Analysis of causes that led to the development of vitiligo in Jeanett's case with recommendations for clinical tests and treatments

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Abstract

At the age of two years, Jeanett developed vitiligo within days of receiving her first MMR vaccine and the fourth injection of DTaP and IPV vaccines. Furthermore, at five years of age, she developed many more unpigmented spots on her body with acrofacial vitiligo, following receipt of the second injection of MMR and the fifth injection of DTaP and IPV vaccines. Jeanett's susceptibility to developing adverse reactions to vaccine was notable a few hours after birth following receiving her first injection of the hepatitis B vaccine. Furthermore, the intensity and the frequency of her adverse reactions to vaccines were significantly increased following receipt of more doses of hepatitis B, DTaP, IPV, Hib, and MMR vaccines. Jeanett's health condition during her second year of life, when she was not given any vaccine was better than during her first year of life, when she received several vaccines.

It is likely that the MMR vaccine induced the depigmentation of Jeanett's skin through local and systemic autoimmune reactions. Synergistic actions between the MMR vaccine and other vaccines given to Jeanett could also be involved in causing the depigmentation of her skin. I believe that Jeanett should not receive any vaccine in the future. Vaccines probably will aggravate her present illness and trigger more illnesses. Jeanett was treated with corticosteroids ointment but the steroid did not help in stopping the depigmentation of her skin. Recommendations for clinical tests and treatment plans are presented in this report that I believe will help Jeanett's pediatrician to better monitor and treat her vitiligo.

Keywords: Amoxicillin; autoimmune reactions; calcipotriol; copper sulfate; corticosteroids; depigmentation; Diphtheria, Tetanus, and Pertussis (DTaP) vaccine; adverse reactions to vaccines; Elccon®; Hib; hepatitis; inactivated polio (IPV) vaccine; Measles, mumps, and rubella (MMR) vaccine; melanin; melanin sysnthesis; melanogenesis; tyrosinase assay; Tylenol®; vitiligo; vitix; Zithromax®.

1. Summary of the case and findings

Jeanett is an 8-year-old white female. She developed white unpigmented spots (vitiligo) on her skin at the age of 2 years and 4 months that appeared on her fingers, toes, ankles, and knees (Figure 1). Vitiligo is pigmentary disorder characterized by areas of depigmented skin resulting from the loss of epidermal melanocytes or the loss of melanocytes' ability to produce melanin. Her vitiligo started within days of receiving her first measles, mumps, and rubella (MMR) vaccine and the fourth injection of Diphtheria, Tetanus, and Pertussis (DTaP) and inactivated polio (IPV) vaccines on May 29, 2001 (Table 2).

Furthermore, Jeanett's vitiligo got worse following receipt of the second injection of MMR vaccine and the fifth injections of DTaP and IPV vaccines on September 1, 2004. She developed many more unpigmented spots on her body and acrofacial vitiligo (Figures 1, 2). In addition, Jeanett's joints became swollen and she developed a limp within 10 days following vaccination. Also, Jeanett's skin became hypersensitive to sunlight. Her skin always burns and never gets tanned when exposed to sunlight. Jeanett was treated with corticosteroid ointment and this treatment did not help in stopping the progress of the depigmentation of her skin.

The review of Jeanett's medical record revealed that Jeanett's susceptibility to developing adverse reactions to vaccine was notable following receipt of her first injection of the hepatitis B vaccine, given a few hours after birth. Jeanett was born on January 22, 1999 in California and appeared healthy. Her birth weight was 5 pounds and 6 ounces (2.4 kg) and her length was 19.5 inches (49.5 cm).

The medical data described in this report show that vaccines had negative impacted on Jeanett's health. For example, her health was significantly better during her second year of life without vaccine than during the first year of life, when she received vaccines (Table 1). Furthermore, the intensity and the frequency of her adverse reactions to vaccines were significantly increased following receipt of more doses of hepatitis B, DTaP, IPV, Hib, and MMR vaccines. Serious systemic adverse reactions to vaccine and even death have been reported in children. The severity of adverse reactions to vaccine is expected to be found more often in genetically susceptible children and sick children. Jeanett was administered vaccines on many occasions while she was sick.

In addition, local and systemic autoimmune illnesses have also been reported in some healthy children and adults who received DTaP, polio, Hib, and MMR vaccines. These include arthritis; rheumatoid arthritis; myelitis; optic neuritis; multiple sclerosis (MS); Guillain Barre Syndrome (GBS); glomerulonephritis; pancytopenia/thrombocytopenia; chronic fatigue; Systemic Lupus Erythematous (SLE); and diabetis (Section 6).

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Clinical and experimental studies have demonstrated that cellular and humoral autoimmune disorders play important roles in the pathogenesis of vitiligo in genetically susceptible individuals. These disorders cause the loss of melanocytes and/or target certain enzymes involved in melanin synthesis or crucial to the survival of melanocytes (Section 7).

MMR vaccine contains attenuated live viruses and others immunogenic substances (Table 14). Viral infections have been known to cause autoimmune illnesses. It is conceivable that attenuated viral vaccines could induce autoimmunity in a manner similar to what has been proposed to explain the viral-autoimmunity association (Section 6).

It is likely that the MMR vaccine induced the depigmentation of Jeanett's skin through local and systemic autoimmune reactions. Synergistic actions between the MMR vaccine and other vaccines given to Jeanett would also explain the depigmentation of her skin. Below are recommendations that I believe will help Jeanett's pediatrician to better monitor and treat her vitiligo and autoimmune condition.

1) Blood tests previously performed in Jeanett's case listed in Section 5 of this report are not specific to identify the autoimmune mechanisms involved in triggering the depigmentation of Jeanett's skin. My review of the medical literature reveled that the following tests can be useful in identifying the specific autoimmune mechanisms involved in Jeanett's vitiligo: (a) Evaluating cutaneous melanogenesis using tyramide-based tyrosinase assay (TTA) as described in Section 7. (b) Measuring the serum levels of antibodies against tyrosinase and other components of melanocytes and performing other immunological tests that are described in Section 7 of this report.

2) Jeanett was treated with corticosteroid locally and systemically on several occasions and these treatments were not helpful in stopping the progress of her vitiligo or reducing the severity of her illness. Clinical studies have shown treatments (application on skin) of children and adults suffering from vitiligo with vitix and 1,25-dihydroxyvitamin D3 (calcipotriol) were helpful in inducing repigmentation of the skin. In addition, clinical study also showed that treatment of children suffering from vitiligo with Aspirin orally at a daily dose of 300 mg for 12 weeks reduced the severity of their illness. These studies are described in Section 7 of this report. The future use of any of these medications and treatment plans in Jeanett's should be done as recommended and supervised by Jeanett's physician(s).

3) My review of Jeanett's medical records revealed that the medical staffs who administered vaccines to Jeanett during her first five years of life did not do benefit/risk analyses prior to administering vaccines to Jeanett. Her medical record clearly shows that she suffered from adverse reactions to vaccines following each treatment with single vaccine or multiple vaccines. In addition, the medical staffs ignored Jeanett's mother warning that vaccines are causing illness in her daughter's case. I believe that Jeanett should not be given any vaccine in the future. Vaccines probably will aggravate her present illness and trigger more illnesses.

2. Jeanett's adverse reactions to vaccines received during her first year of life

Jeanett is a white female child. She was born on January 22, 1999 in Ridgecrest Community Hospital, Ridgecrest, California. Her weight was 5 pounds and 6 ounces (2.4 kg) and her length was 19.5 inches. She appeared healthy at birth. She was discharged from the hospital on January 23, 1999 and her discharge weight was 5 pounds and 3 ounces (2.36 kg). Jeanett was breast-fed and received an Enfamil formula.

She was vaccinated five times during her seven months of life and she suffered from adverse reactions to vaccines. Below are the descriptions of the adverse reactions observed in Jeanett's case [1].

2.1. Jeanett's adverse reactions to hepatitis B vaccine given at birth and 3 days of age

Jeanett received the first hepatitis B vaccine injection in the right thigh at two hours after birth and she developed jaundice within a few hours. Her skin color became dark yellow-brown. Furthermore, Jeanett's jaundice got worse after receiving the second hepatitis B vaccine injection three days later on January 25, 1999. Her jaundice continued for 11 days (Table 1). Furthermore, it was reported that Jeanett's urine had a foul smell [1].

2.2. Jeanett's adverse reactions to vaccines given at two months of age

Jeanett was given inactivated polio vaccine (IPV); Haemophilus influenzae type B (Hib); and Diphtheria, Tetanus, and Pertussis (DTaP) vaccines on March 26, 1999 (Table 1). She developed fever over a period of three days following vaccination. Her eye's crossed and she had seizures. Jeanett's urine had a foul odor and her urine culture tested positive for bacterial infection. Furthermore, her stool contained white puss and she was treated with antibiotic [1].

2.3. Jeanett's adverse reactions to vaccines given at about five months of age

Jeanett was vaccinated again with Polio, DTaP, and Hib vaccines on June 14, 1999 at Sage Community Clinic (Table 1). She developed fever that lasted for a few days and a cough that stayed for more than two weeks. Jeanett also developed fever (101^{o}F or 38.3^{o}C) and cough 2 months after receiving the vaccines. She was seen by a doctor on August 17, 1999 at the Pleasant Valley Pediatric Medical group, Camarillo California [1].

2.4. Jeanett's adverse reactions to vaccines given at seven months of age

Jeanett was vaccinated with DTaP and Hib for the third time on August 23, 1999. She developed a chronic cough that lasted for few weeks and her cough did not clear up with the treatment of the over-the-counter cough medications. She required two emergency trips to the hospital for treatment. She also developed common cold on October 20, 1999. Furthermore, Jeanett suffered from bacterial infection on December 24, 1999 and was treated with Amoxicillin syrup [1].

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Table 1. Vaccines given to Jeanett during the first year of her life and adverse reactions developed following vaccinations

Treatment date	Jeanett's age	Vaccine[1] type	Illness developed and symptoms
1/22/1999	Birth	Hepatitis B	• Jaundice (her skin color became dark yellow brown).
1/25/1999	3 days	Hepatitis B	• Her jaundice got worse and continued for 11 days.
3/26/1999	2 months	Hepatitis B; DTaP; Hib; IPV	• Developed fever for three days, seizures, and bacterial infection.
6/14/1999	About 5 months	DTaP; Hib; IPV	• Developed fever for a few days and chronic cough.
8/23/1999	7 months	DTaP; Hib	• Developed chronic cough.

[1]Diphtheria, Tetanus, and Pertussis (DTaP); Haemophilus influenzae type B (Hib); Inactivated polio vaccine (IPV).

3. The status of Jeanett's health during her second year of life without vaccines

Jeanett did not receive any vaccine during her second year of life (January 1, 2000 to December 31, 2000). Her eyes regained normal function (uncrossed) and she began to develop well. Her body weight on December 21, 2000 was 12.5 kg. Her medical record shows that she had only two episodes of illness between January 1 and December 31, 2000. Her physician saw her on June 19, 2000 for an earache and on December 12, 2000 for a fever and cough [1].

4. Vaccines given and the development of vitiligo and other health problems in Jeanett's case

On May 29, 2001, Jeanett received her first measles, mumps, and rubella (MMR) vaccine and the fourth injection of Diphtheria, Tetanus, and Pertussis (DTaP) and inactivated polio (IPV) vaccines. She developed vitiligo within days following receipt of these vaccines. She was 2 years and 4 months old [1]. Furthermore, Jeanett was injected again with MMR, DTaP, IPV vaccines on September 1, 2004 after which her vitiligo got worse. Jeanett developed many unpigmented spots on her body (Figures 1, 2). Below are the descriptions of Jeanett's skin lesions and her other illness developed following receipt of these vaccines.

4.1. Depigmentation of Jeanett's skin following vaccinations

Jeanett had green mucous discharge from her nose and cold on May 29, 2001 and her mother took her to see her pediatrician. Jeanett was given the first MMR vaccine and the fourth injection of DTaP and IPV vaccines (Table 2). Within days of receiving vaccines, Jeanett developed white unpigmented spots on her skin that appeared on her fingers, toes, ankles, and knees (Figure 1). The vitiligo continued to spread and became more noticeable. Her mother sought out doctors that specialized in this area of treatment. Jeanett was 2 years and 4 months old.

Furthermore, Jeanett was given the second injection of MMR vaccine and the fifth injections of DTaP and IPV vaccines on September 1, 2004 (Table 2). She was five years and 7 months old. Jeanett's vitiligo got worse and she developed many more unpigmented spots on her body (Figure 2). She also developed acrofacial vitiligo (Figure 1). In addition, Jeanett's joints became swollen and she developed a limp within 10 days following vaccination. Furthermore, her skin became hypersensitive to sunlight. Her skin always burns and never gets tanned when exposed to sunlight. She was treated with corticosteroid ointment but it did not help in stopping the depigmentation of her skin.

Furthermore, Jeanett had her first visit with a doctor at the vilitigo and skin pigmentation Institute of Southern California on December 23, 2004 and she was treated with corticosteroid and vitamins. Her blood analysis of January 14, 2005 showed a high level of anti-nuclear Antibody (ANA).

4.2. Jeanett's other health problems associated with the developed of vitiligo

The vaccines cited in Table 2 also caused other systemic health problems in Jeanett's case in addition to vitiligo. Table 3 lists the dates that Jeanett was examined by pediatricians and Table 4 lists Jeanett's medications received during a period of 30 months following the receiving of her fist MMR vaccine on May 29, 2001.

Furthermore, Table 5 contains a list of Jeanett's medications received during a period of 20 months following receiving her second injection of MMR vaccine. The intensity and severity of Jeanett's skin lesion and the incidence of her other systemic illness were significantly increased following receipt of the second MMR vaccine as compared to receipt of her first MMR injection.

Table 2. List of adverse reactions including vitiligo developed following vaccinations

Treatment date	Jeanett's age	Vaccine Type[1]	Reactions type and Symptoms
5/29/2001	2 years and 4 months	MMR; DTaP; IPV	• Developed unpigmented spots on her skin that appeared on her fingers, toes, ankles, and knees.
9/01/2004	5 years and 8 months	MMR; DTaP; IPV	• Developed more unpigmented spots in her skin of her body and her face. • Her joints became swollen. She developed a limp within 10 days following vaccination. • Her skin became hypersensitive to sunlight.

[1]Measles, Mumps, and Rubella (MMR); Diphtheria,Tetanus Toxoids, and acellular Pertussis (DTaP); Inactivated polio vaccine (IPV).

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Table 3. Jeanett's visits to her doctors and her symptoms during 30 months following her first MMR injection[1]

Date	Illness developed
06/04/2001	• Fever and cough
08/06/2001	• Fever and cough
02/13/2002	• Cough and earache
10/25/2002	• Cough, fever, and vomiting
12/09/2002	• Cough
02/03/2003	• Cold for 8-10 days
08/05/2003	• Cold
12/04/2003	• Earache

[1]Jeanett received her first MMR vaccine on 5/29/2001.

Table 4. Jeanett's medications received during a period of 30 months following her first MMR vaccine[1]

Prescription Date	Medications
06/04/2001	Tylenol®
08/06/2001	Amoxicillin
10/15/2002	Elocon® (0.1% cream)
10/25/2002	Zithromax® (200 mg/5 mL syrup)
02/03/2003	Amoxicillin/Clavu (400 mg/5 mL)

[1]Jeanett received her first MMR vaccine on 5/29/2001.

Table 5. Some of Jeanett's medications prescribed during a period of 20 months following her 2nd MMR vaccine[1]

Prescription date	Medications
11/05/2004	Omnicef® (250 mg/5 mL)
12/01/2004	Zithromax® (200 mg/5 mL)
01/18/2005	Apexicon® E 0.05% cream Protopic 0.1% ointment
04/11/2005	Zithromax® (200 mg/5 mL)
07/29/2005	Prednisolone (5 mg/5 mL)
08/16/2005	Augmetin (250 mg/5 mL) Trimethobenzamide (100 mg/Capsule) APAP w/codeine Elixir (120-12/5 mg)
09/18/2005	Amoxicillin (250 mg/5 mL, suspension)
10/30/2005	Sulfamethoxazole/Trimetho (oral suspension)
11/19/2005	Dexamethasone (1 mg/mL)
03/17/2006	Fluticase 50 mg nasal spray Zithromax® (200 mg/5 mL)
04/03/2006	Vigamox® (drops)
04/13/2006	Amoxicillin (250 mg/5 mL, suspension)
04/26/2006	Amoxicillin (250 mg/5 mL, suspension) MAPAP cold medicine Promethazine (6.25 mg/5 mL)

[1]Jeanett received her second MMR vaccine on 09/01/2004.

5. Clinical tests performed to monitor Jeanett's health following the development of her vitiligo and their significance

Jeanett's skin depimentation started within days following receiving her first MMR vaccine and other vaccines on May 29, 2001 (Table 2). She was two years and four months old. The following are the results of Jeanett's clinical tests performed following the development of her skin lesions until June of 2006 and their significance.

5.1. Hematology tests

The blood tests performed during the period of December 2004 and November of 2005 show that Jeanett did not suffer from anemia and her platelet counts were within the normal range (Table 6). Her total white blood cell count and differential count were within the normal range (Table 7). In addition, her CD4T cell and CD8 T cell counts performed on November of 2005 were within the normal range (Table 8). These data indicate that she did not suffer from infection or have any inflammation in tissues during the time of testing.

Table 6. Jeanett's hematology values, Dec. 2004 through Nov. 2005

Measurements	Values 12/23/04	Values 07/25/2005	Values 11/30/2005	Reference range
Red blood cell (x 10^6/μL)	4.96	4.58	4.79	3.83-5.07
Hemoglobin (g/dL)	14.1	13.7	14.4	10.2-15.4
Hematocrit %	43.0	41.1	42.2	32.1-40.9
MCV (fL)	87.0	89.6	88.0	76-91
MCH (pg)	28.4	29.9	30.2	23.3-30.8
MCHC (g/dL)	32.8	33.3	34.2	30.9-35.4
RDW (%)	13.1	12.5	11.8	10.8-14.8
Platelet count (x 10^3/μL)	322	352	406	150-400
ESR mm/HR)	2	-	-	0-20

-: Not measured

Table 7. Jeanett's white blood cell counts, Dec. 2004 through Nov. 2005

Measurements	Values 12/23/04	Values 07/25/05	Values 11/30/05	Reference range
White blood cell (cells/μL)	7,200	11,500	8,900	3,900-13,700
Neutrophils (cells/μL)	3,744	7,418	4,886	1,500-8,500
Lymphocytes (cells/μL)	2,628	3,151	3,364	2,000-8,000
Monocytes (cells/μL)	468	690	579	200-900
Eosinophils (cells/μL)	101	196	62	15-600
Basophils (cells/μL)	245	46	9	0-250

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Table 8. Jeanett's T-cell subsets counts on Nov. 30, 2005

Measurements	Values 11/30/05	Reference range
CD4 (cells/μL)	1,250	670-1,930
CD8 (cells/μL)	623	350-1,160
CD3 (cells/μL)	2,126	1,220-3,000

5.2. Jeanett's liver, kidney, adrenal, and thyroid functions tests

Jeanett's serum and urine analyses indicate that her kidney and liver functions were normal in the period between December of 2004 and November of 2005 (Tables 9, 10). Furthermore, her serum cortisol, thyroid hormone, and TSH were also within the normal range (Tables 10 and 11).

Table 9. Jeanett's serum analyses performed Dec. 2004 through Nov. 2005

Measurements	Values 12/23/04	Values 11/30/05	Reference range
Alk phosphotase (IU/L)	361	340	50-390
AST (IU/L)	32	39	1-45
ALT (IU/L)	27	42	1-55
Total Bilirubin (mg/dL)	0.3	0.6	0.1-1.5
Albumin (g/dL)	4.8	4.6	3.2-4.7
Globulin (g/dL)	2.6	2.3	2.0-3.8
Total protein (g/dL)	7.4	6.9	5.7-8.0
Sodium (mEq/L)	139	141	135-148
Potassium (mEq/L)	4.1	4.4	3.5-5.5
Chloride (mEq/L)	99	107	96-109
CO2 (mEq/L)	23	24	19-31
BUN (mg/dL)	15	10	7-17
Creatinine (mg/dL)	0.5	0.6	0.5-0.8
Calcium (mg/dL)	10.2	10.1	8.7-10.5
Glucose (mg/dL)	96	87	65-99
Cortisol (μg/dL)	-	8.64	3.1-16.7

-: Not measured

Table 10. Jeanett's urine analysis performed on Oct. 30, 2005

Measurements	Values 10/30/2005	Reference range
Clarity	Turbid	Clear
Color	Yellow	Yellow
PH	5.0	5.0-8.0
Specific gravity (g/mL)	1.030	1.005-1.030
Protein (mg/dL)	Negative	0-15
Glucose (mg/dL)	Negative	0-75
Ketones (mg/dL)	Negative	0-5
Bilirubin	Negative	Negative
Urobilinogen (EU/dL)	0.2	0.2-1.0
Nitrite	Negative	Negative
Blood	Small amount	Negative
Leucocytes	Few	Negative
Amorphous crystals	Many	None
Ca oxalate crystals	Moderate amount	None
Bacteria	None	None

Table 11. Jeanett's thyroid function tests performed Dec. 2004 through Jan. 2006

Measurements	Values 12/23 2004	07/25 2005	11/30 2005	01/27 2006	Reference range
T4, Thyroxine (μg/dL)	9.3	8.7	10.2	-	5.3-11.6
Free T3 (pg/mL)	4.4	-	-	-	1.8-4.2
TSH (μIU/mL)	4.32	2.8	1.87	1.87	0.7-6.4
T3 uptake %	-	-	29.9	-	27-37

-: Not measured

5.3. Levels of trace elements and folic acid in Jeanett's blood

Jeanett's blood analysis performed on November 30, 2005 revealed that her levels of zinc, copper, magnesium and folic acid were within the normal range (Table 12). These elements are important for the functions of melanocyte, immune system, and bone marrow.

Table 12. Levels of trace elements and folic acid in Jeanett's blood detected on Nov. 30, 2005

Measurements	Sample Type	Values 11/30/2005	Normal Range
Zinc (μg/L)	Plasma	700	600-1,300
Copper (μg/L)	Plasma	1,136	450-2,200
Magnesium (mg/dL)	Serum	2.0	1.7-2.2
Folic acid (μg/L)	Serum	>20	>5.32

5.4. Autoimmune panel tests

Table 13 contains the list of 21 clinical tests performed in December of 2004 and July and November of 2005 in Jeanett's case to detect autoimmune illness. Her results were within the normal range except for the level of the antinuclear antibody (ANA) in serum that was found slightly elevated on December 23, 2004.

Table 13. Jeanett's autoimmune panel tests performed Dec. 2004 through Nov. 2005

Measurements	Values 12/23/04	Values 7/25/05	Values 11/30/05	Normal range
Anti-Nuclear AB	positive (1:40)	Negative	Negative	Negative (<1:40)
Anti-centromer	<1:40			<1:40
Anti-SCl-70 AB	Negative		Negative	Negative
Anti-SM AB	Negative			Negative
Anti-RNP AB	Negative			Negative
Anti-LA AB	Negative			Negative
Anti-DS AB	2.3			<50.0 U/mL
Anti-Chromatin AB	Negative			Negative
CIQ*			1.1	0-3.9 μg E/mL
Complement C3	131			79-152 mg/dL

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Table 13. Jeanett's autoimmune panel tests performed Dec. 2004 through Nov. 2005 (Continued)

Measurements	Values 12/23/04	Values 7/25/05	Values 11/30/05	Normal range
Complement C4	23			16-47 mg/dL
Cardiolipin, IGG	<15.0			<15.0 GPL
Cardiolipin, IGA	<15.0			<15.0 APL
Cardiolipin, IGM	<12.5			<12.5 MPL
IgA			59	64-246 mg/dL
IgG			732	592-1,723 mg/dL
IgM			148	36-314 mg/dL
Thyroid microsomal AB	<10			<35 IU/mL
Thyroid peroxidase AB		<10		<35 IU/mL
Thyroglobin AB			<20	<41 IU/mL

* Circulating complement binding immune complexes

6. The likely causes of Jeanett's vitiligo and other health problems

Jeanett's susceptibility to developing adverse reactions to vaccine appeared early in life. She suffered from adverse reactions to her first injection of the hepatitis B vaccine that was given a few hours after birth. She developed jaundice and the severity and the duration of her jaundice was significantly increased after receiving her second injection of the hepatitis B vaccine given three days later (Table 1).

Systemic illnesses and autoimmune disorders have been reported in some children who received hepatitis B vaccine. For example, the database from the 1994 National Health Interview Survey (NHIS) in the USA was analyzed to evaluate the vaccine related adverse reactions. It included 6,515 children less than six years of age who received the hepatitis B vaccine. Hepatitis B vaccine was found to be associated with prevalent arthritis, incident of acute ear infections, and incident of pharyngitis/nasopharangitis [2].

Furthermore, hepatitis B vaccine induced autoimmune disorders at 2 to 4 weeks after vaccinations in some individuals. These include erythema nodosum; thrombocytopenia; myasthenia gravis; uveitis; Reiter's syndrome; arthritis; systemic lupus erthematosus; and central nervous system demyelination [3-6].

For example, Geier and Geier examined the adverse events and positive re-challenge of symptoms reported in the scientific literature and to the Vaccine Adverse Event Reporting System (VAERS) following hepatitis B vaccination (HBV) [6]. The VAERS and PubMed (1966-2003) were searched for autoimmune conditions in individuals who received HBV. These conditions included arthritis, rheumatoid arthritis, myelitis, optic neuritis, multiple sclerosis (MS), Guillain Barre syndrome (GBS), glomerulonephritis, pancytopenia/thrombocytopenia, fatigue, and chronic fatigue, and Systemic Lupus Erythematous (SLE). They found that HBV was associated with serious illnesses. There were 415 arthritis, 166 rheumatoid arthritis, 130 myelitis, 4 SLE, 100 optic neuritis, 101 GBS, 29 glomerulonephritis, 283 pancytopenia/thrombocytopenia, and 183 MS events reported in individuals who received HBV. In addition, a total of 465 positive re-challenge adverse events were observed following adult HBV that occurred sooner and with more severity than initial adverse event reports. A case-report of arthritis occurring in identical twins was also identified [6].

Ronchi *et al.* also reported three cases of immune thrombocytopenic purpura after the first dose of recombinant hepatitis B vaccine occurred in infants under 6 months of age. Antiplatelet antibodies were detected in the blood of these children. Other possible causes thrombocytopenic purpura in these children were excluded. [7].

Jeanett was also given inactivated polio (IPV); Haemophilus influenzae type B (Hib); and Diphtheria, Tetanus, and Pertussis (DTaP) vaccines at the age of two months (Table 1). She developed fever over a period of three days, seizures, and her eye's crossed. Jeanett's urine had a foul odor and her urine culture tested positive for bacterial infection. Furthermore, her stool contained white puss and she was treated with antibiotic.

In addition, Jeanett felt sick following vaccination with Polio, DTaP, and Hib vaccines that she received at the age of five months (Table 1). She developed a fever that lasted for a few days and a cough that continued for more than two weeks. Jeanett also developed fever (101^{o}F or 38.3^{o}C) and cough at two months after receiving these vaccines and she was seen by a doctor on August 17, 1999. Furthermore, Jeanett was vaccinated with DTaP and Hib for the third time on August 23, 1999 (Table 1). She developed a chronic cough that lasted for a few weeks and her cough did not clear up with the over-the-counter cough medications. She required two emergency trips to the hospital for treatment.

Local and systemic reactions and autoimmune illnesses have also been reported in some children who received DTaP, Polio, and Hib vaccines. For example, in the USA, reports to the Vaccine Adverse Event Reporting System (VAERS), concerning infant immunization against pertussis between January 1, 1995 and June 30, 1998 were analyzed. During the study period, there were 285 reports involving death, 971 non-fatal serious reports (defined as events involving initial hospitalization, prolongation of hospitalization, life-threatening illness, or permanent disability), and 4,514 less serious reports after immunization with any pertussis-containing vaccine [8].

Furthermore, Rennels reported that extensive local reactions were recognized to occur after administration of the fourth and fifth booster doses of diphtheria-tetanus-acellular pertussis (DTaP) vaccines in children. Retrospective evaluations suggest that entire proximal limb swelling occurs in 2 to 6% of children given booster doses of DTaP vaccines. The pathogenesis of these reactions probably is multifactorial. Evidence suggests that both antigen content and prevaccination immunity have roles [9]. Jeanett received five injections of DTaP during the first four years of her life (Tables 1, 2).

It has been reported that children who react to the first injection of a vaccine also react to the repeated injections of the same vaccine. For example**,** Deloria *et al.* examined the occurrence of common reactions in 2127 infants within 48 hours after

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immunization at 2, 4, and 6 months with one of 13 acellular DTP (DTaP) or whole-cell DTP. Data on at least two consecutive immunizations were available for 357 DTP recipients and 1770 DTaP recipients [10].

For these analyses, reactions evaluated included fever of 100.4°F (38°C) or greater, redness of 21 mm or larger, swelling of 21 mm or larger, moderate or severe pain, moderate or severe fussiness, loss of appetite, drowsiness, and vomiting. They found that reactions after a second or third immunization with either DTP or DTaP vaccine are more likely to occur in infants who had the same reaction after the preceding immunization [10].

In another study, 211 two-month-old infants were vaccinated with IPV and DTaP and some of them developed systemic adverse reactions at 24 hours post-inoculation. These included: Fever > 102.2°F (0.5%); irritability (24.6%); tiredness (31.8%); anorexia (8.1%); and vomiting (2.8%) [11]. Sakaguchi *et al.* also reported eight children who had systemic urticaria within 30 minutes after administration of acellular diphtheria-tetanus-pertussis (DTaP) vaccine which contain gelatin as a stabilizer [12].

Haemophilus influenzae type B (Hib) vaccine has also been known to cause acute and chronic health problems in some children. For example, 365 infants were inoculated with Hib, and some of them developed systemic adverse reactions. The following adverse reactions and their percentages occurred in two-month-old infants during the 48 hours following inoculation: Fever > 100.8°F (0.6%); irritability (12.6%); drowsiness (4.9%); diarrhea (5.2%); and vomiting (2.7%) [11].

Also, Classen and Classen analyzed data from a Hib vaccine trial and identified clusters of extra cases of insulin dependent diabetes (IDDM) caused by the vaccine. IDDM occurred between 36 and 48 months post-immunization. In this study, approximately 116,000 children in Finland were randomized to receive 4 doses of the Hib vaccine beginning at 3 months of age or one dose starting after 24 months of age. A control-cohort included all 128,500 children born in Finland in the 24 months prior to the Hib vaccine study. The difference in cumulative incidence between those receiving 4 doses and those receiving 0 doses is 54 cases of IDDM/100,000 (P = 0.026) at 7- year (relative risk = 1.26).

Most of the extra cases of IDDM appeared in statistically significant clusters that occurred in periods starting at approximately 38 months after immunization and lasting approximately 6 to 8 months [13]. Jeanett received three injections of Hib vaccine during her seven months of life (Table 1).

In a second study, distinct rises in the incidence of IDDM in children occurred 2 to 4 years following the introduction of the MMR and pertussis vaccines [14]. Jeanett also received several injections of these vaccines (Tables 1 and 2).

Jeanett's health was significantly better during her second year of life without vaccine than in her first year of life, when she received vaccines (Table 1). Serious systemic adverse reactions to vaccines and even death have been reported in children who received vaccines and the severity of the adverse reactions is expected to be more in genetically susceptible children and sick children [11, 15-17].

The following is a summary of reports on the adverse events of vaccines reported to the USA Vaccine Adverse Event Reporting System (VAERS) from Jan. 1, 1991, through Dec. 31, 2001. VAERS received 128,717 reports. A total of 14.2% of all reports described serious adverse events, which by regulatory definition include death, life-threatening illness, hospitalization or prolongation of hospitalization, or permanent disability. The most commonly reported adverse event was fever (25.8%) followed by injection-site hypersensitivity (15.8%), rash (11.0%), injection-site edema (10.8%), and vasodilatation (10.8%) [15].

Medical records indicate that Jeanett is very susceptible to developing adverse reactions to vaccine. In addition, she was administered vaccines on many occasions when she was sick which also increased her susceptibility to vaccine injury. It has been reported that ill children have failed to respond adequately to vaccine as compared to healthy children. For example**,** Krober *et al.* examined 47 infants with colds and 51 well infants at the age of 15 to 18 months, who received the standard measles-mumps-rubella (MMR) vaccine, for their response to develop the measles antibody. Pre-vaccination serum samples were obtained prior to vaccine administration and post-vaccination serum samples were obtained 6 to 8 weeks later. Measles antibody was measured in these serum samples by an indirect fluorescein-tagged antibody test. Ten (21%) of 47 infants with colds failed to develop the measles antibody, while only one (2%) of 51 well infants failed to develop an antibody [17].

Jeanett developed vitiligo within days following receipt of her fist injection of the MMR vaccine and the fourth injection of DTaP and IPV vaccines on May 29, 2001 (Table 1). She was two years and four months of age. She developed white unpigmented spots on her skin that appeared on her fingers, toes, ankles, and knees (Figure 1).

Furthermore, Jeanett was given the second injection of MMR and the fifth injections of DTaP and IPV vaccines on September 1, 2004 (Table 2) and her vitiligo got worse. She developed many more unpigmented spots on her body (Figure 2). She also developed acrofacial vitiligo. She was 5 years and 7 months old.

It has been reported that MMR vaccine caused acute and chronic illnesses in some children when given alone or concurrently with other vaccines. These include malaise, sore throat, cough, rhinitis, headache, dizziness, fever (101-102.9 °F), rash, nausea, vomiting, diarrhea, fever, regional lymphadenopathy, parotitis, orchitis, nerve deafness, vasculitis, otitis media, hearing loss, conjunctivitis, aseptic meningitis, measles, thrombocytopenia, allergy, and anaphylaxis [11, 18-23].

MMR contains attenuated lives viruses and others immunogenic substances (Table 14) and viral infections have known to cause autoimmune illnesses. It is conceivable that attenuated viral vaccines can induce autoimmunity in a manner similar to the mechanisms proposed to explain the viral-autoimmunity association [3].

Koga *et al.* described a case of a child who developed bilateral acute profound deafness and aseptic meningitis within 14 days after receiving MMR vaccine. The cause of this deafness was presumed to be the mumps vaccination. The basis for the

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presumption was as follows: The meningitis after MMR vaccination was elicited by the Polymerase Chain Reaction (PCR) method to be caused by the mumps vaccine. The complication of the central nervous system (CNS) after measles vaccination occured within 14 days after injection and the onset of vomiting and gait disturbance of the case occurred at 24 days after vaccination [18].

Furthermore, a 7-year old girl developed unilateral total loss of hearing at 13 days following MMR vaccination and the live attenuated mumps-virus vaccine was suspected to be the cause of the injury [19]. Stewart and Prabhum also reported six individuals who developed hearing loss after the MMR immunization and MMR remained a possible etiology. They stated that any risk associated with attenuated viruses must be weighed against the risks of the natural diseases [20].

Cases of aseptic meningitis associated with measles, mumps, and rubella vaccine were sought in thirteen UK health districts following a reported cluster in Nottingham, which suggested a risk of 1 in 4,000 doses. Cases were ascertained by obtaining vaccination records of children with aseptic meningitis diagnosed from cerebrospinal fluid samples submitted to Public Health Laboratories or discharged from hospital with a diagnosis of viral meningitis. Both methods identified vaccination 15 to 35 days before onset as a significant risk factor and therefore indicative of a causal association. With both, half the aseptic meningitis cases identified in children aged 12 to 24 months were vaccine-associated with onset 15 to 35 days after vaccine. This study confirmed that the true risk was substantially higher than suggested by case reports from pediatricians, probably about 1 in 11,000 doses [21].

Furthermore, in Japan, at least 311 meningitis cases suspected to be vaccine-related were identified among 630,157 recipients of the measles-mumps-rubella trivalent (MMR) vaccine. These cases were identified based on the notification of cases and the testing of mumps viruses isolated from cerebrospinal fluid for their relatedness to the vaccine by nucleotide sequence analysis [22].

MMR vaccine has also caused allergic reactions in some individuals because it contains gelatin and other antigens. For example, Nakayama *et al.* evaluated 366 reports of individuals suffered from adverse reactions after immunization with monovalent measles, mumps, and rubella vaccines containing 0.2% gelatin as stabilizer. These reports were categorized as follows: 34 with anaphylaxis, 76 with urticaria, 215 with nonurticarial generalized eruption, and 41 with local reactions only. In 206 individuals from whom serum was available, IgE antibodies to gelatin were detected in 25 of 27 (93%) with anaphylaxis, 27 of 48 (56%) with urticaria, and 8 of 90 (9%) with a generalized eruption. None of a group of 41 patients with only local reactions at the injected site and none of a control group of 29 subjects with no adverse reaction had such antibodies [23].

In addition to systemic illnesses, vaccines also induced the proliferation of B and T cells in the site of vaccine injection. For example, Maubec *et al.* reported 9 individuals who developed cutaneous and subcutaneous pseudolymphoma at the site of hepatitis B (8 cases) and hepatitis A (1 case) vaccination. Histopathologic studies showed dermal and hypodermal lymphocytic follicular infiltrates with germinal center formation. The center of follicles was mostly composed of B cells without atypia, whereas CD4+ T cells were predominant at the periphery [24].

Molecular analysis of clonality revealed a polyclonal pattern of B-cell and T-cell subsets. Aluminium deposits were evidenced in all cases by using histochemical staining in all cases, and by microanalysis and ultrastructural studies in one case. Associated manifestations were vitiligo (1 case) and chronic fatigue with myalgia (2 cases) [24].

It is likely that the MMR vaccines induced the depigmentation of Jeanett's skin through local and systemic autoimmune reactions. Synergistic actions between the DTaP, IPV, and the MMR vaccines in causing the depigmentation of Jeanett's skin are also possible. The roles of autoimmune disorders in the pathogenesis of vitiligo are described in section 7 of this report.

Table 14. Some of the immunogenic ingredients, preservatives, and additives reported in vaccines administered to Jeanett [11]

Vaccine type	Composition
Hepatitis B	Each 0.5 mL dose contains 0.25 mg aluminum; 10 μg of hepatitis B antigen; 4.5 mg sodium chloride; 0.49 mg disodium phosphate dihydrate; and 0.35 mg sodium dihydrogen phosphate dihydrate.
Diphtheria,Tetanus Toxoids, and acellular Pertussis (DTaP)	Each dose (0.5 mL) contains 0.625 mg aluminum; 25 Lf Diphtheria toxoid; 10 Lf tetanus toxoid; 25μg pertussis toxin; 25 μg filamentous hemagglutinin; 8 μg pertacin; 2.5 mg 2-phenoxyethanol; 4.5 mg sodium chloride; and 0.1 mg formaldehyde.
Inactivated polio vaccine (IPV)	Each 0.5 mL dose contains 40 D antigen units of type 1, 8 D antigen units of type 2, and 32 D antigen units of type 3 poliovirus. Also present are 0.5% of 2-phenoxyethanol and 0.02% of formaldehyde (preservatives), 5 ng neomycin, 200 ng streptomycin, and 25 ng polymyxin.
Haemophilus Influenzae (Hib)	Each 0.5 mL dose contains (0.4% sodium chloride) contains 10 μg of purified Haemophilus capsular polysaccharide.
Measles, Mumps, and Rubella (MMR)	Each 0.5 mL contains no less than the equivalent of 1,000 $TCID_{50}$ (tissue culture infectious doses) of the U.S. Reference Measles live virus; 20,000 $TCID_{50}$ Mumps live virus; and 1,000 $TCID_{50}$ of the U.S. Reference Rubella live virus. The 3 live viruses are mixed before being lyophilized. It also contains additives.

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7. Causes and pathogeneses of vitiligo reported in some cases published in the literature

Vitiligo is pigmentary disorder characterized by areas of depigmented skin resulting from the loss of epidermal melanocytes or the loss of melanocyte's ability to produce melanin. Recent studies have indicated that vitiligo areas contain inactive or dormant melanocytes [25-28].

In human skin, melanin is produced by melanocytes and transferred to epithelial cells. Melanin formation requires the enzyme tyrosinase, which catalyzes multiple reactions in the melanin biosynthetic pathway. Han *et al.* reassess cutaneous melanogenesis using tyramide-based tyrosinase assay (TTA). In the TTA procedure, tyrosinase reacts with biotinyl tyramide, causing the substrate to deposit near the enzyme. These biotinylated deposits are then visualized with streptavidin conjugated to a fluorescent dye [29].

In the skin and eye, TTA was highly specific for tyrosinase and served as a sensitive indicator of pigment cell distribution and status. In clinical skin samples, the assay detected pigment cell defects, such as melanocytic nevi and vitiligo, providing confirmation of medical diagnoses [29]. Below are descriptions of some of the causes and mechanisms reported in the literature in people suffering from vitiligo.

7.1. Evidence of autoimmune disorders causing vitiligo

Clinical and experimental studies have demonstrated that cellular and humoral autoimmune disorders play important roles in the pathogenesis of vitiligo in genetically susceptible individuals. These disorders cause the loss of melanocytes and/or target certain enzymes involved in melanin synthesis or crucial to the survival of melanocytes.

For example, Lucchese *et al.* provided evidence for the presence of humoral immune responses against tyrosinase in the sera of individuals suffering from vitiligo. They analyzed the sera from individuals with vitiligo for reactivity toward tyrosinase peptide sequences and detected five autoantigen peptides that have anti-tyrosinase response [30].

Okamoto *et al.* also demonstrated that individuals with vitiligo had significant anti- tyrosinase-related protein-2 (TRP-2) IgG titers in their serum. TRP-2 is highly expressed in melanocytes [31]. In addition, the serum levels of certain immunologic markers including immunoglobulin G (IgG) anti-melanocyte, vitiligo antibodies (V-IgG), and soluble interleukin-2 receptors (sIL-2R) were increased in individual suffering from vitiligo. These changes are associated with augmented humoral and cellular immunity involved in melanocyte cytotoxicity during the active phase of non-segmental vitiligo [32].

Furthermore, Mandelcorn-Monson *et al.* evaluated T cell reactivity to MelanA/MART-1, tyrosinase, and gp100, in HLA-A2-positive individuals with vitiligo. Antigen-specific T lymphocyte reactivity to gp100 peptides was seen in 15 of 17 (88%) individuals. These findings implicate T cell reactivity to gp100 in individuals with active disease. They support the concept of an immunopathologic mechanism in vitiligo, in which cell-mediated responses to normal melanocyte antigens play a crucial part [33]**.** Palermo *et al.* also reported the presence of cytotoxic T lymphocytes directed to melanocyte antigens in vitiligo patients [26].

Machado *et al.* conducted a study to evaluate the trosinase mRNA presence in normal skin and vitiligo areas. Tyrosinase mRNA was negative in 93.75% of vitiligo areas [28]. Kitamura *et al.* have compared the expression of endothelin (ET)-1, the ET-1 receptor (ET(B)R), granulocyte macrophage colony stimulating factor (GM-CSF), stem cell factor (SCF), the SCF receptor (KIT protein), tyrosinase, and S100 alpha between lesional and non-lesional vitiligo epidermis [34]. They reported the following changes in vitiligo epidermis that may be associated with the dysfunction and/or loss of melanocytes:

1) Analysis by reverse transcription-polymerase chain reaction (RT-PCR) and by western blotting for ET-1 and SCF demonstrated up-regulated expression of these cytokines in lesional vitiligo epidermis.

2) Immunohistochemistry with antibodies to melanocyte markers revealed that at the edge of the lesional epidermis, melanocytes remain and express tyrosinase, S100 alpha and ET(B)R, but not KIT protein or melanocyte-specific microphthalmia-associated transcription factor (MITF-M). Quantitation of the staining revealed a slight or moderate decrease in the number of S100 alpha, tyrosinase, and ET(B)R-positive cells at the edge of the lesional epidermis. In contrast, the number of cells expressing KIT protein was markedly decreased at the edge of the lesional epidermis compared with the non-lesional epidermis. At the center of the lesional epidermis, there was complete loss of melanocytes expressing KIT protein, S100 alpha, ET(B)R, and/or tyrosinase.

3) Western blotting revealed down-regulated expression of c-kit and MITF-M proteins at the edge of the lesional epidermis in vitiligo [34].

Zailaie found that low-dose oral aspirin treatment of active vitiligo patients caused significant reduction in the acute serum immunologic markers of T cell activation, V-IgG activity and sIL-2R concentration with concomitant arrest of disease activity [32].

In this study, 18 female and 14 male individuals with a recent onset of non-segmental vitiligo were divided into 2 equal groups. One group received a daily single dose of oral aspirin (300 mg) and the second group received only placebo for a period of 12 weeks.

Serum V-IgG activity and sIL-2R concentration were determined before and at the end of treatment period. The V-IgG activity was measured using cellular enzyme-linked immunosorbent assay (ELISA) following incubation of IgG antibodies with an adult cultured melanocytes. Serum sIL-2R concentration was measured using the highly sensitive quantitative sandwich ELISA utilizing a commercially available kit.

The serum V-IgG activity and sIL-2R concentration of the active vitiligo patients (0.81 +/- 0.23 optical density (O.D.), 1428 +/- 510 pg/ml) were significantly increased compared with that of controls (0.27 +/- 0.1 O.D., 846 +/- 312 pg/ml; $p<0.05$, $p<0.01$). Aspirin-treated vitiligo patients showed significant decrease in serum V-IgG activity and sIL-2R concentration (0.32 +/- 0.08 O.D., 756 +/- 216 pg/ml) compared with that of placebo-treated patients (0.83 +/- 0.19 O.D., 1327 +/- 392 pg/ml; $p<0.01$) [32].

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7.2. Exposure of individuals to certain chemicals and oxidative stress caused vitiligo

Boissy and Manga reported that the exposure of individuals to phenolic/catecholic derivatives at workplace has caused vitiligo in some individuals. Phenolic/catecholic derivatives are structurally similar to the melanin precursor tyrosine and are preferentially cytotoxic to melanocytes, with high-dose exposure resulting in the initiation of apoptosis [27].

They suggested that tyrosinase-related protein-1 facilitates toxicity possibly by catalytic conversion of the compounds, which results in the generation of radical oxygen species. The ensuing oxidative stress then triggers activation of cellular free radical scavenging pathways to prevent cell death. Genetic inability of melanocytes to tolerate and/or respond to the oxidative stress may underlie the etiology of contact/occupational vitiligo [27].

Furthermore, a number of experiments showed that keratinocytes derived from vitiligo lesions produce increased number of superoxide anions (hyperactive oxygen and nitric oxide). Tsiskarishvili studied the effectiveness of complex treatment with cuprum sulfate and vitix in children with vitiligo. Melanin is formed from tyrosine by enzyme tyrosinase and cuprum is a cofactor of this photochemical process. A total of 27 children 7-17 years old with vitiligo (15 boys and 12 girls) were included in this study and the duration of illness varied from 1 month to 11 years [35].

Preparation vitix was applied directly to the lesions and surrounded affected area. Duration of the treatment was 6 months. Restoration of pigmentation was observed by the following patterns: diffuse in 9, follicular in 5 and peripheral in 3 cases. Improvement of clinical condition was observed in 56% of patients. Erythema with mild itching and erythema with peeling were observed as the side effects. Due to the ability to re-establish the free radicals physiological equilibrium in epidermal cells (melanocytes and keratinocytes) vitix shows principally new impact on skin with depigmentation. The effect of this preparation is based on melon's extract rich in antioxidants [35].

7.3. Treatment with vitamin D3 helped in repigmentation of skin in vitiligo cases

It has been reported that 1,25-dihydroxyvitamin D3 and the vitamin D3 analog calcipotriol play important role in the maturation of the immature melanocytes and treatment with vitamin D helped individuals with vitiligo to regain pigmentation of their skin. Cherif *et al.* performed a prospective study including twenty-three individuals with essentially bilateral symmetrical lesions of vitiligo to evaluate efficacy of the combination of calcipotriol and psoralen plus ultraviolet A (PUVA) in the treatment of vitiligo. Calcipotriol (0.005 %) ointment was applied twice daily over the right side of the body, and the other side was not treated. PUVA was performed three times per week and all individuals received at least forty-five sessions of PUVA [36].

Individuals were evaluated clinically and photographed all fifteen weeks. At the fifteenth session, 69 percent of the individuals had minimal to moderate improvement on the calcipotriol side compared to 52 percent on the PUVA-only side ($p = 0.015$). At the forty-fifth session, 52 percent showed marked improvement on the calcipotriol side compared to 30 percent on the PUVA-only side ($p = 0.13$), with more intense repigmentation on calcipotriol-treated areas. Treatment was well tolerated, and no adverse effect was noted [36].

Furthermore, Watabe *et al.* studied the effects of 1,25-dihydroxyvitamin D3 on the differentiation of immature melanocyte precursors using the NCC-/melb4 cell line which is an immature melanocyte cell line established from mouse neural crest cells. They found that 1,25-Dihydroxyvitamin D3 inhibited the growth of NCC-/melb4 cells and the growth inhibition was accompanied by the induction of tyrosinase and a change in L-3,4-dihydroxyphenylalanine reactivity from negative to positive. In primary cultures of murine neural crest cells, L-3,4-dihydroxyphenylalanine-positive cells were increased after 1,25-dihydroxyvitamin D3 treatment. These findings indicate that 1,25-dihydroxyvitamin D3 stimulates the differentiation of immature melanocyte precursors [37].

In this study, electron microscopy also demonstrated that melanosomes were in more advanced stages after 1,25-dihydroxyvitamin D3 treatment. Moreover, immunostaining and reverse transcription-polymerase chain reaction analysis revealed that endothelin B receptor expression was induced in NCC-/melb4 cells following treatment with 1,25-dihydroxyvitamin D3. The induction of endothelin B receptor by 1,25-dihydroxyvitamin D3 was also demonstrated in neural crest cell primary cultures, but not in mature melanocytes. These findings suggest a regulatory role for vitamin D3 in melanocyte development and melanogenesis, and may also explain the working mechanism of vitamin D3 in the treatment of vitiligo [37].

7.4. Zinc deficiency can cause vitiligo

Bruske and Salfeld reported significant low blood-levels of zinc in individuals suffering from vitiligo as compared to healthy individuals and individuals suffered from other skin problems. Their study included data on serum zinc levels of 380 individuals with alopecia areata, alopecia androgenetica, psoriasis vulgaris, vitiligo, rosacea, venous ulcer and atopic eczema. In addition, data on zinc levels from 31 healthy people were also included [38].

8. Conclusions and recommendations

The medical evidence described in this report clearly indicates that vaccines are the likely cause of vitiligo in Jeanett's case and her illness probably resulted from autoimmune disorder. Jeanett's susceptibility to developing adverse reaction to vaccine was notable following receiving her first injection of hepatitis B vaccine given after birth. Furthermore, the intensity of her adverse reactions to the hepatitis B, DTaP, Polio, and Hib vaccines increased following receiving more doses of these vaccines. In addition, the intensity and severity of Jeanett's skin lesions and the incidence of her other systemic illness were significantly increased following receiving the second injection of MMR vaccine as compared to receiving her first MMR injection.

My review of Jeanett's medical records revealed that the medical professionals who administered vaccines to Jeanett during her first five years of life did not do benefit/risk analyses

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prior to administering vaccines to Jeanett. Her medical records clearly show that she suffered from adverse reactions to vaccines following each treatment with single vaccine or multiple vaccines. In addition, the medical staffs ignored Jeanett's mother warning that vaccines are causing illness in her daughter's case. In my opinion, Jeanett should not be given any vaccine in future. Vaccine(s) probably will aggravate her present illness and trigger more illnesses.

It seems that the blood tests previously performed in Jeanett's case (Section 5) are not specific to identify the autoimmune mechanisms involved in triggering the depigmentation of Jeanett's skin. My review of the medical literature reveled that the following tests may be useful in identifying the specific autoimmune mechanisms involved in Jeanett's vitiligo: (1) Evaluating cutaneous melanogenesis using tyramide-based tyrosinase assay (TTA) as described by Han *et al.* 2002 (Section 7). (2) Measuring the serum levels of antibodies against tyrosinase and other components of melanocytes and performing other immunological tests that are described in Section 7 of this report.

Jeanett was treated with corticosteroids locally and systemically on several occasions and these treatments were not helpful in reducing the severity of her vitiligo. Clinical studies have shown treatment of children and adults suffering from vitiligo with vitix or 1,25-dihydroxyvitamin D3 (calcipotriol) were helpful in inducing repigmentation of the skin. Clinical study also showed that treating children suffering from vitiligo with Aspirin orally at a daily dose of 300 mg for 12 weeks reduced the severity of their illness. These studies are described in Section 7 of this report. In my opinion implementing these treatments or some of them under medical supervision could be helpful to inducing skin repigmentation in Jeanett case and reducing the severity of her illness.

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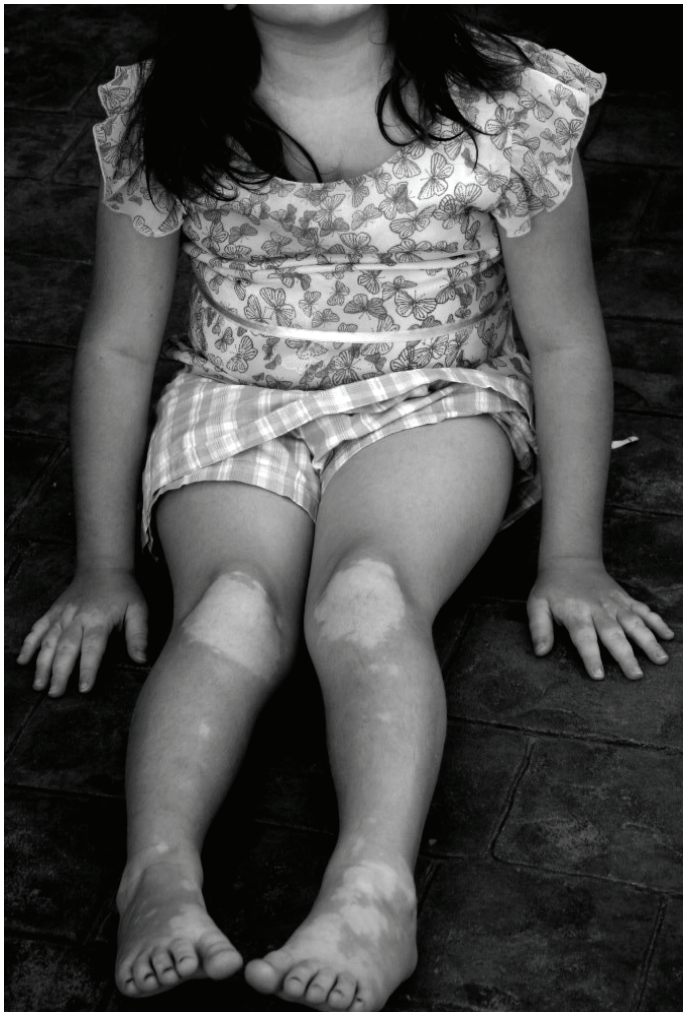

Figure 1. Front view of vitiligo on legs and hands

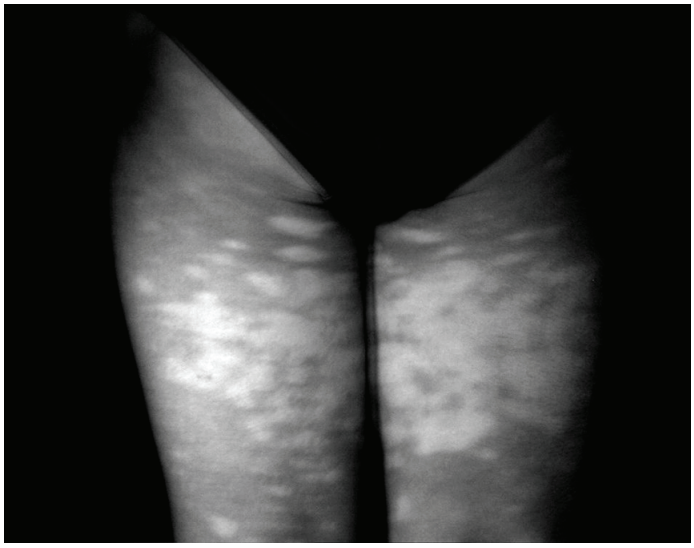

Figure 2. Back view of vitiligo on legs

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