# **Atopic Dermatitis Game**

## **Department of Bioengineering, Imperial College London**

Mohima Ahmed, Aidan Acquah, Anisha Malde, Yomna Genina and Nasreen Razak,

Jenna Stevens-Smith, Reiko Tanaka

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#### 1. Introduction

There are a large number of people who suffer from Eczema. For our BEng group project, we are working on developing a tool to educate children –aged 9 to 13- to learn the biology behind eczema, as well as how to deal with eczema symptoms and to prevent them from happening. We have chosen to deliver this information in the best way to capture their attention – in the form of a computer game (both website/mobile based).

The game will place particular emphasis on the effects of scratching, and the importance of using emollients/corticosteroids. We will make 4 levels of games with increasing difficulties (complexities), alongside tutorials, each with a different educational point. The idea of the game is that as the levels progress, we will go deeper and deeper into the skin layers, with tutorials, before each level, along the way to explain to the children what is going on.

**Overall objective of the project:** To develop an educational game for children aged 9-13 on the science behind Eczema as well as how to deal with and prevent Eczema symptoms.

## 2. Overview of the game

#### Level 0

**Learning objective:** To understand the "itch-scratch cycle" and the effects of scratching on itchiness and inflammation of skin.

**Level objective:** The players should stop the hand from excessive scratching of the skin.

The level consists of:

- a slapping hand
- a falling hand to scratch
- skin cells (the redness of the cells reflects the inflammatory level and the itchiness)

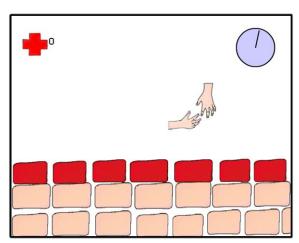


Figure 1: Current version of Level 0

**Rules:** The players control the horizontal movement of a slapping hand so as to block the falling hand trying to scratch the inflamed skin. The game will begin with the top layer of skin cells being a red colour to denote itchiness. Initially, the players should let the falling hand touch the red skin cell once — as some scratching can reduce itchiness — and this will reduce the redness of the cell. After allowing the falling hand to touch the red skin cell once however, they must prevent it from scratching the same skin cell again. If it does, the redness will increase and on the third touch, the cell will break away. This will then expose the layer of white cells beneath it, which if the hands touch, will become red and break away as well if the hand continues to touch. There will be a "itchy monster" character in the corner that will release more scratching hands if the cells break to express an increase in levels of itchiness.

**Success Scenario:** If at the end of the level (which lasts 30 seconds), the large majority of cells are a white or light red colour, and not too many have broken away, the player has "won" the level, as it corresponds to the player dealt with the itchiness well.

**Failing Scenario:** If however, at the end of the level (which lasts 30 seconds), the large majority of cells are a red colour, and too many have broken away, the player has "lost" the level.

**Point Accumulation:** The player will gain "health points" depending on the number of white cells at the end of the game. Health points will be useful in the last level of the game.

**Transition into next level:** Upon finishing this level, if the level is won, the player will move on to the next level which is focused on teaching the players about the need for/use of steroids. If the level is lost however, they need to restart it.

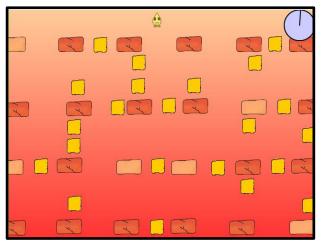
#### Level 1

**Learning objective:** To understand the importance of using steroids/emollients at the appropriate times and for the prescribed amount of time.

**Level objective:** To get the steroid/emollient avatar to the end of the maze.

The level consists of:

- An avatar that is either an emollient or a steroid
- A maze the avatar must go through.



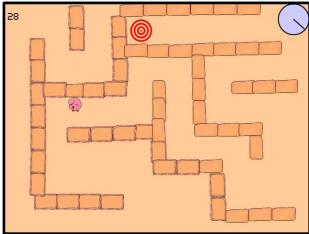


Figure 2a: Level 1 - Steroid Maze

Figure 2b: Level 1 – Emollient Maze

**Rules:** Level 1 will open with the steroid maze, to achieve the remission. The maze will be made of inflamed cells and healthy cells. The steroid avatar should be directed along the path to apply itself to the inflamed cells. Throughout the level, the steroid will start to fade and the player must press the spacebar to make it reappear, reflecting the cream finishing and the player must obtain a new tube after the length of time they've been using it. Certain "healed" cells may also become red once again (re-inflammation) and this is to

emphasise the importance of continuing to apply the steroid for the prescribed amount of time. At the end of the pre-allocated time, if the cells are mostly healthy, the steroid stage has been won and the player will move on to the emollient maze, corresponding to the maintenance therapy.

The emollient maze will be placed on a healthy patch of skin that has a path that covers the entire skin. The only way to reach the end of the maze is to cover the entire patch of skin and apply the emollient to all the cells. This reinforces the message that emollients should be used even if there is no inflammation and everywhere on the body.

**Success scenario:** If in the steroid level, 80% of the cells are healthy, the level is won. If in the emollient stage, the player applies emollient to all the cells before the time is up, the level is won.

**Failing scenario:** If in the steroid level, there are still many red inflamed cells left, the level is lost. If in the emollient level, the player doesn't apply emollient to all the cells before the time is up, they have lost.

**Transition into next level:** If the player fails the steroid maze level, they must repeat it until they win. If the player wins the steroid maze level, they will be moved to the emollient maze level. If they lose the emollient level, they will be moved to the steroid level – this emphasises the message that not using emollients for appropriate maintenance can lead to inflammation. If the emollient level is won, the player will proceed to Level 2.

#### Level 2

**Learning objective:** To understand the role of LEKTI to regulate the activity of KLK, which activates PAR2, leading to inflammation, and degrades corneodesmosomes, leading to barrier damage.

Level objective: To stop the degredation of corneodesmesomes. The level consists of:

- Active and Inactive KLK
- LEKTI
- Keratinocytes
- Corneodesmosomes
- PAR2

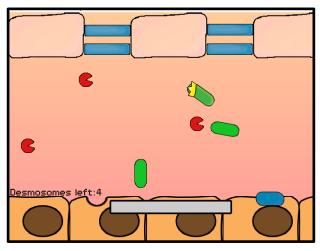


Figure 3: Current Version of Level 2

**Background information:** When the skin is scratched, it will damage the skin barrier, causing it to turn red KLK. When inactive KLKs are activated in a self-catalytic manner, active KLK causes desquamation of the skin as it breaks the binding proteins (corneodesmosomes). You can inactivate KLK by its inhibitor, LEKTI (note there is no way of controlling the amount of LEKTI). PAR2 is activated by active KLK and once this happens, the PAR2 produces inactive KLK and causes inflammation. Therefore KLK activity is appropriately regulated to avoid the excessive skin desquamation and inflammation, which are the two main causes of AD. In this case therefore, the main symptoms of Eczema are the thinning of the skin barrier and inflammation as a result of excessive

KLK activity. It is important to note that we still need some KLK activity to ensure the natural skin shedding process still takes place. This will be reflected in the level by having a new skin barrier being developed in the background.

**Rules:** The players will be controlling LEKTI and trying to inactivate the active KLK before they start destroyng too many links (corneodesmesomes) between the keratinocytes(skin cells). It will be made clear to the players, during the tutorial, you cannot control how much LEKTI is present; the aim of this level is to help them understand the role of KLK/LEKTI on Eczema. The players will also try to stop the active KLK from activating the PAR2 as, if activated, this produce more inactive KLK and this will in turn mean more active KLK is present resulting in inflammation. If the KLK touches the Corneodesmesome, it will start to crack and with every hit, it will weaken and eventually break off.

**Success scenario:** If there are still corneodesmosomes still present, then the level has been won.

Failing scenario: If there are no more corneodesmosomes present, the level has been lost.

**Transition into next level:** If level 2 is lost, the player will have to repeat it until they win. If level 2 is won, the player will be moved to the Boss Level.

#### **Boss Level**

**Learning objective:** To understand the interplay between skin desquamation, itchiness, treatment, and pH on Eczema.

**Game objective:** To try and maintain the right level of active and inactive KLK in reaction to external conditions and to stop the scartching of the skin.

The level consists of:

- Active and Inactive KLK
- LEKTI
- pH bar
- Skin cells and Corneodesmosomes
- Falling/slapping hands

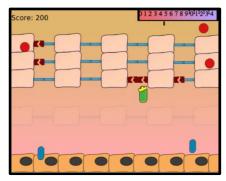


Figure 4a: Beginning stages of Boss Level

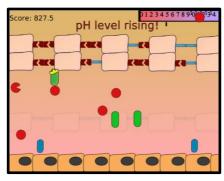


Figure 4b: Boss Level during Emergancy Mode

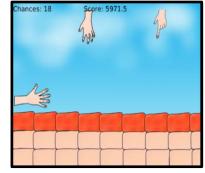


Figure 4c: Last stage of Boss Level

**Background Information**: The normal pH of skin is around 4.5. If the pH reaches 7.5, the enzymatic activity of the KLK increases and the enzymatic activity of the LEKTI decreases; this results in stronger activity of KLK relative to LEKTI.

**Rules:** This is the final and hardest level; the idea is that the extracellular space acts as the control system and there is a timer telling the player how long they have before the game ends (we recommend it would be around 2 minutes.)

Initially the players will be controlling LEKTI and trying to inactivate the active KLK before they start destroyng too many corneodesmesomes between the keratinocytes and causing inflammation. The aim here is to reinforce their understanding of the role of LEKTI and KLK on Eczema.

The pH of the extracellular layer will randomly increase at times and this increases the catalytic activity of the KLK; if this happens there will be an increased auto-activation of inactive KLK. From here:

- The increased KLK activity will mean increased probability of desquamation of the skin barrier, making the inter-epidermal layer more vulnerable to stimulants and pathogens.
- Stronger PAR2 activation will be triggered by the increased activity of KLK, and this will cause stronger inflammation.
- The increased PAR2 activation will cause more release of inactive KLK and LEKTI but the existing high active KLK means that chances of the inactive KLK being activated is increased. This makes it harder for the players to protect the corneodesmosomes from breaking and preventing inflammation.

If inflammation occurs, we call this part of the level to be in Emergency Mode. At this point, a scratching hand will start to appear just like level 0; initially, the players should let the falling hand touch the red skin cell once – as some scratching can reduce itchiness – and this will reduce the redness of the cell. After allowing the falling hand to touch the red skin cell once however, they must prevent it from scratching the same skin cell again. If it does, the redness will increase and on the third touch, the cell will break away. This will then expose the layer of white cells beneath it, which if the hands touch, will become red and break away as well if the hand continues to touch.

In addition to this, there will also be a falling hand with steroid on it, which players should allow to touch the skin cells as applying steroids when inflammation occurs is the correct thing to do.

We will also have a vortex in the top corner that will suck up the scratching hands if you can direct the scratching hand to it.

**Success scenario:** If when the timer ends, the corneodesmosomes are still intact or the large majority of the skin cells are still white, the player has won the level and the game.

**Failing scenario:** If the large number of skin cells are red/destroyed however at the end of the game, the level is lost.

**Transition:** If the level is won, the player has won the game and a congratulations screen will come up. If the level is lost, they will have to repeat it until they win.

## 3. Ongoing themes throughout the game

We still plan on doing a number of things:

- 1) There will be tutorial videos before each level to explain the science of atopic dermatitis to the children in simple language and to help them complete the levels.
- 2) There will be a points system, where the players will get scores depending on their performance throughout the game.

#### 4. Summary

To conclude, we have decided to code a game that will inform young children of the roles of LEKTI and the relationship of LEKTI with KLK. We also hope to emphasise the importance of using emollients/steroids as well as why scratching can be good or bad depending on the amount of it done.

## **Appendix**

## Overall Flow of the game

