives a single 'point in time' measurement without repeat testing (which often isn't viable).
- A **Continuous Temperature Monitor** (CTM) - a small non-invasive device which sits on the upper arm and gives temperature readings to a mobile App every 5 minutes could be a powerful tool in this field.

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Real time temperature monitoring – Detection of COVID-19

- A CTM that provides accurate temperature readings / trends over an extended period of time would have multiple advantages over the current systems including:
  - A trend over time would allow the user to see if their body temperature is (gradually) increasing indicating the onset of fever and so infection. This would allow them to 'self-isolate' quicker and so reduce the chance of infecting others.
  - Monitoring over an extended time reduces the chance of inaccurate results that are characteristic of any 'one time' measurement.
  - Some authority guidance documents recommend taking your temperature at least twice a day[3] with others suggesting using two separate temperature monitoring systems at a time in order to improve accuracy[4]. An accurate CTM would avoid these issues.

Real time temperature monitoring – Detection of COVID-19

- Global travel is now the norm with airports like London Heathrow having nearly 220,000 passengers land or depart every day[5].
- During viral outbreaks, attempts have been made to screen passengers showing signs of fever using infrared thermal imaging[6]
- This is effective up to a point but literature[7] has shown that the positive predictive value (PPV) of infrared thermoscanners for detecting fever is insufficient to actively detect febrile influenza cases among passengers.
- If passengers could readily provide a real time temperature profile on their Smart Device when passing through immigration this, allied with the thermoscanners could have huge benefits in detecting positive cases and avoiding false negatives.
- In addition, as the data would already be available this would prevent immigration officials having to perform temperature monitoring so reducing interaction and spread.

Real time temperature monitoring – Detection of COVID-19

- In the detection / diagnosis of COVID-19, a non-invasive device providing ‘real time’ temperature monitoring data and trends could be a powerful tool for:
  - **Users**: An accurate up to date temperature chart would allow them to see if their body temperature is increasing and hence take measures both to seek treatment options but to also consider ‘self-isolating’ at the earliest possible moment in order to reduce the chance of spreading the infection.
  - **Immigration:** If a passenger can provide a temperature profile for the past 10-14 hours to an immigration official or indeed the official can download the data direct from the device this would allow the rapid processing of cases without officials having to perform a possibly inaccurate ‘point in time’ test which also involves close interaction with the passenger.
  - **Hospitals:** If accurate temperature trends can be provided on arrival, this should allow healthcare professionals to more rapidly diagnose cases and so improve wait times / prioritise resources for the most needed cases.
  - **Businesses / Government Bodies:** If supplied to employees, this would allow users to detect any sign of fever at the earliest moment and so reduce the chance of spreading it to their colleagues.

Real time temperature monitoring – Diagnosis of other diseases

- COVID-19 may be at the front of the world's mind at this time but there are many other infectious diseases which are characterised by fever and diagnosis of many of these could benefit greatly from continuous rather than 'point in time' monitoring.

- Fever in lay terms is generally considered to be a 'high temperature' but, in some disease states the temperature can fluctuate considerably meaning a graphic temperature chart rather than point in time measurements can be indispensable to the clinician approaching and treating the febrile patient.

- Different diseases are often associated with a certain type of temperature curve so **easily** and **accurately** monitoring and tracking temperature over time as opposed to taking potentially inaccurate and laboursome point in time measurements can quickly point the clinician in the right direction when it comes to diagnosis. Faster accurate diagnosis results in faster targeted treatment which in the case of e.g. sepsis could be the difference between life and death.

Real time temperature monitoring – Diagnosis of other diseases

- In hospital settings, medical workers check the temperature frequently to form the temperature curve that doctors then interpret. If this function was performed by a simple non-invasive device which transmitted the readings to a mobile App this would:
  - Simplify this process considerably
  - Avoid unnecessary contact between patient and nurse
  - Free up nursing resource for other tasks
  - Avoid the use of often inaccurate existing temperature monitors
- In addition if a patient presented at hospital with a temperature curve from the point that they began to feel unwell (or before) this would be an even more powerful tool to a faster diagnosis and start of treatment.
- The following slides present different fever states where a trend from a CTM rather than a point in time temperature measurement would be invaluable in accurate diagnosis and treatment.

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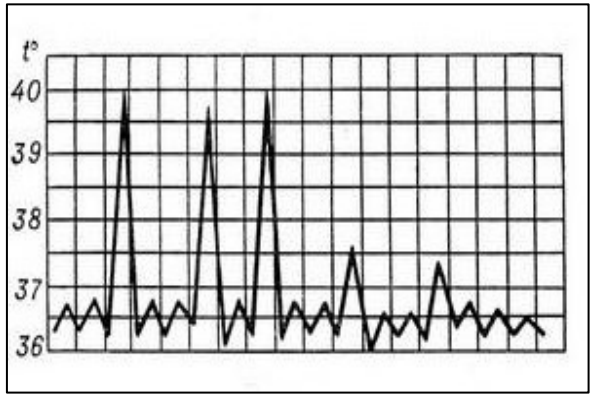
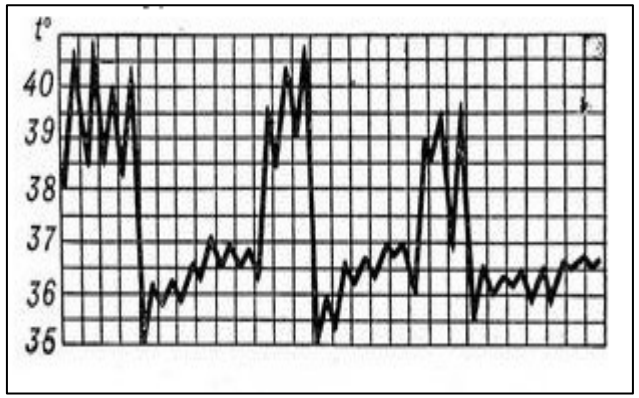
Real time temperature monitoring – Diagnosis of other diseases

- **Febris intermitens** (Intermittent Fever)[8]: Temperature rises to 39 / 40°C, with fluctuations resulting in drops below even 37°C sometimes for a day or more. Febris intermittens is a typical temperature curve for malaria but also occurs in infectious mononucleosis and cytomegalovirus infection.



- **Febris recurrens** (Recurrent Fever)[8]: Several days of fever alternate with days of normal temperature. Febris reccurens occurs in recurrent typhus, Hodgkin's disease (Pel-Epstein fever) and *Borrelia* infection.



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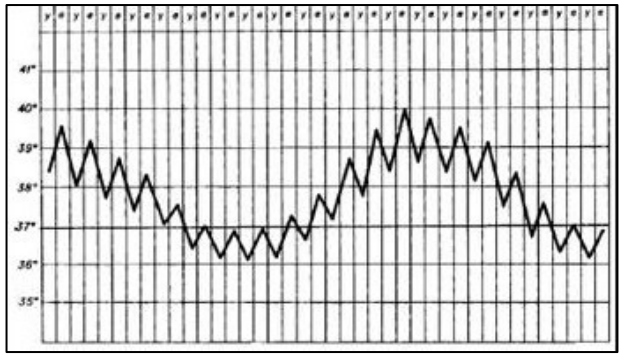
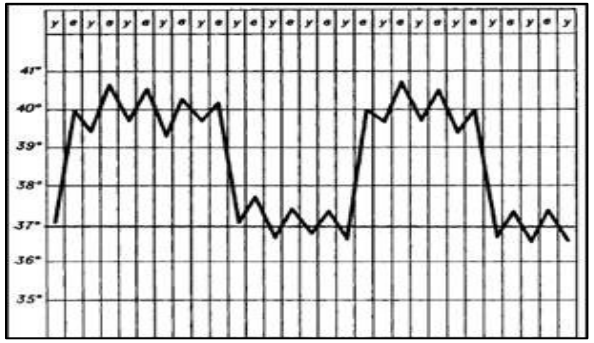
Real time temperature monitoring – Diagnosis of other diseases

- **Febris undulans** (Undulating Fever)[8]: Temperature gradually rises every day, sometimes reaching 39 / 40°C and then slowly falls, followed by a period of afebrile days until the onset of a new wave of febrility. Characteristic of lymphogranulomatosis, brucellosis. Such a second wave of fever occurs in acute viral infections such as haemorrhagic fever, polio etc



- **Febris irregularis** (Irregular Fever)[8]: One of the most common types of fever in children. The temperature curve shows various irregular fluctuations without any regularity. Occurs in flu, other acute viral respiratory infections, sepsis, bronchopneumonia, collagenosis, etc.



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Real time temperature monitoring – Diagnosis of other diseases

- All of the above fever states and others including **septic fever** (seen in sepsis and osteomyletis) and **hectic fever** (seen with tuberculosis and sepsis) display fluctuating temperature profiles.

- **Continuous temperature monitoring** providing accurate, real-time readings every five minutes in numerical and graphical form would be a formidable weapon in both the accurate diagnosis of and treatment monitoring of these potentially serious conditions.

Real time temperature monitoring – Pregnancy

- It is well known that checking and plotting basal (‘at rest’) body temperature is helpful to predict when a woman will ovulate.
- Before a woman ovulates, her basal body temperature will usually be about 36.1 - 36.4°C (97 - 97.5°F).
- During ovulation, progesterone is released, which brings on a slightly raised temperature a day or two later - usually by 0.5°F. This temperature then usually stays high until the next cycle begins.
- A woman is generally most fertile for 1-2 days either side of the egg being released so by charting temperature every day over several cycles, a pattern should emerge as to when fertility is greatest and so the best chance of conception will occur (or alternatively to know when not to have sex if you are trying to avoid falling pregnant)..

Real time temperature monitoring – Pregnancy

- Current methods require women to take their temperature every morning before getting out of bed and charting this themselves or using an App.

- This ‘point in time’ measurement approach has a number of limitations / disadvantages:
  - Inaccurate readings due to the limitations of the device (previously explained) and / or user error
  - Change in basal temperature by other factors such as stress, alcohol, disrupted sleep, shift work etc
  - It is onerous on the user as the measurement must be taken at the same time each day in the exact same way.

- A continuous temperature monitor would obviate the above disadvantages providing the user with not only an accurate daily trend but following repeated wear a larger dataset to better predict ovulation.

Real time temperature monitoring – Pregnancy

- Combine this accurate temperature dataset with data such as heart rate, sleep quality etc from other wearable devices plus information from user input and the potential to create using predictive analytics / artificial intelligence, a **personalised** dataset which could provide the user with prompts and advice to further increase the chances of conception is possible.

- It would be an extremely useful tool that can predict the ovulation date through temperature monitoring / other data and can then via an App, prompt or send notifications to:

    - Remind the woman on or just before her most fertile days to free her diary…….!
    - Prompt the woman before her most fertile days of the importance of maintaining a healthy lifestyle to increase her chances of conception so to:
        - Ensure she sleeps as well as she can
        - Eat healthily
        - Avoid alcohol
        - Avoid stressful situations……..

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Real time temperature monitoring – Foot complications in diabetes

- People with diabetes can develop many different foot problems often caused by nerve damage (neuropathy) but also by poor blood flow or changes in the shape of the feet or toes[9].
- These foot problems can range from the minor (calluses) to the serious (ulcers) which can in severe and unmonitored cases become infected and ultimately lead to amputation.
- Foot temperature monitoring has been suggested as a tool for predicting diabetes related foot complications for more than 25 years[10] since the onset of ulceration (tissue injury) will lead to an increase in temperature.
- Since then multiple studies have demonstrated the benefits of regular temperature monitoring in the prevention of foot ulcers. As an example, in three randomized controlled trials, the incidence of re-ulceration was reduced by 3–10-fold when patients used self-temperature assessment and standard of care compared to standard of care alone.[11-13]

Real time temperature monitoring – Foot complications in diabetes

- As the window to identify an increase in foot temperature indicating a potential ulcer is wide – 37 days prior to ulceration[14], patients do not need to monitor their temperature every day but do need to do it regularly. As such patient compliance is a key part of the success of this preventative measure.

- An accurate non-invasive continuous temperature monitor which connects to and automatically transmits the data to an App would be a useful tool for both users and healthcare professionals (HCP) alike as:
  - It is easy for the patient to use = increased compliance.
  - Avoids the already discussed disadvantages of 'point in time' thermometers = gives a more accurate data set;
  - It potentially allows the HCP to check the data remotely = saved time / resource / visits and additionally allows them to check patient compliance i.e. are they regularly performing agreed temperature checks.

Device Regulations in the US

- Any medical device will be regulated by FDA if it meets the definition in Section 201(h) of the Food, Drug, and Cosmetic Act[15]:

Per Section 201(h) of the Food, Drug, and Cosmetic Act, a device is:
An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

1. *recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,*
2. *intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or*
3. *intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and*

which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o).

Device Regulations in the US

- Medical Devices in the US currently fall into three categories:
  - **Class I** – Low risk to user. General controls are adequate to control it.
  - **Class II** – Medium risk to user. General controls plus special (specific) controls required
  - **Class III** – High risk to user. General controls and Pre-Market Approval (PMA) required.
- FDA classifies medical devices on the *intended use* of the device and its *indications for use*. As an example a scalpel is intended to cut tissue but a scalpel designed to cut cornea tissue will require different and more stringent controls than a standard scalpel.
- All three classes generally require **prior approval** from FDA before marketing via PMA, 510(k) or 'De Novo' application route.

Summary – Uses and Benefits of a Continuous Temperature Monitoring Device?

- Monitoring body temperature has multiple uses from the (self)-diagnosis of fever in diseases like COVID-19 to helping to predict ovulation date in order to increase the chances of conception.
- Currently available and easy to use systems are often inaccurate and mainly offer ‘point in time’ measurements which can result in issues with diagnosis / mis-diagnosis.
- A simple, non-invasive and accurate continuous temperature monitoring device which sits on the upper arm and sends real time temperature data to a mobile app which then displays that in trends over days / weeks could be a game changer in this field.
- Potential use for rapid self-diagnosis of COVID-19 and so self-isolation could be a powerful tool in reducing the spread of the infection.

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