INTRODUCTION

Immunity is the state of protection against infectious disease conferred either through an immune response generated by immunization or previous infection or by other non-immunological factors ***(Baxter, 2007).***

Infectious agents such as viruses, bacteria and parasites are responsible for the major childhood diseases. Viruses cause measles and polio while bacteria cause tetanus, diphtheria and pertussis. Vaccinations work through stimulating the immune system, the natural disease-fighting system of the body. The healthy immune system is able to recognize invading bacteria and viruses and produce substances (antibodies) to destroy or disable them. Immunizations prepare the immune system to ward off a disease. To immunize against viral diseases, the virus used in the vaccine has been weakened or killed. To only immunize against bacterial diseases, it is generally possible to use a small portion of the dead bacteria to stimulate the formation of antibodies against the whole bacteria. In addition to the initial immunization process, it has been found that the effectiveness of immunizations can be improved by periodic repeat injections or "boosters ***(Janeway et al., 2001).***

Classification of vaccines:

1) Live attenuated vaccines
2) Killed and inactivated vaccines
3) Subunit vaccines

(Baxter, 2007)

1) Live attenuated vaccines:

The virulence properties of the virus are reduced so that it does not cause disease in healthy individuals. The attenuated vaccine virus multiplies to a limited extent in host tissue and induces an immune response similar to wild virus infection in the majority of subjects. Live vaccines are generally very effective and induce long-lived immunity ***(Minor, 2015).***

2) Killed and inactivated vaccines:

The term 'killed' is generally used for bacterial vaccines and the term 'inactivated' for viral vaccines. Generally these organisms remain intact and whole. They generate an immune response (to a broad range of antigens) but cannot cause an infection because they are dead and so cannot reproduce ***(Lee et al., 2012).***

Subunit vaccines:

They can be further categorized as follows.

- ***Toxoid vaccines***

Toxoid vaccines induce antibodies that neutralize the harmful exotoxins released from these bacteria ***(Plotkin, 2014).***

Recombinant vaccines

They are made using a gene from the (disease-causing) pathogen as an antigen, which generates a protective immune response ***(Nascimento and Leite, 2012).***

- ***Polysaccharide and conjugate vaccines***

Contain carrier proteins that are chemically attached to the polysaccharide antigens. Attaching relatively non-immunogenic polysaccharides to the highly immunogenic carrier proteins means that by activating a T-cell response, conjugate vaccines induce both high-affinity antibodies against the polysaccharide, and immune memory ***(Peeters et al., 1991).***

Other subunit vaccines:

They are made from 'chunks' of the outer membrane of the cell. They contain a range of antigens ***(Moyle and Toth, 2013).***

AIM OF THE WORK

The aim of this work was to assess the vaccination status in Al Qualaubya Governorate to detect children with improper vaccination status and to increase children caregiver awareness about the children vaccination needs.

Research questions

Are people giving their children their vaccines according to the schedule in Al Qualaubya Governorate? Are they giving them extra vaccines? And if they are satisfied with the vaccination services introduced to them?

Hypothesis of the study

Before we started this study the expectations were that some children in Al Qualaubya Governorate would not be taking their obligatory vaccines properly. Those children's caregivers would to have increased awareness about vaccines (Null hypothesis).

Chapter 1

History of Vaccination Development

The story of vaccines did not begin with the first vaccine where Edward Jenner's used material from cowpox pustules to provide protection against smallpox. Rather, it began with the long history of infectious disease in humans, and in particular, with early uses of smallpox material to provide immunity to that disease. Evidence exists that the Chinese employed smallpox inoculation (or variolation, as such use of smallpox material was called) as early as 1000 CE. It was practiced in Africa and Turkey as well, before it spread to Europe and the Americas ***(Fitzpatrick, 2007).***

Edward Jenner is considered the founder of vaccinology in the West in 1796, after he inoculated a 13 year-old-boy with vaccinia virus (cowpox), and demonstrated immunity to smallpox. In 1798, the first smallpox vaccine was developed. Over the 18th and 19th centuries, systematic implementation of mass smallpox immunization culminated in its global eradication in 1979 ***(Riedel, 2005).***

Louis Pasteur's experiments spearheaded the development of live attenuated cholera vaccine and inactivated anthrax vaccine in humans (1897 and 1904, respectively) ***(Smith, 2012).***

Plague vaccine was also invented in the late 19th Century. Between 1890 and 1950, bacterial vaccine development proliferated, including the Bacillis-Calmette-Guerin (BCG) vaccination, which is still in use today ***(Oldstone, 2009).***

In 1923, Alexander Glenny perfected a method to inactivate tetanus toxin with formaldehyde. The same method was used to develop a vaccine against diphtheria in 1926. Pertussis vaccine development took considerably longer, with a whole cell vaccine first licensed for use in the US in 1948 ***(Thaysen-Andersen et al., 2007).***

Viral tissue culture methods developed from 1950-1985, and led to the advent of the Salk (inactivated) polio vaccine and the Sabin (live attenuated oral) polio vaccine. Mass polio immunization has now eradicated the disease from many regions around the world ***(Oshinsky, 2005).***

Attenuated strains of measles, mumps and rubella were developed for inclusion in vaccines. Measles is currently the next possible target for elimination via vaccination ***(Baker, 2011).***

The past two decades have seen the application of molecular genetics and its increased insights into immunology, microbiology and genomics applied to vaccinology. Current successes include the development of recombinant hepatitis B vaccines, the less reactogenic a cellular pertussis vaccine, and

new techniques for seasonal influenza vaccine manufacture ***(Ravin et al., 2015).***

Molecular genetics sets the scene for a bright future for vaccinology, including the development of new vaccine delivery systems (e.g. DNA vaccines, viral vectors, plant vaccines and topical formulations), new adjuvants, the development of more effective tuberculosis vaccines, and vaccines against cytomegalovirus (CMV), herpes simplex virus (HSV), respiratory syncytial virus (RSV), staphylococcal disease, streptococcal disease, pandemic influenza, shigella, HIV, malaria and schistosomiasis among others. Therapeutic vaccines may also soon be available for cancer, allergies, autoimmune diseases and addictions ***(Nascimento and Leite, 2012).***

Chapter 2

CHILDHOOD VACCINATION PROGRAMS

In the African Region, one child dies every minute of measles or from its fatal complications of diarrhea, pneumonia and malnutrition. Those who survive can suffer deafness, blindness and brain damage. Infections such as diphtheria and pertussis (whooping cough) can lead to pneumonia that is caused by *haemophilus influenza* type b, a leading killer in the Region. Hepatitis B virus infects many infants and children. When infected with hepatitis B, children have a 90% chance of developing a life-long, chronic infection that can cause liver failure ***(Shen et al., 2014).***

Why do different countries have different vaccination schedules?

The vaccination schedule is chosen by the official authorities in each country. It is decided based on various criteria, including in particular the incidence of a contagious disease, the availability of certain vaccines, the epidemiological situation, financial resources, prices of vaccines ***(Oxford Vaccine Group, 2016).***

According to WHO a child is considered fully immunized if he receives:

1. BCG vaccination against tuberculosis
2. 3 doses of the DPT vaccine to prevent diphtheria, pertussis, and tetanus
3. 3 doses of polio vaccine
4. Measles vaccination during the first year of life ***(Mutua et al., 2016).***

Examples of vaccination schedules:

1) United states specific schedule:

The most up-to-date schedules are available from CDC's National Center for Immunization and Respiratory Diseases. In the US, the National Childhood Vaccine Injury Act requires all health-care providers to provide parents or patients with copies of Vaccine Information Statements before administering vaccines fig (1) ***(Kroger, 2011)***.

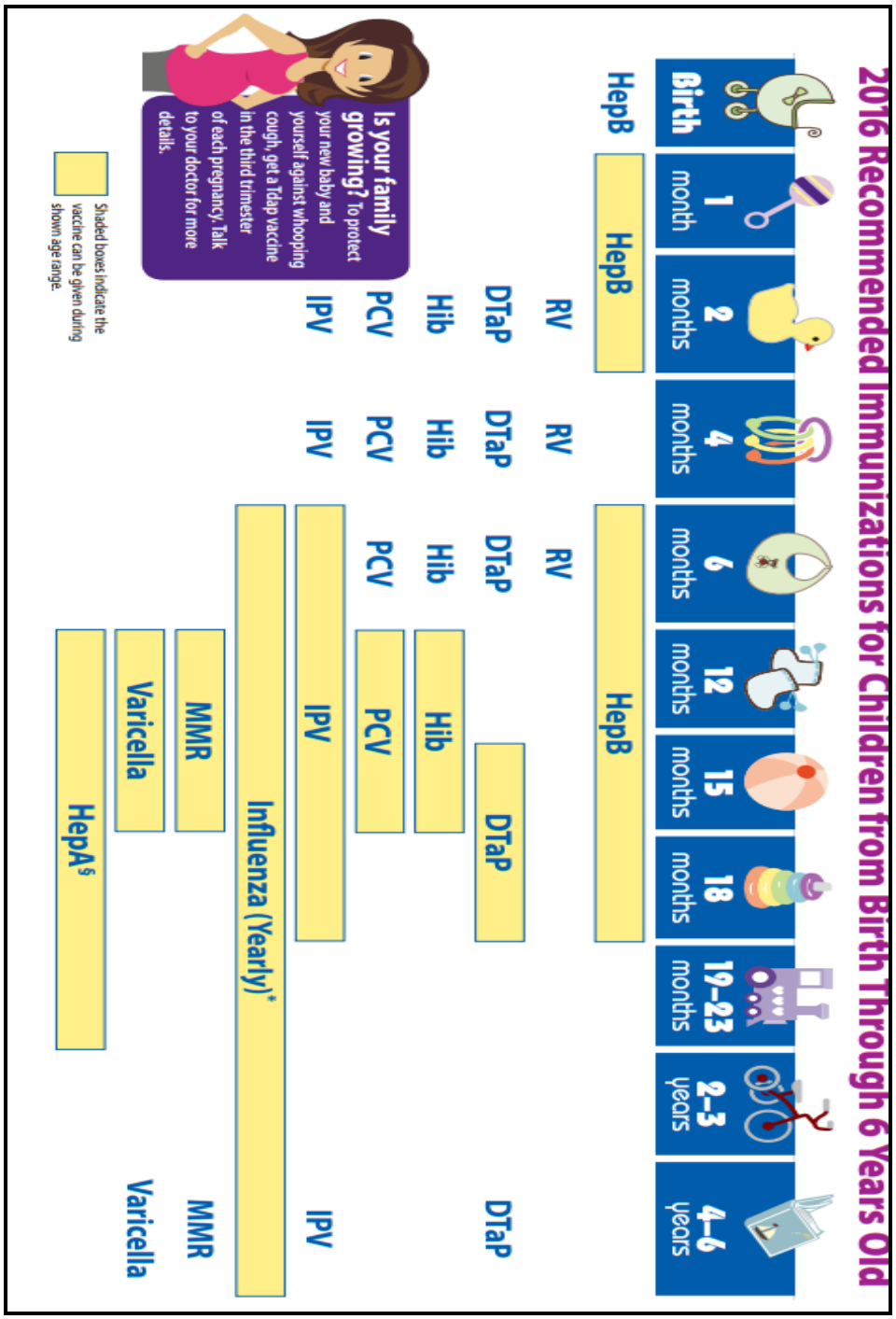

Figure (1): Vaccination schedule: from birth through 6 years old- 2014 recommended schedules ***(CDC, 2017).***

2) World Health organization recommended schedule:

The World Health Organization monitors vaccination schedules across the world, noting what vaccines are included in each country'9s program, the coverage rates achieved and various auditing measures ***(WHO, 2016).***

Table (1): Recommendations for routine immunization according to WHO

Vaccine			Doses
BCG			One dose
Hepatitis B			3 to 4 doses
Polio vaccine			3 to 4 doses at least one dose of IPV with DTP
DTP		3 doses	Booster DTP 1 to 6 years
Haemophilus influenza b	Option 1		3 doses with DTP
	Option 2		2 or 3 doses with booster at least 6 months after last dose
Pneumococcal conjugate	Option1		3 doses with DTP
	Option 2		2 doses before 6 months of age plus booster dose at 9-15 months of age
Rota vaccine			Rotarix : 2 doses oral 2 doses with DTP
			Rota teq :3 doses with DTP
Measles			2 doses
Rubella			1 dose

http://www.who.int/immunization/policy/Immunization_routine_table2.pdf?ua=1.

Immunization in Egypt:

In 1960, the Expanded Program on Immunization started in Egypt targeting 6 diseases for eradication: diphtheria, whooping cough, tetanus, measles, poliomyelitis and tuberculosis. 4 additional vaccines have now been added to the routine infant immunization schedule; including hepatitis B, German measles, mumps and Haemophilus influenza type b ***(Sayed et al., 2011).***

In Egypt, there are two types of recommended vaccination: obligatory and non-obligatory vaccines*:*

Obligatory vaccines:

According to the recommendations of the World Health Organization and in line with the policy of Ministry of Health of Egypt, vaccinations against certain diseases are required for every child.

Table (2): Immunization schedule in Egypt

Vaccine	**Time of administration**
BCG	At birth
Pentavalent (DPT-Hep B-Hib)	2,4,6 and 18 months
OPV	At birth ,2,4,6,9,12 and 18 months
MMR	12 and 18 months

(Ministry of Health and Population, Immunization Schedule, 2015 available (https://www.unicef.org/egypt/eg_ Ch4. Immunization_and_ Health_2015.pdf)

Non -Obligatory vaccines:

Vaccines not included in national program of immunization.

Table (3): Recommended but not included in expanded program of immunization

Age	Vaccine
2 months	PCV (pneumococcal) vaccine Rota vaccine
4 months	PCV(pneumococcal) vaccine Rota vaccine
6 months	PCV(pneumococcal)
12 months	Chicken pox vaccine Hepatitis A vaccine
18 months	Booster doses of both Hib (haemophilus influenza) PCV(pneumococcal)
2 years	Meningococcal vaccine (1^{st} dose) Hepatitis A vaccine (2^{nd} dose)
4 to 6 years	Booster dose of BCG vaccine 2^{nd} dose of chicken pox vaccine Meningococcal vaccine (2^{nd} dose)

This schedule was obtained from vacsera an Egyptien company for production of vaccines.

Obligatory and non-obligatory vaccines given in Egypt:

1. BCG vaccine:

- *Type of vaccine:*

Live attenuated vaccine, Bacille Calmette-Guérin (BCG) is a live strain of *Mycobacterium bovis* developed by Calmette and Guérin for use as an attenuated vaccine to prevent tuberculosis and other mycobacterial infections. The vaccine was first administered to humans in 1921 and remains the only vaccine against tuberculosis in general use. Several new vaccines against tuberculosis are also in development, and many are designed to boost the effects of BCG ***(McShane, 2011).***

- *Route of administration:*

Intradermal (ID) injection administers the vaccine in the topmost layer of the skin. BCG is the only vaccine with this route of administration. Intradermal injection of BCG vaccine reduces the risk of neurovascular injury ***(Prakash et al., 2001).***

- *Time of administration:*

BCG should be given as early as possible in life, before the child comes in contact with tuberculosis. It can be given up to 5 years of age ***(Luca et al., 2013).***

Virtually everyone who has a BCG vaccination will develop a raised blister at the site of the injection immediately afterwards, two to six weeks after the injection, a small spot

may appear at the site of the injection. It can grow into a circle up to 7mm across and may become crusty where fluid has dried on the surface. The spot can be painful and bruised for a few days, but will eventually heal. It usually leaves a small scar fig (2). Occasionally, there may be a more severe skin reaction, but this should heal within a few weeks ***(Dhanawade et al., 2015).***

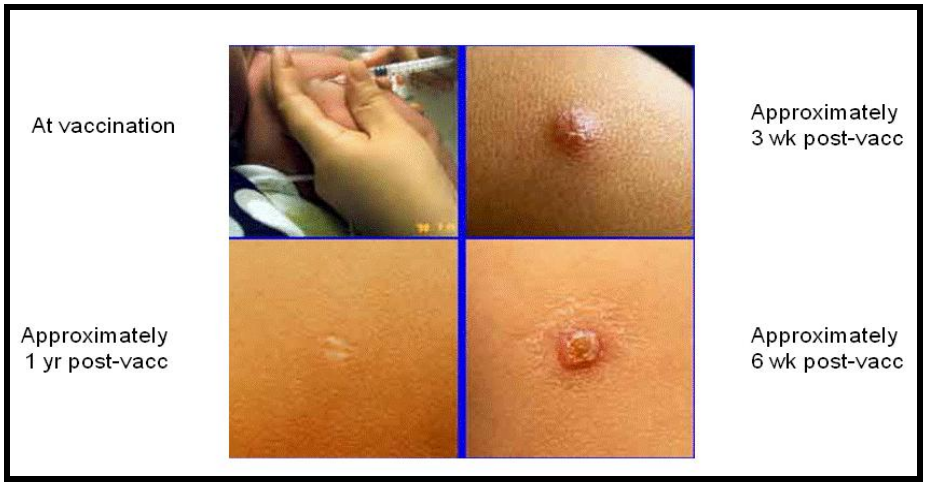

Figure (2): Showing normal reaction course to BCG vaccination ***(Kim, 2001)***

- ***Side effects:***

Serious side effect to the BCG vaccine, such as an anaphylactic reaction is very rare. It occurs in less than one in a million cases ***(Barari et al., 2016).***

- *Contra indications:*

Contraindications to BCG vaccination may be either relative (weight < 2 kg, skin reactions at the vaccination site; severe diseases use of immunosuppressants or absolute as immunosuppression. BCG vaccination should not be given to