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MATH 2590 – Thinking Mathematically
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PODCAST ON KIDNEY AND MATH

KIDNEY FUNCTION AND TRANSPLANT - AND ITS CONNECTION WITH MATH

<u>Introduction:</u>

Hello and welcome to our first podcast for Math 2590. This is Sarah Tang and Caroline Wadid; we are going to talk about kidney function and transplant. Before we begin, it is important to know that each person has two kidneys; the kidney is a bean-shaped organ, the size of a fist, and its main function is to filter the blood from waste products and excess water; the waste then leaves the body in the form of urine [1]. A human being can live normally with only one kidney operating. However, serious health problems can occur to individuals if less than 25% of the kidney is functioning, and if it drops to 10 – 15 %, then one needs either blood-cleansing treatments (such as dialysis) or a kidney transplant [1]. Statistics reveal that 11.5% of adults in the states suffer from some kind of a chronic kidney malfunction.

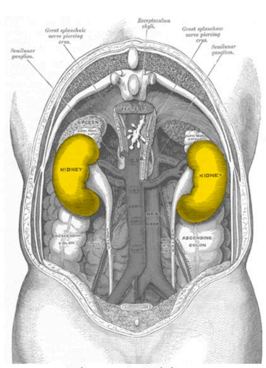


Figure 1: Kidney
(Source: http://en.wikipedia.org/wiki/Kidney)

Have you ever imagined that a medical procedure, such as kidney transplant, has connection with math? Indeed, it does, but before we get into the math behind this procedure, it should be noted that the most common causes of a chronic kidney disease (which might lead to the need for kidney transplant) are diabetes and high blood pressure [2]. The indication for kidney transplantation is End-Stage Renal Disease (ESRD), regardless of the primary cause.

We, nursing students and teachers, are not surprised about the way math is involved in this procedure. In this particular assignment, we will discuss two specific ways in which math is involved in the processes related to kidney function and transplant. Math is used first to ***diagnose*** a malfunctioning kidney through blood tests that reveal the estimated glomerular filtration rate (eGFR), which is calculated to assess the function of a kidney and it corresponds to the percentage of kidney function available. Secondly, we will discuss the optimization method used to match suitable kidney donors with patients. It is important to know that a kidney donor must be matched with a recipient and that there are some factors that come into play when finding a match. In this project, we will only focus on blood-type compatibility.

Kidney function and the eGFR:

The kidney is made up of millions of units known as nephrons; each of which consists of a small filter called glomerulus; this filter separate waste products and excess water from the blood, and lead them through tubules to the bladder so they are eliminated under the form of urine [2] (please see figure 1)

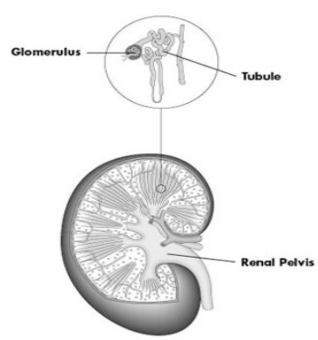


Figure 1: structure of a kidney
(Source: The kidney foundation of Canada; http://www.kidney.ca/Page.aspx?pid=318)

The eGFR, or estimated glomerular filtration rate is the volume of filtered blood flowing per unit time. The eGFR is a test that is used to monitor kidney function to detect early kidney damage, and is calculated by ordering a creatinine test. This test is reliable as the calculations give a good estimation of the reduced renal function. According to the national kidney foundation (NKF); an eGFR below 60ml/min suggests that kidney damage has occurred [3]. Please refer to table 1 for a brief overview of the calculations and their meaning:

Table 1: eGFR values and the level of kidney damage

KIDNEY DAMAGE STAGE	DESCRIPTION	GFR	OTHER FINDINGS
1	Normal or minimal kidney damage with normal GFR	90+	Protein or albumin in urine are high, cells or casts seen in urine
2	Mild decrease in GFR	60-89	
3	Moderate decrease in GFR	30-59	
4	Severe decrease in GFR	15-29	
5	Kidney failure	<15	

Glomerular filtration rate (GFR) can be calculated using the following formula [4]:

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

If the eGFR was more than 60; doctors usually order more tests to ensure that there is no decreasing kidney function and that everything is normal; this includes; looking at the urine (for pH, blood and protein); for wastes and toxins in the blood; the blood pressure (high blood pressure is indicative of potential problems) and others… If the eGFR levels are less than 60, there is a chronic kidney disease and treatment becomes essential.

Moreover, eGFR can be calculated from the creatinine data (mL/min/1.73m^2) and other data. As figure 2 shows, there have been many calculations and equations developed (each is used under different conditions (as in health conditions) or based on available data and ethnic backgrounds)**:**

Table 44. Equations Developed to Predict GFR in Adults Based on Serum Creatinine

Equation Author, Year (No. of Subjects)	Equation	Studies Reviewed (Abstracts)*
Cockcroft-Gault Equation Cockcroft,[121] 1976 (N = 236)	$C_{Cr}\,(\text{ml/min}) = \frac{(140 - Age) \times Weight}{72 \times S_{Cr}} \times (0.85 \text{ if female})$	58 (5)[a]
MDRD, Serum Variables Levey,[17] 1999 (N = 1,070, 558 in validation set)	$GFR\,(\text{ml/min/1.73 m}^2) = 170 \times (S_{Cr})^{-0.999} \times (Age)^{-0.176} \times (SUN)^{-0.170} \times (Alb)^{+0.318} \times (0.762 \text{ if female}) \times (1.180 \text{ if black})$	1 (6)
Jelliffe Equation, 1973 Jelliffe,[130] 1973 (No data)	$C_{Cr}\,(\text{ml/min}) = \frac{98 - 0.8 \times (Age - 20)}{S_{Cr}} \times (0.90 \text{ if female})$	15 (1)
Mawer Equation Mawer,[131] 1972 (N = 16)	Men: $C_{Cr}\,(\text{ml/min}) = \frac{Weight \times [29.3 - (0.203 \times Age)] \times [1 - (0.03 \times S_{Cr})]}{(14.4 \times S_{Cr})} \times \frac{Weight}{70}$ Women: $C_{Cr}\,(\text{ml/min}) = \frac{Weight \times [25.3 - (0.175 \times Age)] \times [1 - (0.03 \times S_{Cr})]}{(14.4 \times S_{Cr})} \times \frac{Weight}{70}$	13 (1)
Hull Equation Hull,[132] 1981 (N = 103, 144 measurements)	$C_{Cr}\,(\text{ml/min}) = \left(\frac{145 - Age}{S_{Cr}} - 3\right) \times \frac{Weight}{70} \times (0.85 \text{ if female})$	12
Jelliffe Equation, 1971 Jelliffe,[122] 1971 (No data)[b]	Men: $C_{Cr}\,(\text{ml/min}) = \frac{100}{S_{Cr}} - 12$ Women: $C_{Cr}\,(\text{ml/min}) = \frac{80}{S_{Cr}} - 7$	7
Reciprocal Serum Creatinine Equation	$C_{Cr}\,(\text{ml/min}) = \frac{100}{S_{Cr}}$	7 (1)
Gates Equation Gates,[133] 1985 (N = 90, 100 measurements)	Men: $C_{Cr}\,(\text{ml/min}) = (89.4 \times S_{Cr}^{-1.2}) + ((55 - Age) \times (0.447 \times S_{Cr}^{-1.1}))$ Women: $C_{Cr}\,(\text{ml/min}) = (60 \times S_{Cr}^{-1.1}) + ((56 - Age) \times (0.3 \times S_{Cr}^{-1.1}))$	6
Bjornsson Equation Bjornsson,[134] 1983 (N = 50, validation set)	Men: $C_{Cr}\,(\text{ml/min}) = \frac{27 - (0.173 \times Age) \times Weight \times 0.07}{S_{Cr}}$ Women: $C_{Cr}\,(\text{ml/min}) = \frac{25 - (0.175 \times Age) \times Weight \times 0.07}{S_{Cr}}$	6
Articles with equations reviewed in ≤3 studies:	Agarwal,[135] Davis-Chandler,[136] Edwards,[137] Hallynck,[138] Levey,[17,18] Mogensen,[139] Nankivell,[140] Robinson,[141] Rowe,[142] Salazar-Corcoran,[143] Sanaka,[144] Siersbaek-Nielsen,[145] Toto,[146] Tourgaard,[147] Walser,[181] Yukawa[148]	26 (3)
	Total number of articles examined:	**64**

Includes equations whose initial development was to predict creatinine clearance subsequently validated as predictors of GFR.

* Total number of studies reviewed for each equation, including abstracts, in parentheses. Individual studies that examined multiple equations are included in the count for each equation.

[a] Includes studies that corrected or did not correct for both gender and body surface area.
[b] Equation presented without a demonstration set.

Abbreviations and units: C_{Cr}, creatinine clearance; S_{Cr}, serum creatinine in mg/dL; Age, in years; Weight in kg; SUN, serum urea nitrogen in mg/dL; Alb, serum albumin in g/dL

Figure 2: Equations developed to predict eGFR in adults
(Source: © 2002 National Kidney Foundation, Inc
http://www.kidney.org/professionals/kdoqi/guidelines_ckd/p5_lab_g4.htm)

We can clearly see here that math is indispensible for interpreting results and for the proper assessment of kidney function.

Case study:

(Modified from source: © Copyright 2007 American Kidney Fund; http://www.kidneyfund.org/assets/pdf/gfr-fact-sheet.pdf)

In many cultures, the eGFR factor is calculated differently; in the case of African Americans for example, the eGFR result has to be multiplied by a factor of 1.2 for a more accurate interpretation.

Norma is a 5 year old African American women; her blood test revealed an eGFR of 52. Use the data in table 1 to assess the kidney function of Norma.

Answers:

Actual eGFR result: 62.5, which means Norma has a normal kidney function and the doctor should do more tests to ensure there is no potential problems.

Kidney transplant and blood type:

A successful kidney transplant requires a pair of a matching blood type between donor and recipient. The participants are usually siblings or close family relatives [5]. Unfortunately, it is very hard to find a perfect match because the chances that their kidneys will be compatible are low. In fact, there are always many people on the waiting list, simply waiting to donate or to receive a kidney; and even those who are healthy and are willing to help their loved ones with this process might still be rejected due to incompatibilities[5].

So how do we find a match? In order to find a match, the first step is to start with figuring out the blood type of the donor and the recipient. For example, if a female patient has blood type O, she can only accept a kidney from a donor with blood type O[7]. Even if her closest family members are willing to donate a kidney, it would be a mismatch if their blood type is different. The reality is that many people die waiting for a donor with a perfect match.

If the first step failed because there was a blood mismatch, then the next step is to wait for a deceased donor or someone who just passed away that is willing to donate his/her kidney[6]. It is important to keep in mind that live donor kidney grafts tend to perform better than those from deceased donors. Again, once there is a mismatch, which means that the kidneys were incompatible, the plan is automatically dismissed and the patients are usually sent home[8]. Sending patients home might not be the best solution because there will always be another pair with a mismatch who cannot produce a transplant that **can still be cross-matched with another pair**; and if a donor is willing to donate his/her kidney to their relative or their friend, who is not a match, **that person can still donate his/her kidney to another recipient who is a match**[8/9]. This kidney roundabout procedure is step three *(please refer to figure 3 below)* and is referred to as the Kidney Paired Donation program (KPDP) [7]. In a kidney paired donation program, a potential recipient and a willing, but incompatible donor, are cross-matched with another recipient and a willing incompatible donor. Through this program, donors who are incompatible with their recipients can still help their loved ones get a kidney by getting a match with another incompatible pair[7]. This creates a win-win situation for everyone.

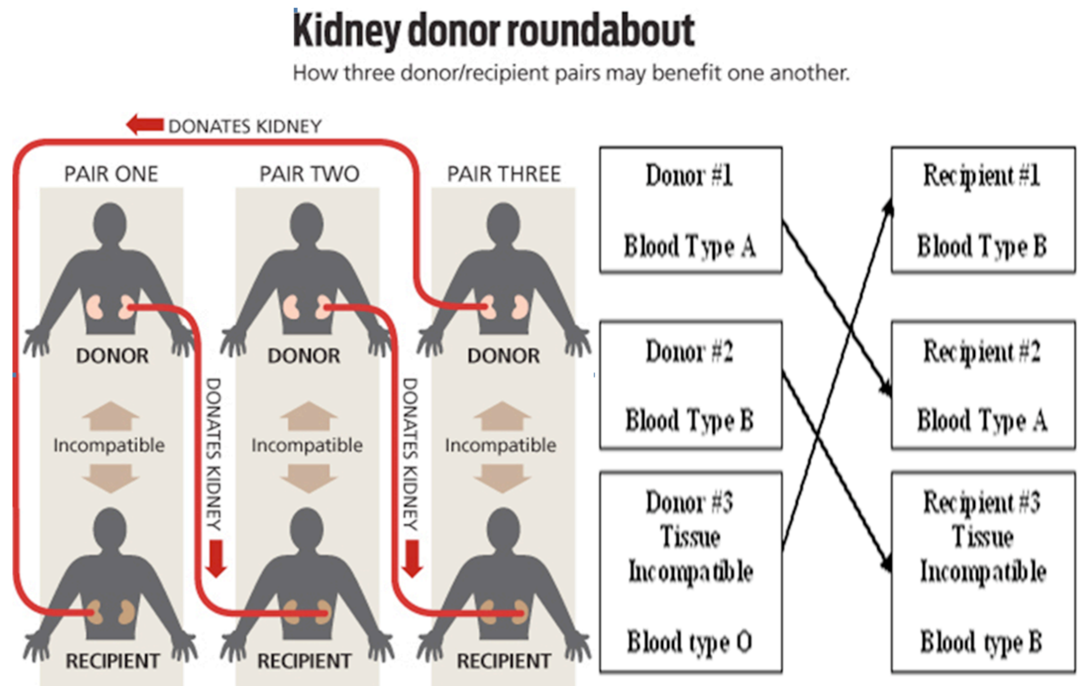


Figure 2: Kidney donor roundabout
(Source: Paired Kidney Exchange Program. http://www.hopkinsmedicine.org/transplant/Programs/InKTP/kidneypaireddonation.html)

The basic idea of matching pairs, is that the first donor can donate his/her kidney to the second recipient, and the second donor can donate his/her kidney to the third recipient, and the third donor can donate his/her kidney back to the first recipient. In other words, the incompatible pair will be matched with other pairs in such a way that swapping is beneficial.

A pair of donor and recipient with different blood types may have many potential matches[8]. For example, a type O donor can donate his/her kidney to thousands of recipients because type O is a universal blood type, which can match most blood types (such as O, A and B). On the other hand, type O recipients can only accept from type O donors[7]. Here is one place math plays an important role through optimization. Optimization is the branch of mathematics that calculates which choices will offer the best results from a limited resource. This method is based on a matching algorithm from the ***graph theory***[5/7]**.** The graph theory involves the construction of graphs consisting of nodes (or circles) and edges (or lines) in the purpose of making connections[8] *(please refer to figure 4 in the next page).*

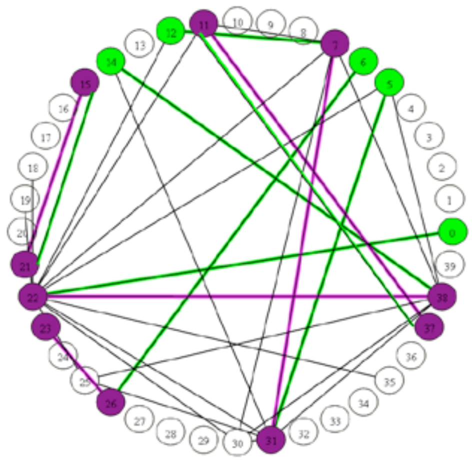


Figure 3: Matchmaking for kidneys through the graph theory
(Source: American mathematical society; Matching Vital Needs http://www.ams.org/mathmoments/mm75-kidney.pdf)

In this graph, the incompatible pair is a small circle, and the edge is the line connecting the circles. The incompatible pair can be connected to another incompatible pair by a line. Each line represents a potential kidney transplant. The graph shows the suboptimal matching (in purple) and an optimal matching (in green).The graph is completed by connecting all the circles. The purpose of the graph is to find the maximum amount of matches because once a circle has been connected twice, other possibilities will be withdrawn automatically[8]. Again, the goal is to find maximum matches without wasting willing donors.

Exercise:

Now it is your turn to draw the graph. This exercise is a very simplified form of the graph theory. Its goal is to give you an idea of how they match pairs in a way that satisfies most of the patients in need of kidneys. In order to complete this exercise, you will need to refer *the Red Blood Cell Compatibility Table* shown below in figure 5.

Red blood cell compatibility table

Recipient	Donor							
	O−	O+	A−	A+	B−	B+	AB−	AB+
O−	✓							
O+	✓	✓						
A−	✓		✓					
A+	✓	✓	✓	✓				
B−	✓				✓			
B+	✓	✓			✓	✓		
AB−	✓		✓		✓		✓	
AB+	✓	✓	✓	✓	✓	✓	✓	✓

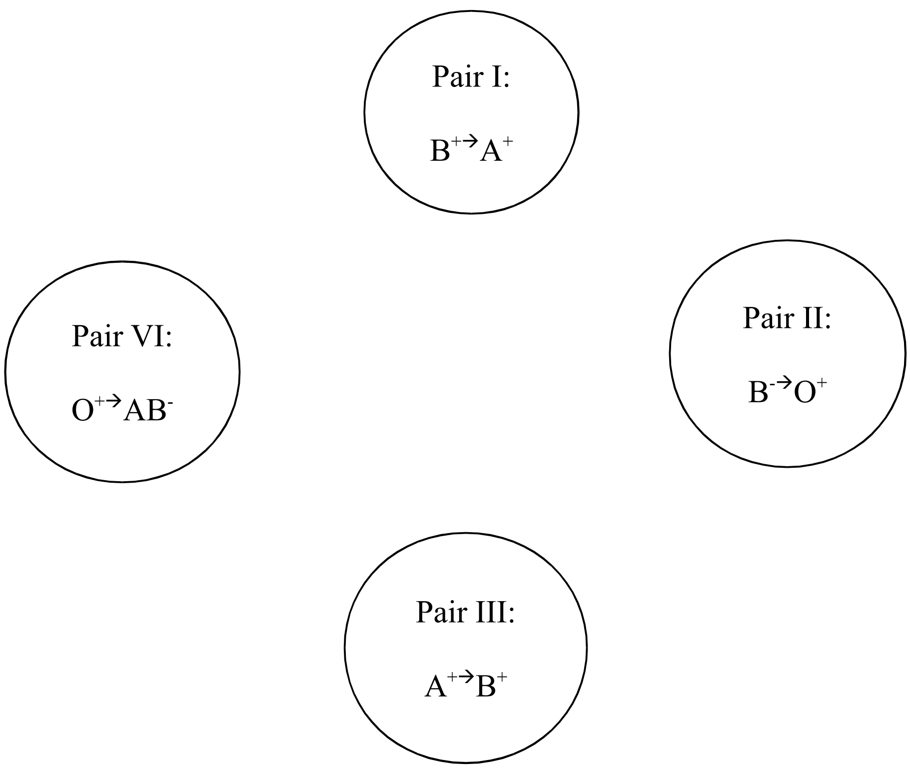
Figure 5: Blood Type
(Source: http://en.wikipedia.org/wiki/Blood_type)

- First, look at the donor/recipient blood type information below

Donor-Recipient	**Donor Blood Type**	**Recipient Blood Type**
Pair I	B^+	A^+
Pair II	B^-	O^+
Pair III	A^+	B^+
Pair IV	O^+	AB^-

Note: According to the Red Blood Cell Compatibility Table above, all these pairs are incompatible.

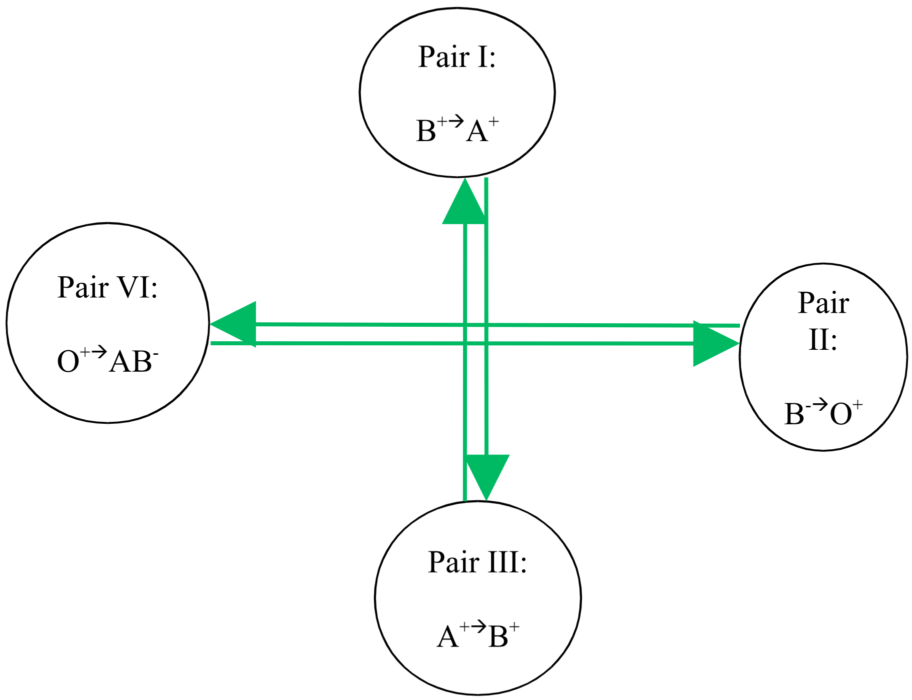
- Second, draw a circular graph with 4 nodes, each node representing a pair.



- Third, look at the recipient/donor blood types and then try to match them. To make it easier, let us draw a table that shows all the possibilities.

Donor Blood Type	**All** Possible Match	Possible **Recipients**
D_1: $\mathbf{B^+}$	B^+, AB^+	$\mathbf{R_3}$ (B^+)
D_2: $\mathbf{B^-}$	B^+, AB^+, B^-, AB^-	$\mathbf{R_4}$ (AB^-)
D_3: $\mathbf{A^+}$	A^+, AB^+	$\mathbf{R_1}$ (A+)
D_4: $\mathbf{O^+}$	A^+, B^+, O^+, AB^+	$\mathbf{R_2}$ (O^+)

- Fourth, connect all possible matches.



<u>Conclusion:</u>

When one first hears about kidney diseases, or about a person with malfunctioning kidneys he thinks that it is nothing but a medical problem. As our project discussed, diagnosing a malfunctioning kidney, or finding the right donor for transplantation is a sophisticated process. This process involves more than medicine, it involves **Mathematics**; although at first it seems to be a medical problem, it ends up being a combination of a medical and a mathematical issue, and this proves that math is implicated in everything in our life. Unfortunately, not all people are aware of this fact.

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