Abstract

With the ever increasing number of infant mortalities in developing countries and the lack of adequate methods for neonatal urine collection, there is an immediate need for our product: The Diaper Detective. This pad will act as an early indicator for dehydration and bacterial infection by utilizing an array of chemical indicators, which will elicit a physical color change to the respective analyte that is present when the infant urinates. This paper based lateral flow device will provide healthcare professionals and everyday users with a simple, effective method of determining if further medical attention is needed for the infant.

Description of clinical need or problem, including background and current methods available

Our project represents the intersection of solutions to three pre-existing problems. First, infant mortality in developing nations makes up an estimated 32% of global deaths per year.[1] Second, current neonatal urine collection requires external adhesion of a plastic reservoir to an infant's genital area, which is both inconvenient and uncomfortable. Lastly, Pixie Scientific's Smart Diaper[2], the only product functionally similar to ours, hinges on the availability of smartphone technology primarily available only in developed nations. Our product bypasses this requirement making similar diagnostics readily available in resource-limited settings. Of the estimated 3.9 million annual neonatal deaths, 98% occur in developing countries and could be prevented with access to low cost, point-of-care diagnostics. Therefore, the primary focus of this project is to develop a neonatal diaper insert capable of indicating basic pathologies, such as severe dehydration, bacterial infection, and the like, which could be easily interchanged based on regional needs.

Design, including a discussion of the innovative aspects

This diaper insert will utilize lateral flow channels that guide the user's urine to the respective reactive regions where a color change will take place through means of a bioassay.

[1] "Children: Reducing Mortality." World Health Organization. World Health Organization, Sept. 2013. Web. 08 May 2014.
[2] "Pixie Scientific - Prevention for the 21st Century." Pixie Scientific - Prevention for the 21st Century. N.p., n.d. Web. 08 May 2014.

The comprehensive unit that will incorporate these aspects will be known as The Diaper Detective. This insert will utilize bioassays within the reactive regions similar to those that have been developed within urine dipsticks that are used in clinics today. This ensures accurate colorimetric results and allows for proper indication of numerous urinary analytes such as leukocytes, nitrites, bilirubin, pH, specific gravity, and more. In addition to this resource, our team has tested the feasibility of our product as a complete unit and has ensured absorbency utilizing sodium polyacrylate, functionality, and timely readout through testing. After performing several blinded reader studies, our technical feasibility has been confirmed with a specificity of 82% and a sensitivity of 55% for bacterial infection and a specificity of 99% and sensitivity of 100% for dehydration.

Some key product specifications than can be highlighted as advantageous are: the product does not require electricity, cold storage, advanced education to interpret, or a coupled device. The Diaper Detective also has the potential to be customizable to the primary health concerns of a specific region by utilizing multiple bioassays within the reactive regions of our device. For example, if a region had a history of child mortality caused by kidney complications, the device can be modified to detect excess proteins in the urine. This will result in a potential expansion of the diagnostic market available to developing countries.

After examining the potential for intellectual property for our product, we determined that the integration of lateral flow channels, using patterned barriers, into a pad is unique to our product. Due to the novelty of our idea, we currently have patent pending on the concept of “Lateral Flow Channels Within Diaper Insert For Urine Collection in Inexpensive Diagnostics” with application number 61985701. Our invention will utilize patterned, hydrophobic channels within a urinalysis device to collect and assess urine from the user. This method of lateral flow will allow directed movement of urine towards regions in which a bioassay can take place.

Evidence of a working prototype (results/graphics obtained with the designed solution)

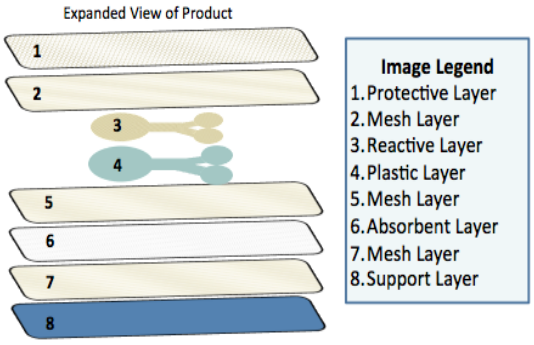


Figure 1: Expanded View of Prototype

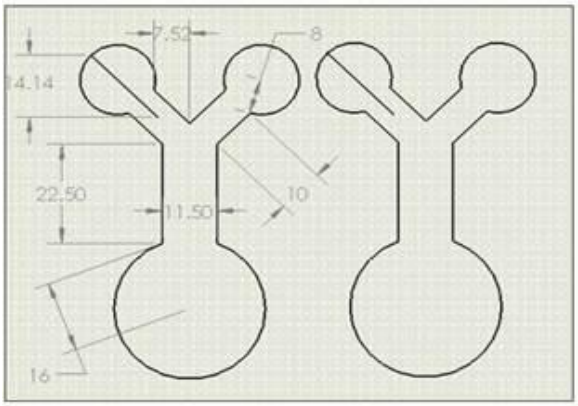


Figure 3: Dimensions of Prototype (in mm).

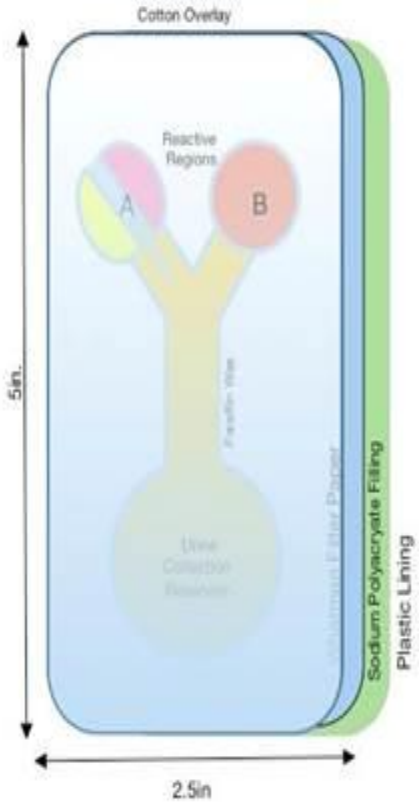


Figure 2: Collapsed View of Prototype

Reactive Region A, as labeled above in Figure 2, is impregnated with Bromophenol Blue. This will elicit a yellow color change if the urine is acidic and serve as an indicator of dehydration. Reactive region B, as labeled above in Figure 2, is impregnated with a Griess reagent. This reagent elicits a pink color change if nitrites are present in the urine, and serves as an indicator for bacterial infection.

To optimize the functionality of the lateral flow channels within our device, multiple prototypes were drawn using Crayola crayons to create a hydrophobic barrier system. These barriers were melted down to evaluate how effectively wax could contain and direct fluid flow within the channels and into the reactive regions. Due to the blockage of fluid flow, the implementation of wax barriers evolved to wax printing using paraffin wax as demonstrated in Figures 3 and 4.

Figure 3:

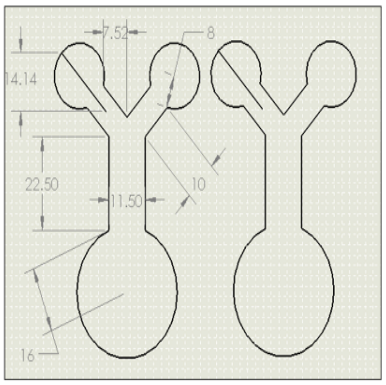
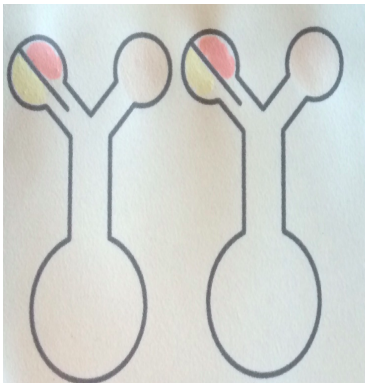


Figure 4:



This was achieved using a laser printer fitted with a paraffin wax cartridge capable of printing our SolidWorks drawing onto filter paper. Our final prototype resulted in the use of this alternative method, as we were able to standardize the precision and template for our design.

We evaluated the viability of the reactive regions with several ratios of synthetic urine mixed with nitrite ion standard solution and an acidic solution to determine if our expected results would take place. Based on a study done by 50 blinded readers, we were able to present the below statistics. Blinded readers were asked to identify colorimetric readouts for four different solutions on four different prototypes (Appendix 3). Based on the blinded reader results for detecting bacterial infection and dehydration, the values for specificity and sensitivity were calculated.

	Nitrites	**Without Nitrites**
Yes Change	55	18
No Change	45	82

Specificity: $\frac{82}{100} = 82\%$

Sensitivity: $\frac{55}{100} = 55\%$

	Dehydration	**Without Dehydration**
Yes Change	100	1
No Change	0	99

Specificity: $\frac{99}{100} = 99\%$

Sensitivity: $\frac{100}{100} = 100\%$

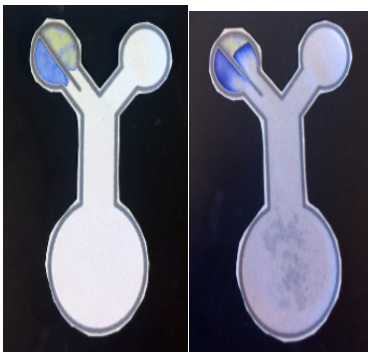
For the colorimetric aspect of our device, we optimized the bioassays taking place within the reactive regions through extensive experimentation and testing. The region representing dehydration utilizes a detection of pH within the fluid as well as specific gravity. The pH analysis is done by impregnation with bromophenol blue to elicit a yellow color change if the urine is acidic. Specific gravity represents the density of urine to water and can be detected based off of a change in pKa of a pretreated electrolyte (in our case poly methyl vinyl ether-alt-maleic acid) in relation to the ionic concentration of the urine. This is then jointly used with bromophenol blue to elicit a yellow color change when specific gravity is too high. This method of detecting specific gravity has been proven to work by researchers, however, due to limited resources we are in the process of optimizing the colorimetric readout. Finally, for the detection of nitrites, we have utilized a common method known as the Griess test. For this chemical reaction, the sulfanilamide reagent (Griess reagent) is converted to a diazonium salt by present nitrites in the sample. The diazonium salt is then reacted with a diazonium salt to form an azo colored dye with a pink color. The degree of pink color directly corresponds to the amount of nitrites in the urine.

After optimizing the colorimetric readouts within our device, a blind study was conducted with 50 participants to validate the technical feasibility of the diagnosis. They were asked to observe 4 different reaction scenarios listed in the table below:

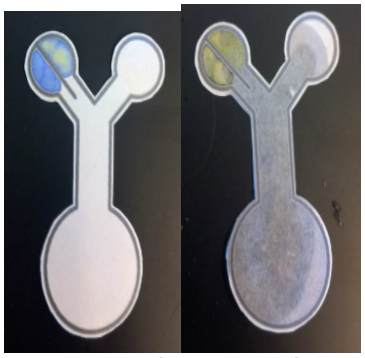
Scenario 1	Control
Scenario 2	Dehydration
Scenario 3	Bacterial Infection
Scenario 4	Dehydration and Bacterial Infection

Below are the visual representations of the expected readouts of the 4 scenarios.

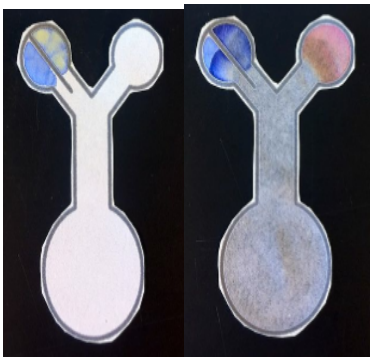
Scenario 1: Before and After



Scenario 2: Before and After



Scenario 3: Before and After



Scenario 4: Before and After

Dehydration is characterized by urine with a pH level lower than 4.6. We tested pH at different levels and in Figure 8, we were able to obtain standardized readouts for different increments. In addition to this, we were able to demonstrate that at trace levels of nitrites present in the urine, a pink color change was elicited indicating bacterial infection. To prove this, we tested different nitrite concentrations shown in Figure 9 below.

Figure 8:

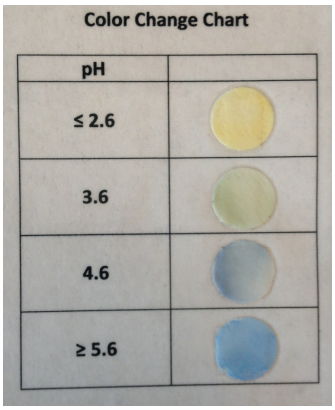
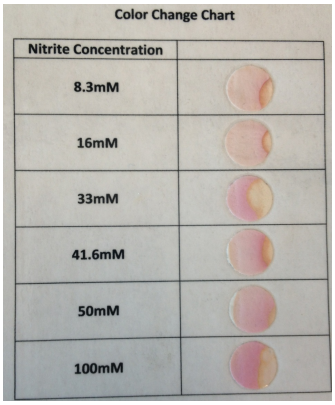


Figure 9:



Supplementary Video Link: http://www.youtube.com/watch?v=VzFio1Wfwe0

The Procter & Gamble Company
Mason Business Center
8700 Mason-Montgomery Road
Mason, OH 45040
www.pg.com

May 29, 2014

To: DEBUT 2014 Challenge Organizers

Subject: "Diaper Detective" – University of California, Riverside (UCR), Undergraduate DEBUT 2014 Competition

I was introduced to this innovative undergraduate design team and their project by a colleague and a fellow member of the American Institute of Medical and Biological Engineering. After following their progress over the past few months I am delighted to add my support for the "Diaper Detective" project, and the student team who developed this product, and to wish them success in the upcoming DEBUT 2014 competition.

As a Global R&D and Innovation Executive at Procter & Gamble, I have the opportunity to review inventions and innovation around the world. In this role, I encourage serious consideration for commercializing projects that demonstrate masteries of fundamental sciences and engineering principles, and have the potential to make a difference in peoples' lives. The "Diaper Detective" is an excellent candidate for such consideration. The team has creatively demonstrated that they understand the important R&D steps needed to go from idea to market and the related business development program. Specifically, they clearly understand the consumer and market needs, have identified a robust technical strategy, and led the required product design and qualification action plan to bring the idea to life. They have effectively assessed the project's intellectual property potential, tested the invention for validations, and effectively established external Open Innovation connections to expedite the journey to market.

Overall, it is rare to see the level of maturity and mastery of the science, engineering and innovation principles that has been exhibited by these undergraduate students. For these reasons and for the project leadership demonstrated by these young ladies on this novel, broadly relevant and affordable product idea, The Procter & Gamble Co. has taken interest in the design and intellectual property of the device.

Net, I enthusiastically support the efforts of the UCR team and their product, the "Diaper Detective", as they compete in the Debut 2014 Challenge.

Sincerely,

Ghebre E. Tzeghai, Ph.D.
Global R&D and Innovation Executive
The Procter & Gamble Company - Tzeghai.ge @pg.com