Vitamin D and VDR

Part II

Disclosure:

Relationship with commercial interests - None
Disclosure of commercial support - None
Conflict of interest - None

Autoimmune diseases and infections: controversial issues.

Baio P[1], Brucato A, Buskila D, Gershwin ME, Giacomazzi D, Lopez LR, Luzzati R, Matsuura E, Selmi C, Sarzi-Puttini P, Atzeni F.

Author information

Abstract

The etiology and pathogenesis of certain types of disease remain controversial and stand like a bridge that crosses infectious, autoimmune and autoinflammatory pathways. Infection, for example, may initiate a disease, although it is the genetic regulation in the host, the interplay between virus or bacteria persistence and autoimmunity that produces the later phases of disease, the antigenic determinants responsible for inducing autoimmune disease, and the pathogenetic effector mechanisms. Infections agents cause pericarditis, but in 85% of cases it is "idiopathic". It has also been shown that persistent Clamydia pneumoniae, Porphyromonas gingivalis, and Helicobacter pylori infections cause host immunity and promote atherogenesis. A number of infectious agents have been suggested as potential triggers for primary biliary cirrhosis. Infections and vaccinations have also been linked to the pathogenesis of fibromyalgia syndrome, a common, chronic syndrome of widespread pain. Many factors are also responsible for fever of unknown origin such as: infections, autoimmunity disease, etc. However, it is difficult to determine a direct correlation between the infections agents in such a large group of diseases. The aim of this review is to analyze some of the controversies about the role of infections in autoimmune diseases.

Vitamin D metabolites as clinical markers in autoimmune and chronic disease.

Blaney GP[1], Albert PJ, Proal AD.

Author information

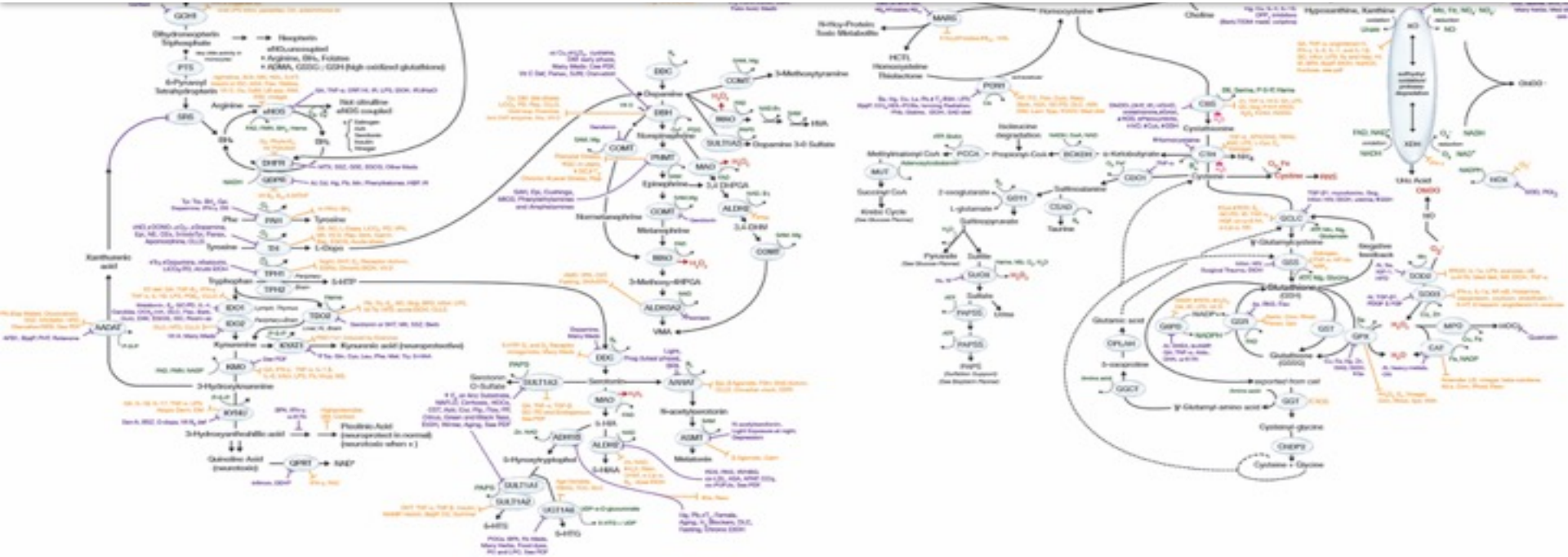
Abstract

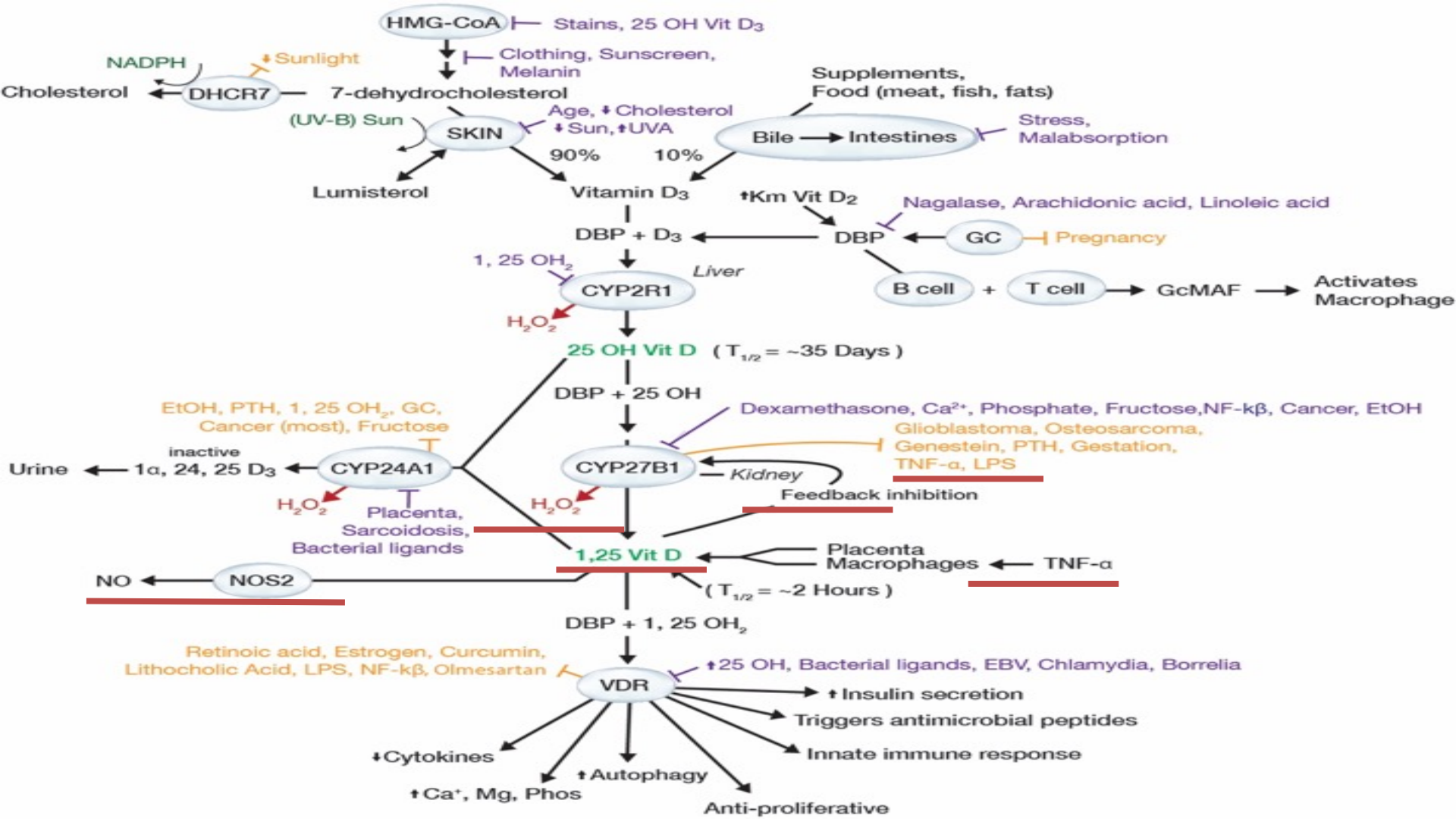
Recent research has implicated vitamin D deficiency (serum levels of 25-hydroxyvitamin D <50 nmol/L) with a number of chronic conditions, including autoimmune conditions such as multiple sclerosis, lupus, and psoriasis, and chronic conditions such as osteoporosis, osteoarthritis, metabolic syndrome, fibromyalgia and chronic fatigue syndrome. It has been assumed that low levels of 25-hydroxyvitamin D (25-D) accurately indicate vitamin D storage and vitamin D receptor (VDR)-mediated control of calcium metabolism and innate immunity. To evaluate this assumption, 25-D and 1,25-dihydroxyvitamin D3 (1,25-D) levels were measured in 100 Canadian patients with these conditions. Additionally, other inflammatory markers (CK, CRP) were measured. Results showed a strong positive association between these autoimmune conditions and levels of 1,25-D >110 pmol/L. However, there was little association with vitamin D deficiency or the other inflammatory markers, meaning that the results challenge the assumption that serum levels of 25-D are a sensitive measure of the autoimmune disease state. Rather, these findings support the use of 1,25-D as a clinical marker in autoimmune conditions. High levels of 1,25-D may result when dysregulation of the VDR by bacterial ligands prevents the receptor from expressing enzymes necessary to keep 1,25-D in a normal range.

I will test for 25 OH and 1,25 OH.

Great. Now What?

Practical	Logical	Strategic
Alignment	Plot	Plan
Foundations	Response	Remove
Timeline	Trigger	Restore

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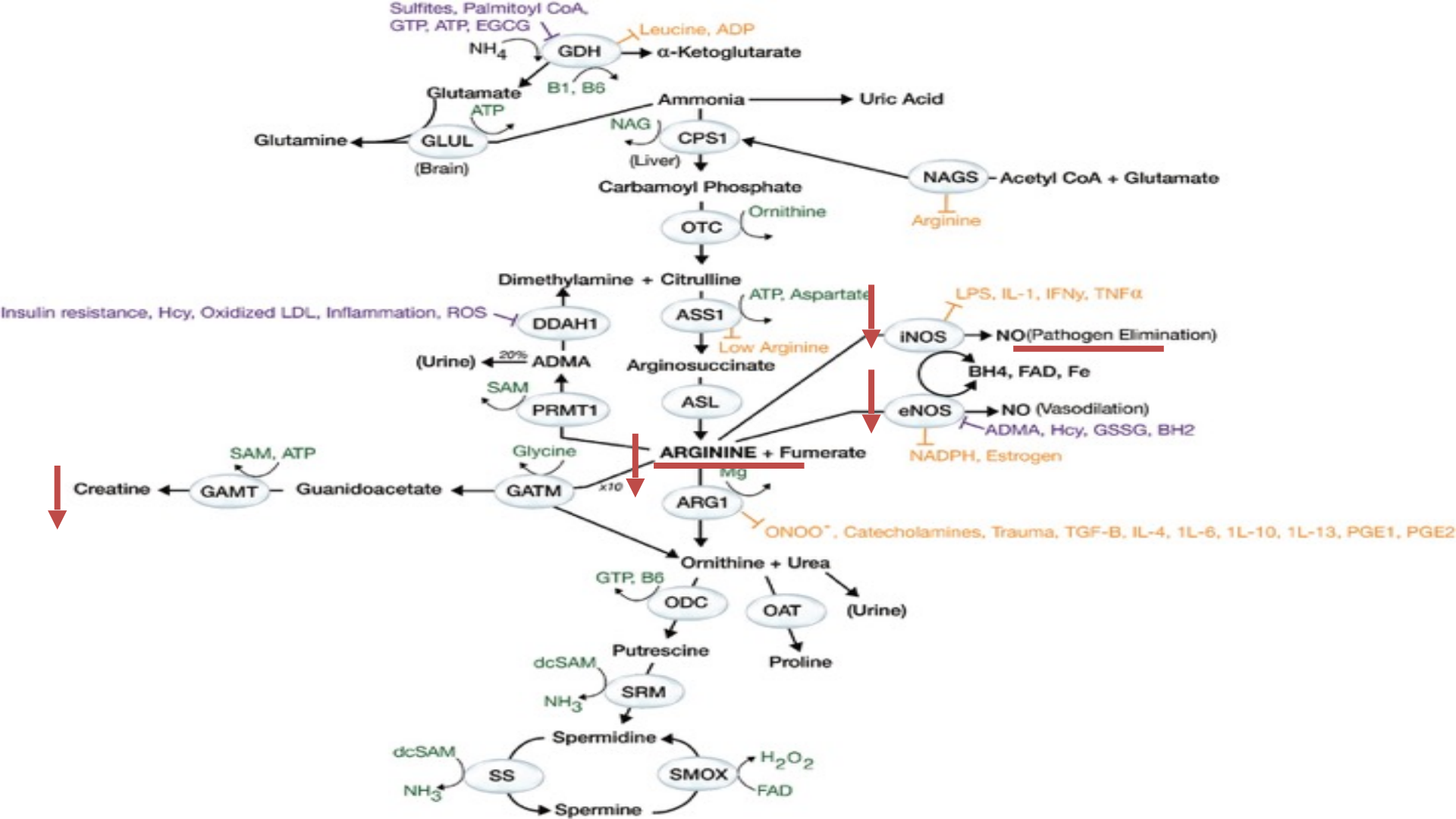
NADPH
Sunlight
Cholesterol
DHCR7
7-dehydrocholesterol
Supplements, Food (meat, fish, fats)
(UV-B) Sun
SKIN
Age, Cholesterol
Sun, UVA
Bile
Intestines
Stress, Malabsorption
90%
10%
Lumisterol
Vitamin D3
Km Vit D2
Nagalase, Arachidonic acid, Linoleic acid
DBP + D3
DBP
GC
Pregnancy
1, 25 OH2
Liver
CYP2R1
B cell
+
T cell
GcMAF
Activates Macrophage
H2O2
25 OH Vit D
(T1/2 = ~35 Days)
DBP + 25 OH
EtOH, PTH, 1, 25 OH2, GC, Cancer (most), Fructose
Dexamethasone, Ca2+, Phosphate, Fructose, NF-kβ, Cancer, EtOH
Glioblastoma, Osteosarcoma, Genestein, PTH, Gestation, TNF-α, LPS
inactive
Urine
1α, 24, 25 D3
CYP24A1
CYP27B1
Kidney
Feedback inhibition
H2O2
H2O2
Placenta, Sarcoidosis, Bacterial ligands
1,25 Vit D
Placenta
Macrophages
TNF-α
NO
NOS2
(T1/2 = ~2 Hours)
DBP + 1, 25 OH2
Retinoic acid, Estrogen, Curcumin, Lithocholic Acid, LPS, NF-kβ, Olmesartan
VDR
25 OH, Bacterial ligands, EBV, Chlamydia, Borrelia
Insulin secretion
Triggers antimicrobial peptides
Innate immune response
Cytokines
Autophagy
Ca+, Mg, Phos
Anti-proliferative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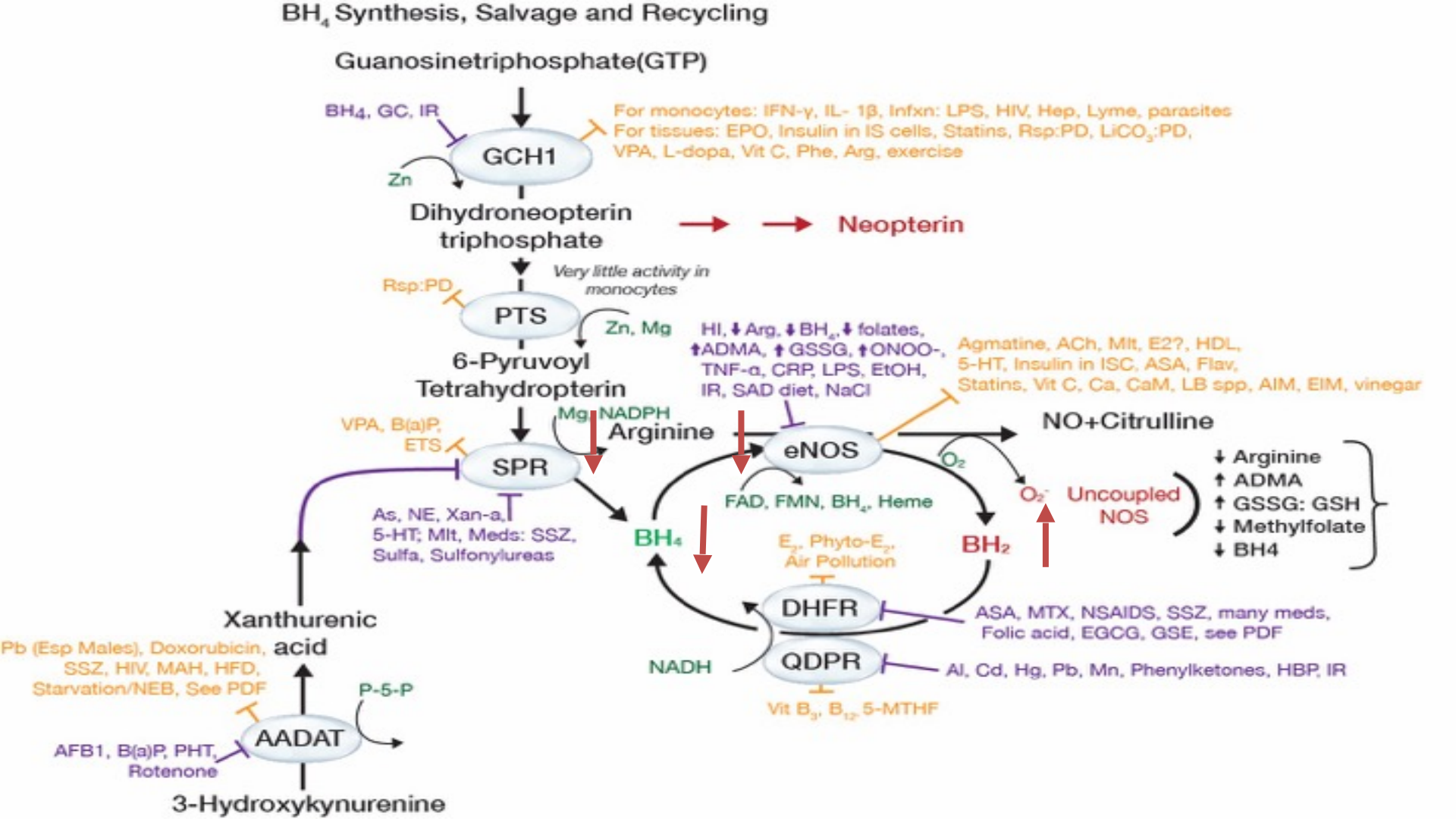
Leucine, ADP
NH4
GDH
α-Ketoglutarate
B1, B6
Glutamate
Ammonia
Uric Acid
ATP
Glutamine
GLUL
(Brain)
NAG
CPS1
(Liver)
NAGS
Acetyl CoA + Glutamate
Carbamoyl Phosphate
Arginine
OTC
Ornithine
Dimethylamine + Citrulline
ATP, Aspartate
LPS, IL-1, IFNγ, TNFα
Insulin resistance, Hcy, Oxidized LDL, Inflammation, ROS
DDAH1
ASS1
iNOS
NO(Pathogen Elimination)
(Urine)
20%
ADMA
Low Arginine
Arginosuccinate
BH4, FAD, Fe
SAM
PRMT1
ASL
eNOS
NO (Vasodilation)
ADMA, Hcy, GSSG, BH2
SAM, ATP
Glycine
ARGININE + Fumerate
NADPH, Estrogen
Creatine
GAMT
Guanidoacetate
GATM
x10
Mg
ARG1
ONOO⁻, Catecholamines, Trauma, TGF-B, IL-4, 1L-6, 1L-10, 1L-13, PGE1, PGE2
Ornithine + Urea
GTP, B6
ODC
OAT
(Urine)
Putrescine
Proline
dcSAM
NH3
SRM
Spermidine
dcSAM
SS
SMOX
H2O2
NH3
FAD
Spermine


BH4 Synthesis, Salvage and Recycling
Guanosinetriphosphate(GTP)
BH4, GC, IR
GCH1
Zn
For monocytes: IFN-γ, IL- 1β, Infxn: LPS, HIV, Hep, Lyme, parasites
For tissues: EPO, Insulin in IS cells, Statins, Rsp:PD, LiCO3:PD,
VPA, L-dopa, Vit C, Phe, Arg, exercise
Dihydroneopterin triphosphate
Neopterin
Very little activity in monocytes
Rsp:PD
PTS
Zn, Mg
6-Pyruvoyl Tetrahydropterin
VPA, B(a)P, ETS
SPR
Mg
NADPH
Arginine
HI, ↓Arg, ↓BH4, ↓folates, ↑ADMA, ↑GSSG, ↑ONOO-, TNF-α, CRP, LPS, EtOH, IR, SAD diet, NaCl
Agmatine, ACh, Mlt, E2?, HDL, 5-HT, Insulin in ISC, ASA, Flav, Statins, Vit C, Ca, CaM, LB spp, AIM, EIM, vinegar
eNOS
NO+Citrulline
O2
O2-
Uncoupled NOS
↓ Arginine
↑ ADMA
↑ GSSG: GSH
↓ Methylfolate
↓ BH4
FAD, FMN, BH4, Heme
As, NE, Xan-a, 5-HT; Mlt, Meds: SSZ, Sulfa, Sulfonylureas
BH4
BH2
E2, Phyto-E2, Air Pollution
DHFR
ASA, MTX, NSAIDS, SSZ, many meds, Folic acid, EGCG, GSE, see PDF
NADH
QDPR
Al, Cd, Hg, Pb, Mn, Phenylketones, HBP, IR
Vit B3, B12, 5-MTHF
Xanthurenic acid
Pb (Esp Males), Doxorubicin, SSZ, HIV, MAH, HFD, Starvation/NEB, See PDF
P-5-P
AADAT
AFB1, B(a)P, PHT, Rotenone
3-Hydroxykynurenine

Autism and Vit D

TABLE 1. CLINICAL CHARACTERISTICS OF STUDY SUBJECTS

Variable	*Children with autism*	*Healthy controls*
Number	70	42
Age (years)	5.3 ± 2.8	6.1 ± 1.8
Calcium (mg/dL)	8.9 ± 0.8**	9.5 ± 0.8
25(OH)D (ng/mL)	28.5 ± 16.4***	40.1 ± 11.8
$1,25(OH)_2D$ (ng/mL)	27.1 ± 10.7*	32.8 ± 9.1

Data expressed as mean ± standard deviation.
*$p < 0.005$ versus healthy controls.
**$p < 0.0001$ versus healthy controls.
***$p < 0.00001$ versus healthy controls.

Reduced Serum Levels of 25-Hydroxy and 1,25-Dihydroxy Vitamin D in Egyptian Children with Autism

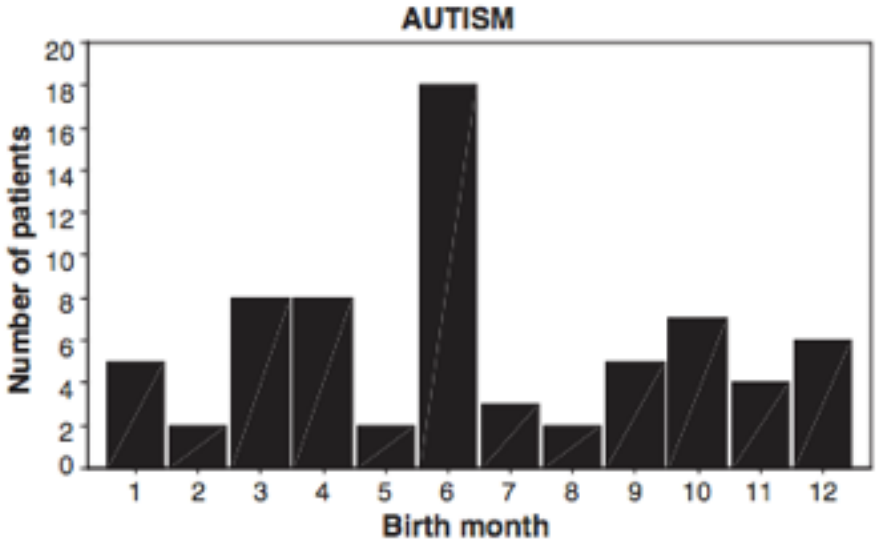


FIG. 2. Distribution of birth months for children with autism.

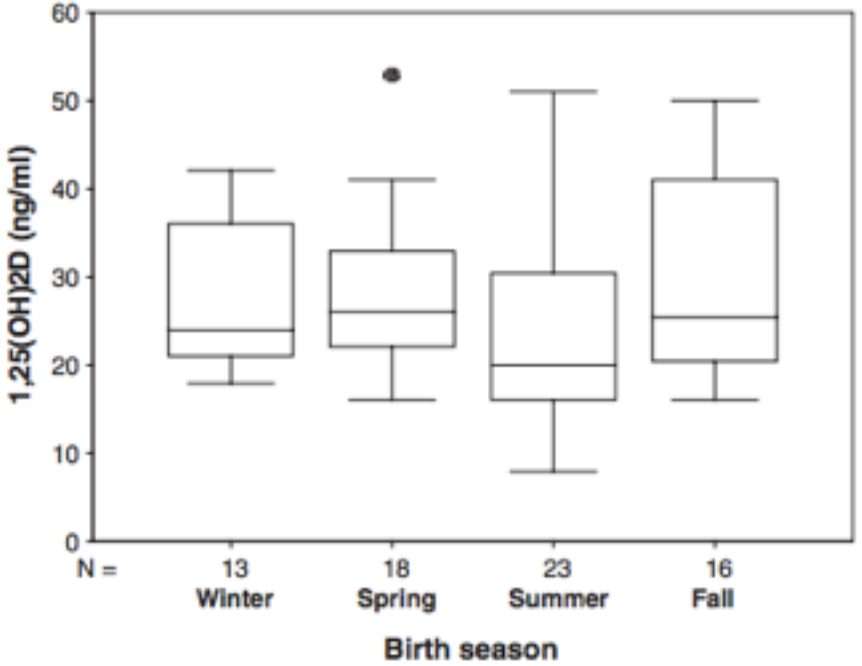
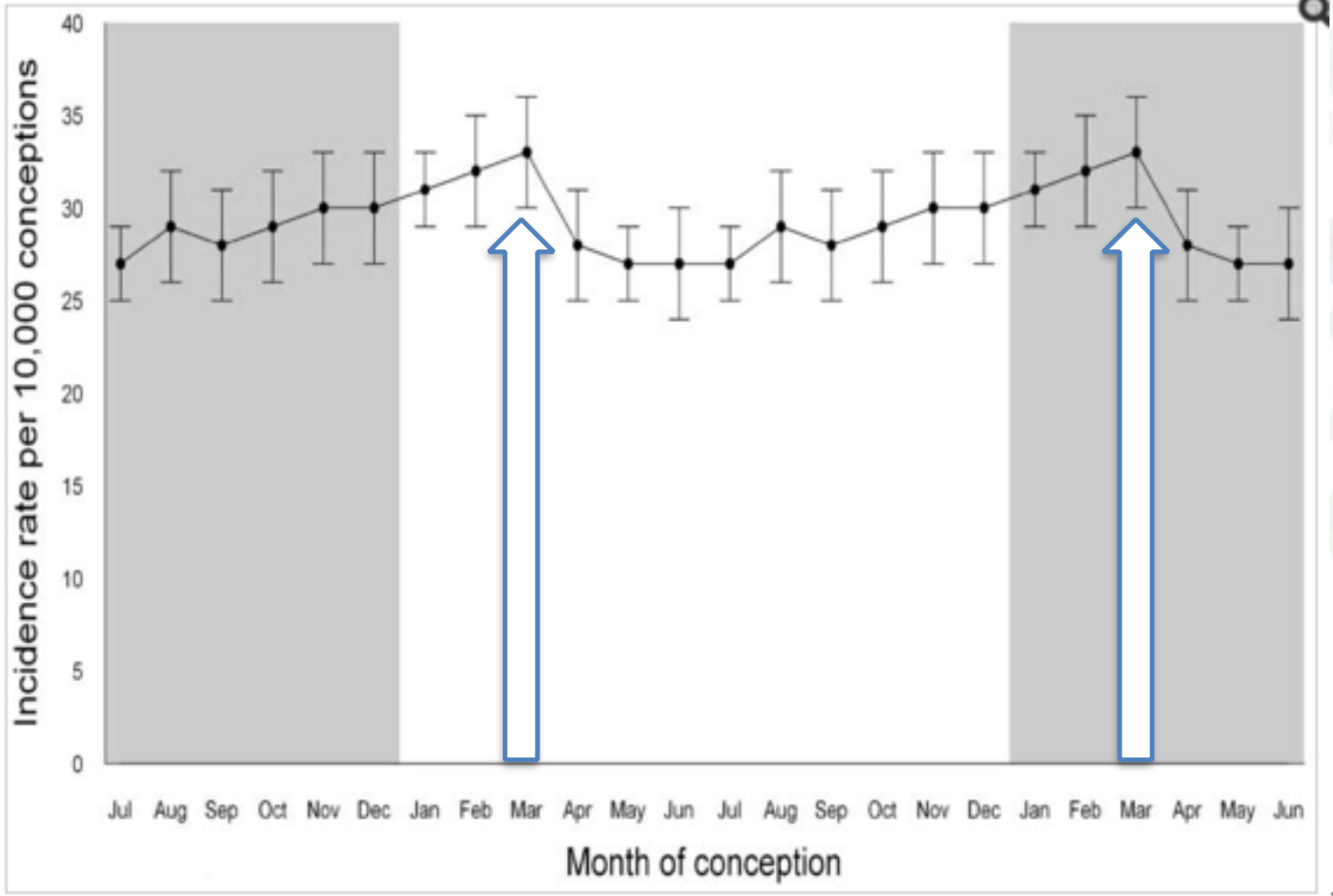


FIG. 4. Box plots of birth seasons for $1,25(OH)_2D$ in children with autism.

Reduced Serum Levels of 25-Hydroxy and 1,25-Dihydroxy Vitamin D in Egyptian Children with Autism



Month of Conception and Risk of Autism

This knowledge is particularly relevant and timely, because infants and children appear more susceptible to viral rather than bacterial infections in the face of vitamin D deficiency. The connection between vitamin D, infections and immune function in the pediatric population indicates a possible role for vitamin D supplementation in potential interventions and adjuvant therapies.

Vitamin D treatment during pregnancy prevents autism-related phenotypes in a mouse model of maternal immune ac

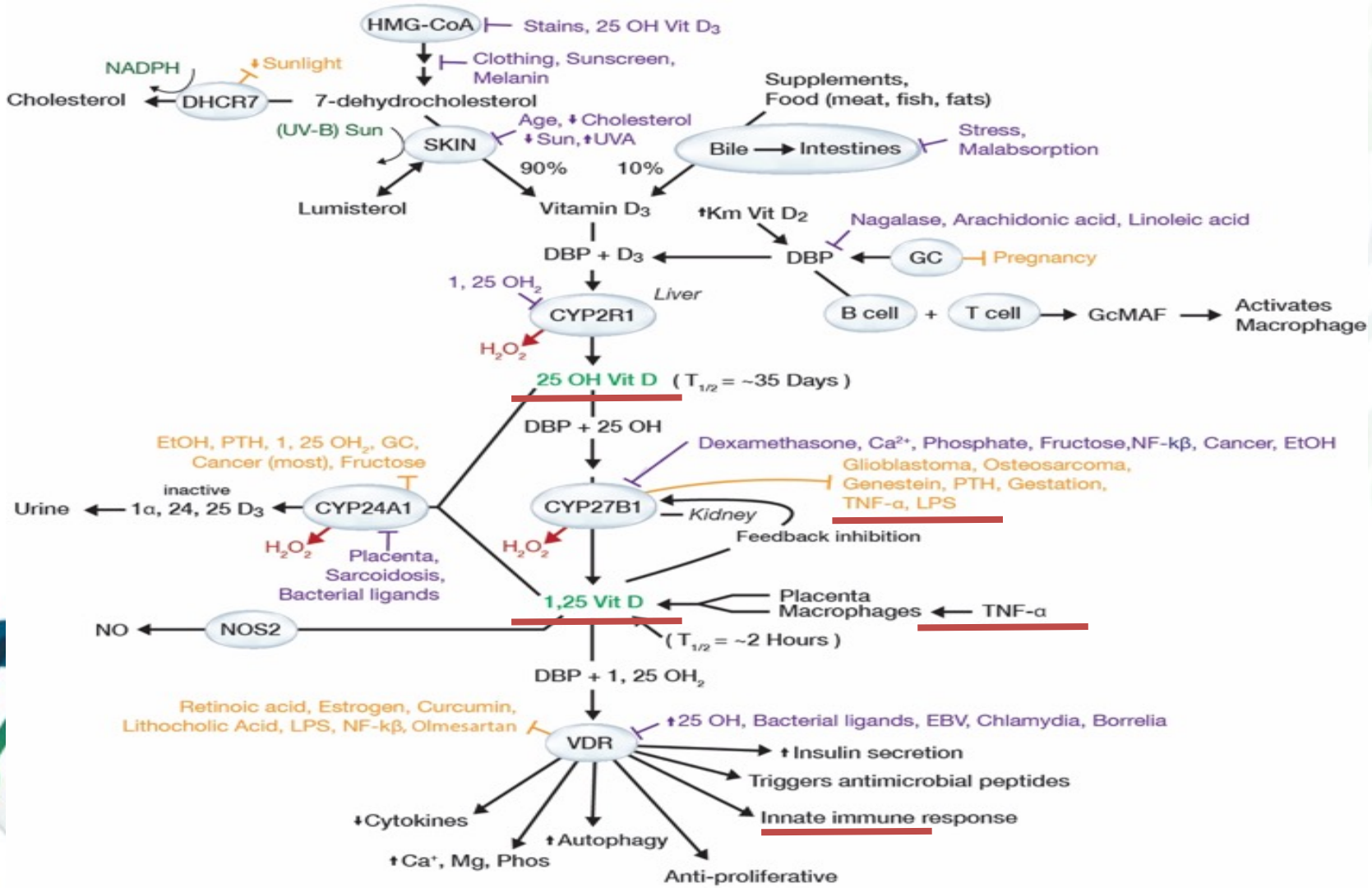
Developmental vitamin D deficiency has further been shown to induce persistent alterations in immune function, by increasing central immune organ size and inducing a pro-inflammatory lymphocyte phenotype [32].

Vitamin D treatment during pregnancy prevents autism-related phenotypes in a mouse model of maternal immune activ

Vitamin D association with IFNγ response to *M.tb* PPD

Vitamin D has been shown to play an immuno-regulatory role [20,23], and in particular has been shown to regulate IFNγ production [38,39]. It is possible that Vitamin D is produced as part of the immuno-regulatory mechanism to control the pro-inflammatory response produced following vaccination. Our results show that 25(OH)D concentration is inversely associated with the IFNγ response to *M.tb* PPD following BCG vaccination 3 months post vaccination, but that this effect is weaker at 12 months. The weakening of the effect at 12 months could be due to lower levels of Vitamin D being present at 12 compared to 3 months.

BCG Vaccination: A Role for Vitamin D?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Cholesterol
DHCR7
7-dehydrocholesterol
Supplements, Food (meat, fish, fats)
(UV-B) Sun
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Stress, Malabsorption
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Km Vit D2
Nagalase, Arachidonic acid, Linoleic acid
DBP + D3
DBP
GC
Pregnancy
1, 25 OH2
Liver
CYP2R1
B cell
+
T cell
GcMAF
Activates Macrophage
H2O2
25 OH Vit D
(T1/2 = ~35 Days)
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EtOH, PTH, 1, 25 OH2, GC, Cancer (most), Fructose
Dexamethasone, Ca2+, Phosphate, Fructose, NF-kβ, Cancer, EtOH
Glioblastoma, Osteosarcoma, Genestein, PTH, Gestation, TNF-α, LPS
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Urine
1α, 24, 25 D3
CYP24A1
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(T1/2 = ~2 Hours)
DBP + 1, 25 OH2
Retinoic acid, Estrogen, Curcumin, Lithocholic Acid, LPS, NF-kβ, Olmesartan
VDR
25 OH, Bacterial ligands, EBV, Chlamydia, Borrelia
Insulin secretion
Triggers antimicrobial peptides
Innate immune response
Cytokines
Autophagy
Ca+, Mg, Phos
Anti-proliferative

Prenatal exposure to infection is a recognized environmental risk factor for neuropsychiatric disorders of developmental origins. This epidemiological association has been most widely studied in the context of schizophrenia [1]. Since the first report in 1971 [2], however, evidence has accumulated to suggest that prenatal infection also is a risk factor for autism spectrum disorder (ASD) [3, 4]. For example, studies of the Danish health registry show that from more than one million children born between 1980 and 2005 there was an almost threefold increase in the rate of ASD diagnosis in children born to mothers who were hospitalized for viral infection during pregnancy [5]. A similar (albeit somewhat less strong) association has been found in a large Swedish nationwide register-based birth cohort born 1984–2007 with follow-up through 2011 [6]. Experimental work in animals indicates that this link is mediated by maternal immune activation (MIA) involving an interplay between cytokine-associated inflammatory events [7, 8, 9], oxidative stress [10], and other pathophysiological processes such as hypoferremia [11] and zinc deficiency [12]. The centrality of

Vitamin D treatment during pregnancy prevents autism-related phenotypes in a mouse model of maternal immune activa

Another epidemiologically valid developmental risk factor for later psychiatric disease is developmental vitamin D (DVD) deficiency [22]. Besides its role in schizophrenia etiology, there is a growing body of evidence linking vitamin D deficiency with autism [23]. Birth cohort studies have provided evidence that maternal vitamin D deficiency is associated with a range of later autism-related outcomes including impaired language development [24] and cognitive development in offspring [25]. Most recently, we have shown that low levels of vitamin D at birth are associated with increased incidence of autism in children [26]. Low vitamin D would also appear to be prevalent in children diagnosed with autism [27].

Vitamin D treatment during pregnancy prevents autism-related phenotypes in a mouse model of maternal immune act

working memory [51]. Finally, in the context of this study, an even more important finding was that maternal treatment with the active vitamin D hormone 1,25OHD was capable of preventing this altered social behavior in juvenile MIA offspring.

there is initial evidence to suggest that Vit_D supplementation in children with ASD may be effective in treating this condition [71]. Unfortunately, 1,25OHD as the active Vit_D hormone cannot be used in pregnancy due to its potential hypercalcaemic effects on the developing fetus. However, our findings suggest that future studies with the safe-to-use dietary form of Vit_D, cholecalciferol, are warranted. If dietary supplementation with cholecalciferol was shown to be successful in the prevention of MIA-induced behavioral abnormalities relevant to ASD (and related neurodevelopmental disorders), then this may open new avenues for the establishment of novel therapeutic public health preventative interventions in a similar manner to the use of folate to prevent spina bifida.

Vitamin D treatment during pregnancy prevents autism-related phenotypes in a mouse model of maternal immune act

Serious GI Issues?

The gastrointestinal (GI) tract is a selectively permeable barrier that permits water and nutrient transport whilst inhibiting systemic pathogenic infection. Evidence from VDR knockout mice suggests that vitamin D has a role in regulating the GI tract barrier. The knockout mice showed a heightened vulnerability to lipopolysaccharides and chemically induced GI inflammation (DSS colitis) [30]. The integrity of the epithelial barrier was lost in the mice that had been exposed to DSS [30]. Compared to wild-type (WT) mice, VDR mice treated with DSS displayed a reduction in expression of E-cadherin, claudin-1, ZO-1, and occluding proteins [31]. In GI epithelial cells 1,25D stimulated transcription of E-cadherin [32]. The permeability of the gut increased in line with the loss of tight junction proteins in VDR knockout mice and vitamin D deficient mice [31]. Furthermore, elevated levels of inflammatory cytokines, such as TNF-α, were found to contribute to the loss of GI barrier integrity in vitamin D deficient and VDR knockout mice [30]. Together, the evidence from these studies indicates that vitamin D has an important regulatory role in maintaining the GI epithelium and its barrier function.

PMCID: PMC492596 **Crosstalk between Vitamin D Metabolism, VDR Signalling, and Innate Immunity**

Paul and Judy -

Are you checking vitamin D levels in kids who are responding poorly to vaccines?

Be good to see three ratios and inflammatory markers BEFORE kids are vaccinated:
- vitamin D 25 : vitamin D 1, 25
- neopterin : biopterin
- SAM : SAH
- hsCRP or lipid peroxidation
- RBC glutathione

I highly suspect all of these are out of whack in kids who are becoming autistic or challenged by vaccines

If we can identify consistent markers of what predisposes kids to vaccine injury, then we can create standard guidelines of practice to have kids exempt from vaccinations until these markers are normalized.

Can you get another IRB Paul?

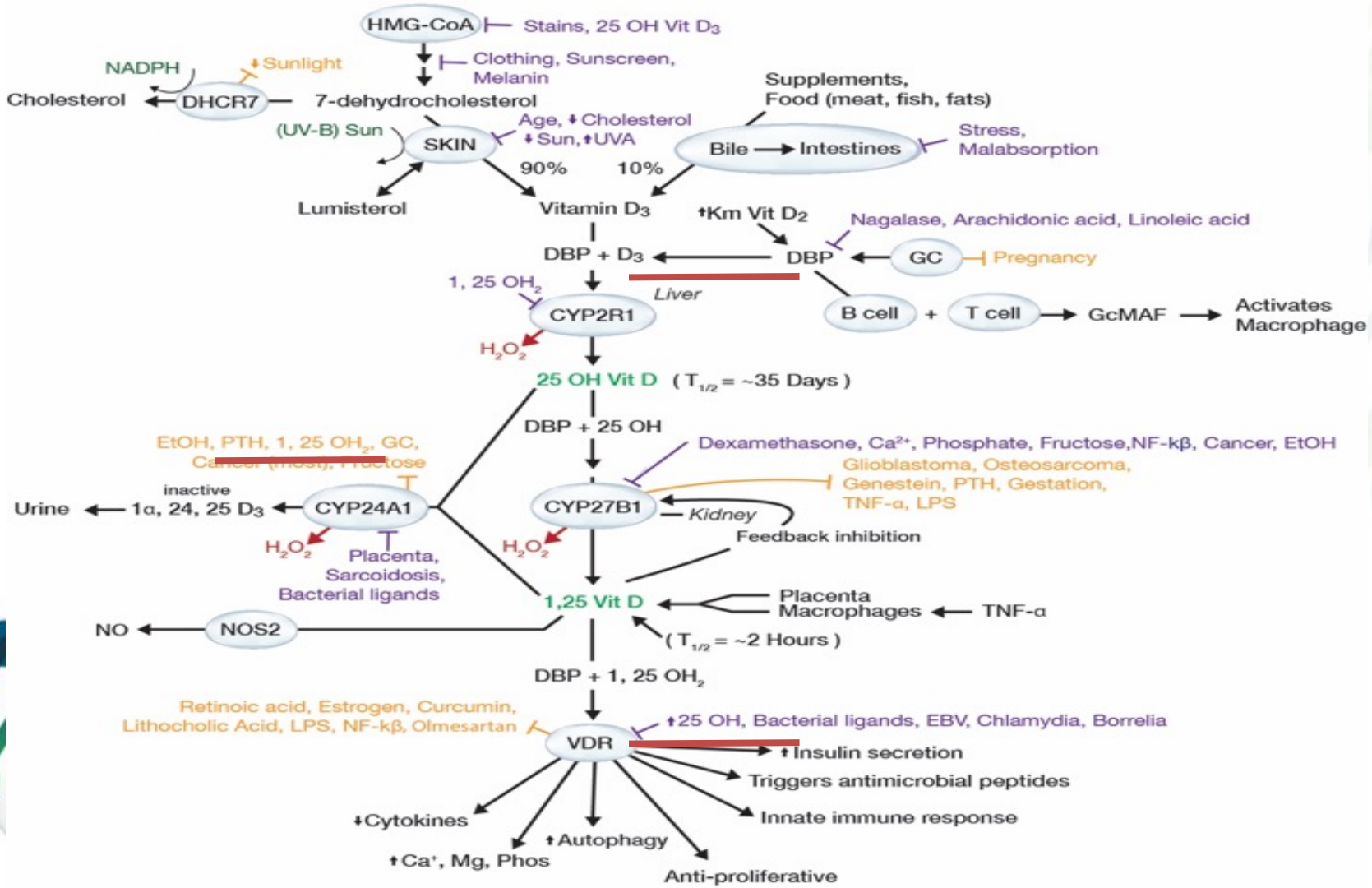
Thanks

Ben

General Dosing

Why might use of bolus dose vitamin D be ineffective for prevention of acute respiratory tract infection? One explanation relates to the potentially adverse effects of wide fluctuations in circulating 25-hydroxyvitamin D concentrations, which are seen after use of bolus doses but not with daily or weekly supplementation. Vieth has proposed that high circulating concentrations after bolus dosing may chronically dysregulate activity of enzymes responsible for synthesis and degradation of the active vitamin D metabolite 1,25-dihydroxyvitamin D, resulting in decreased concentrations of this metabolite in extra-renal tissues.[38] Such an effect could attenuate the ability of 25-hydroxyvitamin D to support protective immune responses to respiratory pathogens. Increased efficacy of vitamin D supplementation in those with lower baseline vitamin D status is more readily explicable, based on the principle that people who are the most deficient in a micronutrient will be the most likely to respond to its replacement.

http://www.bmj.com/content/356/bmj.i6583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Insulin secretion
Triggers antimicrobial peptides
Innate immune response
Cytokines
Autophagy
Ca+, Mg, Phos
Anti-proliferative

Maternal Versus Infant Vitamin D Supplementation During Lactation: A Randomized Controlled Trial.

Hollis BW[1], Wagner CL[2], Howard CR[3], Ebeling M[4], Shary JR[2], Smith PG[2], Taylor SN[2], Morella K[4], Lawrence RA[3], Hulsey TC[4].

⊕ Author information

Abstract

OBJECTIVE: Compare effectiveness of maternal vitamin D3 supplementation with 6400 IU per day alone to maternal and infant supplementation with 400 IU per day.

METHODS: Exclusively lactating women living in Charleston, SC, or Rochester, NY, at 4 to 6 weeks postpartum were randomized to either 400, 2400, or 6400 IU vitamin D3/day for 6 months. Breastfeeding infants in 400 IU group received oral 400 IU vitamin D3/day; infants in 2400 and 6400 IU groups received 0 IU/day (placebo). Vitamin D deficiency was defined as 25-hydroxy-vitamin D (25(OH)D) <50 nmol/L. 2400 IU group ended in 2009 as greater infant deficiency occurred. Maternal serum vitamin D, 25(OH)D, calcium, and phosphorus concentrations and urinary calcium/creatinine ratios were measured at baseline then monthly, and infant blood parameters were measured at baseline and months 4 and 7.

RESULTS: Of the 334 mother-infant pairs in 400 IU and 6400 IU groups at enrollment, 216 (64.7%) were still breastfeeding at visit 1; 148 (44.3%) continued full breastfeeding to 4 months and 95 (28.4%) to 7 months. Vitamin D deficiency in breastfeeding infants was greatly affected by race. Compared with 400 IU vitamin D3 per day, 6400 IU/day safely and significantly increased maternal vitamin D and 25(OH)D from baseline ($P < .0001$). Compared with breastfeeding infant 25(OH)D in the 400 IU group receiving supplement, infants in the 6400 IU group whose mothers only received supplement did not differ.

CONCLUSIONS: Maternal vitamin D supplementation with 6400 IU/day safely supplies breast milk with adequate vitamin D to satisfy her nursing infant's requirement and offers an alternate strategy to direct infant supplementation.

Prevalence and risk factors for vitamin D insufficiency and deficiency at birth and associated outcome.

Marshall I[1], Mehta R[2], Ayers C[2], Dhumal S[2], Petrova A[2].

⊕ Author information

Abstract

BACKGROUND: Occurrence and consequence of cord blood (CB) vitamin D insufficiency/deficiency has not been adequately explored despite rising concern regarding this topic in pediatrics. This study was designed to determine the rate, maternal risk factors, and clinical outcomes in infants in association with vitamin D insufficient/deficient status at birth.

METHODS: American Academy of Pediatrics (AAP) defined levels (ng/mL) were utilized to categorize the vitamin D status in CB samples as deficient (5-15), insufficient (16-20), and sufficient (21-100). We used descriptive statistics and multiple regression models to identify the rate and factors associated with vitamin D deficiency/insufficiency and related outcomes in the enrolled mother-infant pairs.

RESULTS: This prospective study was conducted at a single center on postpartum women and their infants. Vitamin D deficiency and insufficiency was recorded in 38.9 and 29.8% respectively of the 265 CB samples. Deficient CB vitamin D levels in infants were associated with maternal Black, Hispanic, or Asian race/ethnicity, younger age, and increased number of pregnancies. The likelihood for infants to be born with an insufficient vitamin D level increases with younger maternal age and the number of pregnancies as well as Asian ethnicity. We did not find an association between the vitamin D status at birth and pre-discharge clinical characteristics of the neonates.

CONCLUSIONS: The likelihood for an infant to be born with vitamin D deficiency/insufficiency is relatively high and is related mainly to younger maternal age, gravidity, and non-White race/ethnicity. Our findings raise a question regarding the adequacy of the AAP recommended vitamin D supplementation requirements without knowing the infant's vitamin D status at birth.

Respiratory Tract Infections

PLOS ONE

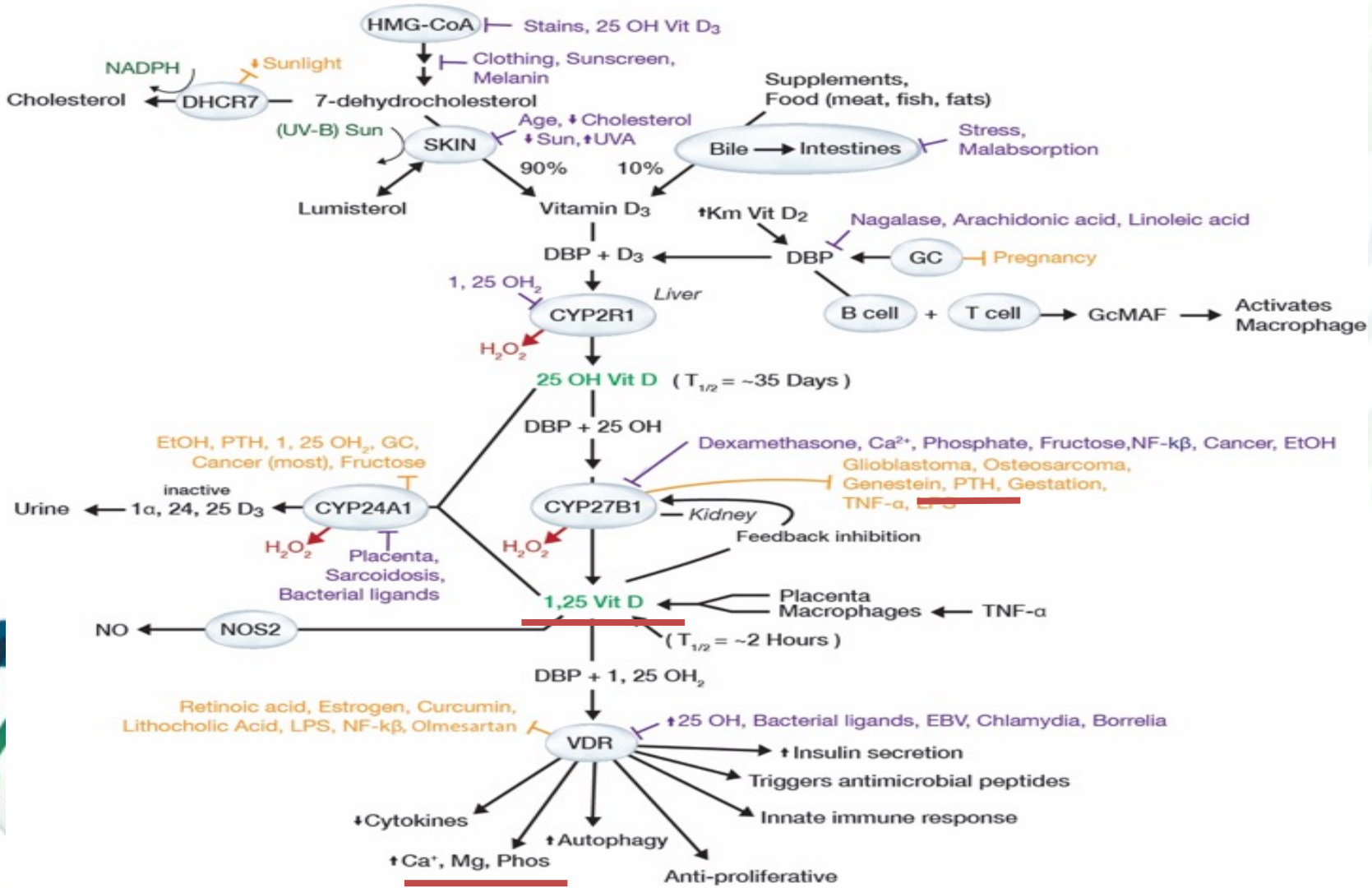
Vitamin D_3 and Antibiotic Prescription at an Immune-Deficiency Unit

Table 3. Type of Antibiotics prescribed the year before and after starting vitamin D supplementation.

	Type of Antibiotics	Prescriptions Before (n)	Prescriptions After (n)	Difference
	Respiratory tract antibiotics[1]			
1	Amoxicillin	225	199	-26
2	Cefadroxil	18	5	-13
3	Doxycycline, Tetracycline	195	141	-54
4	Erythromycin, Clarithromycin, Azithromycin	56	47	-9
5	Phenoxymethylpenicillin	100	67	-33
			Summary:	**-135**

Surprisingly, the subgroup analysis for the different vitamin D levels at inclusion showed that the patients with lowest levels at inclusion (25OHD levels < 30 nmol/L), had less benefit of vitamin D_3 supplementation than patients with 25OHD levels > 50 nmol/L. This might be explained by the fact that half of the patients with levels < 30 nmol/L at baseline never reached above 75 nmol/L, which in previous studies have been shown to be the critical threshold level protection against RTIs [19, 20]. In addition, patients who actually reached above 75 nmol/L might have obtained these levels too late in order to experience any benefit with regard to RTIs in the current study-protocol. In contrast, patients with 25OHD levels >50 nmol/L at baseline reached median levels of 90 nmol/L and the majority of the patients reached 25OHD-levels above 75 nmol/L (Table 3).

(Table 1). Use of serum 25-D and 1,25-D levels as markers of inflammation requires first ruling out secondary hyperparathyroidism as a result of low calcium intake or elevated phosphorus from kidney disease.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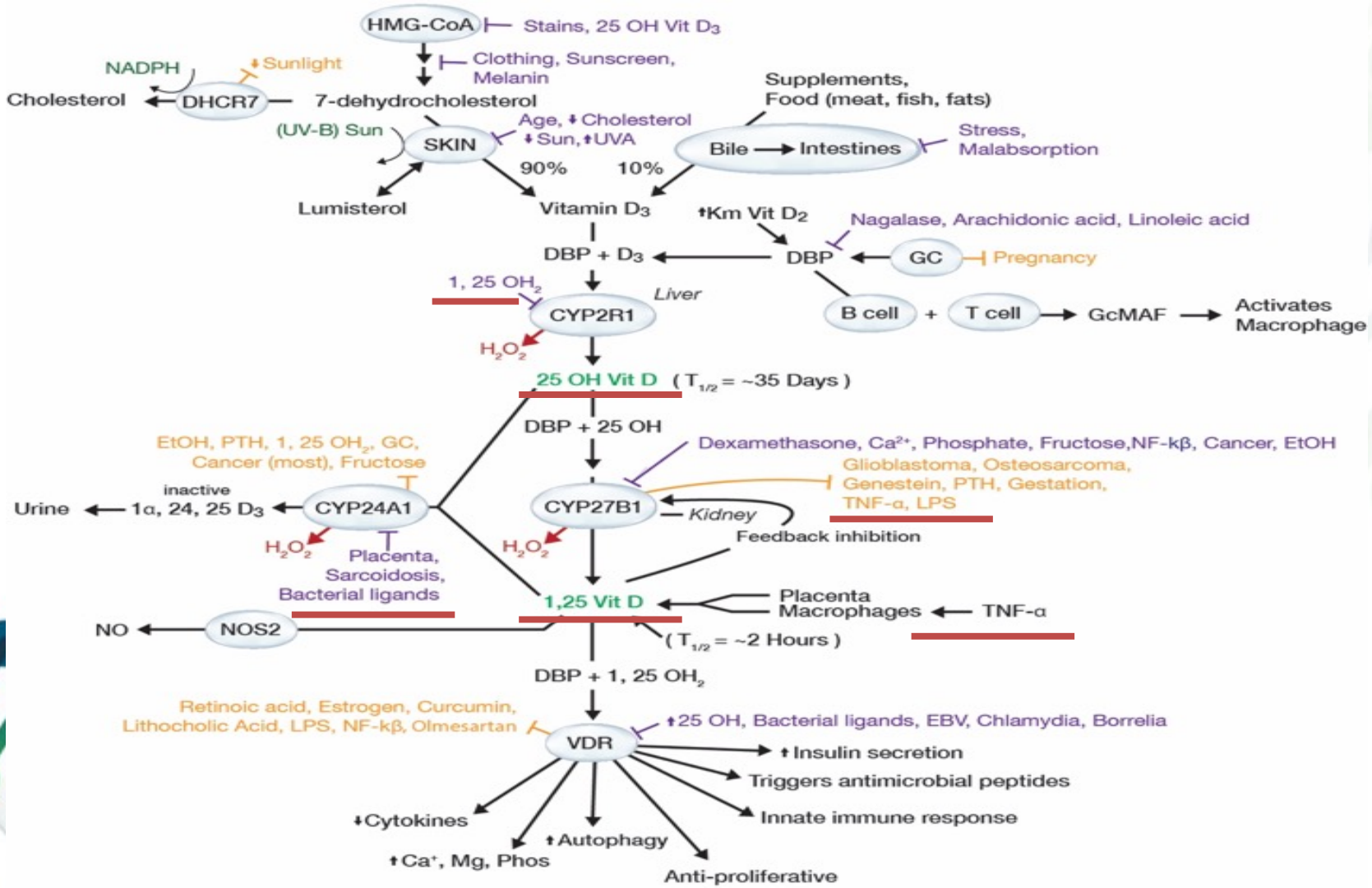
Nagalase, Arachidonic acid, Linoleic acid
DBP + D3
DBP
GC
Pregnancy
1, 25 OH2
Liver
CYP2R1
B cell
+
T cell
GcMAF
Activates Macrophage
H2O2
25 OH Vit D
(T1/2 = ~35 Days)
DBP + 25 OH
EtOH, PTH, 1, 25 OH2, GC, Cancer (most), Fructose
Dexamethasone, Ca2+, Phosphate, Fructose, NF-kβ, Cancer, EtOH
Glioblastoma, Osteosarcoma, Genestein, PTH, Gestation, TNF-α, LPS
inactive
Urine
1α, 24, 25 D3
CYP24A1
CYP27B1
Kidney
Feedback inhibition
H2O2
H2O2
Placenta, Sarcoidosis, Bacterial ligands
1,25 Vit D
Placenta
Macrophages
TNF-α
NO
NOS2
(T1/2 = ~2 Hours)
DBP + 1, 25 OH2
Retinoic acid, Estrogen, Curcumin, Lithocholic Acid, LPS, NF-kβ, Olmesartan
25 OH, Bacterial ligands, EBV, Chlamydia, Borrelia
VDR
Insulin secretion
Triggers antimicrobial peptides
Innate immune response
Cytokines
Autophagy
Ca+, Mg, Phos
Anti-proliferative

Marshall *et al.*[3] found an elevated D ratio ranging from 2.0 to more than 4.5 in sarcoidosis. An abnormal ratio has also been observed in a number of different autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus, and Sjogren's syndrome.[3,7]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Clothing, Sunscreen, Melanin
NADPH
Sunlight
Cholesterol
DHCR7
7-dehydrocholesterol
Supplements, Food (meat, fish, fats)
(UV-B) Sun
SKIN
Age, Cholesterol, Sun, UVA
Bile
Intestines
Stress, Malabsorption
90%
10%
Lumisterol
Vitamin D3
Km Vit D2
Nagalase, Arachidonic acid, Linoleic acid
DBP + D3
DBP
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Pregnancy
1, 25 OH2
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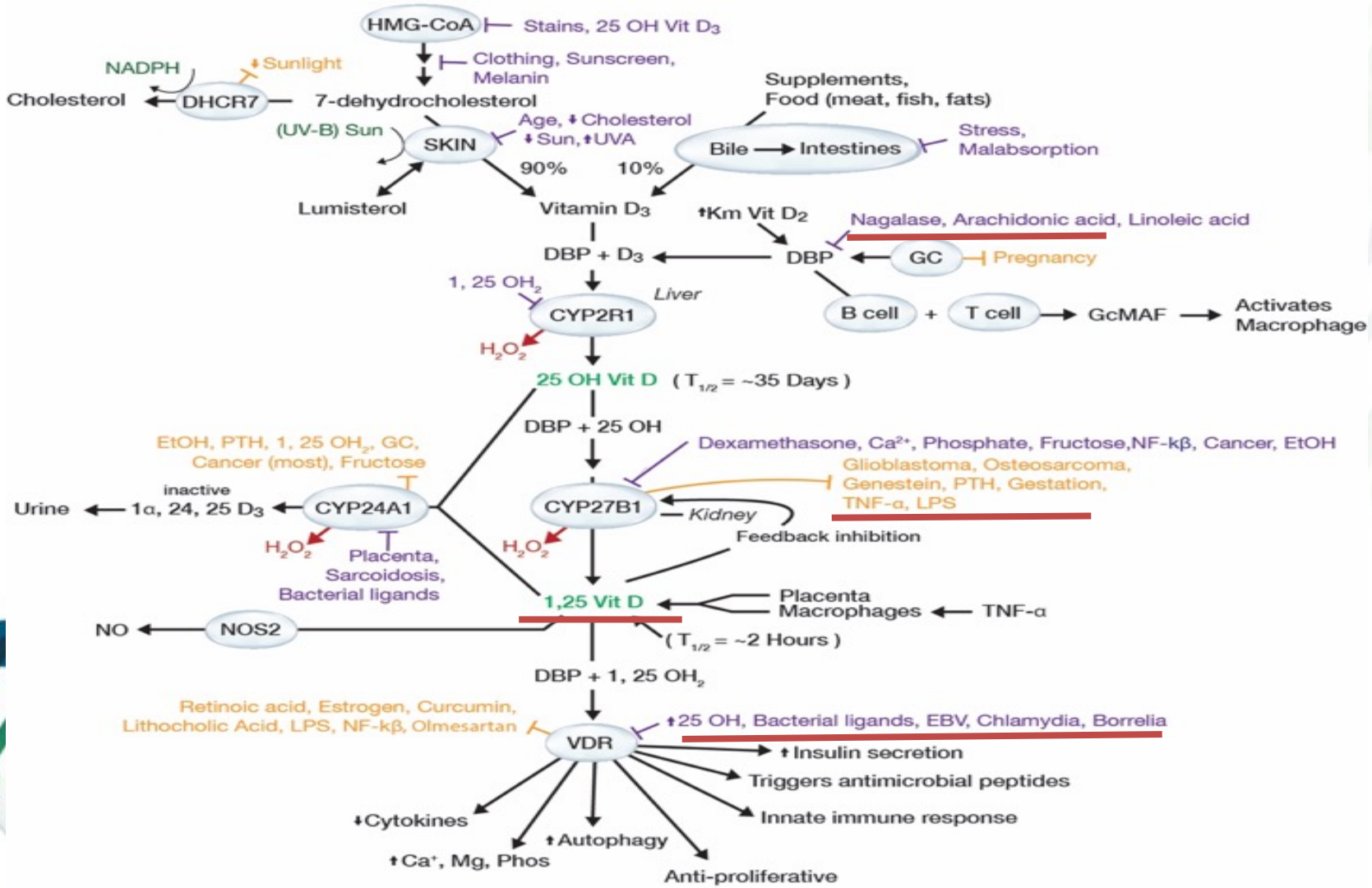
However, a very high 1,25-D (e.g., >80 pg/mL or 200 nmol/L) suggests involvement of one or more highly perfused tissues, such as the lungs, heart, or gastrointestinal tract.[7]

As with nearly all diagnostic tests, serum vitamin D tests can give false negatives. For instance, VDR dysfunction may be so high that bacterial killing is minimized and inflammation is relatively low, leading to lower 1,25-D than expected. Alternatively, regulation of

Reversing Bacteria-induced Vitamin D Receptor Dysfunction Is Key to Autoimmune Disease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Clothing, Sunscreen, Melanin
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Sunlight
Cholesterol
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Age, Cholesterol, Sun, UVA
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Vitamin D3
Km Vit D2
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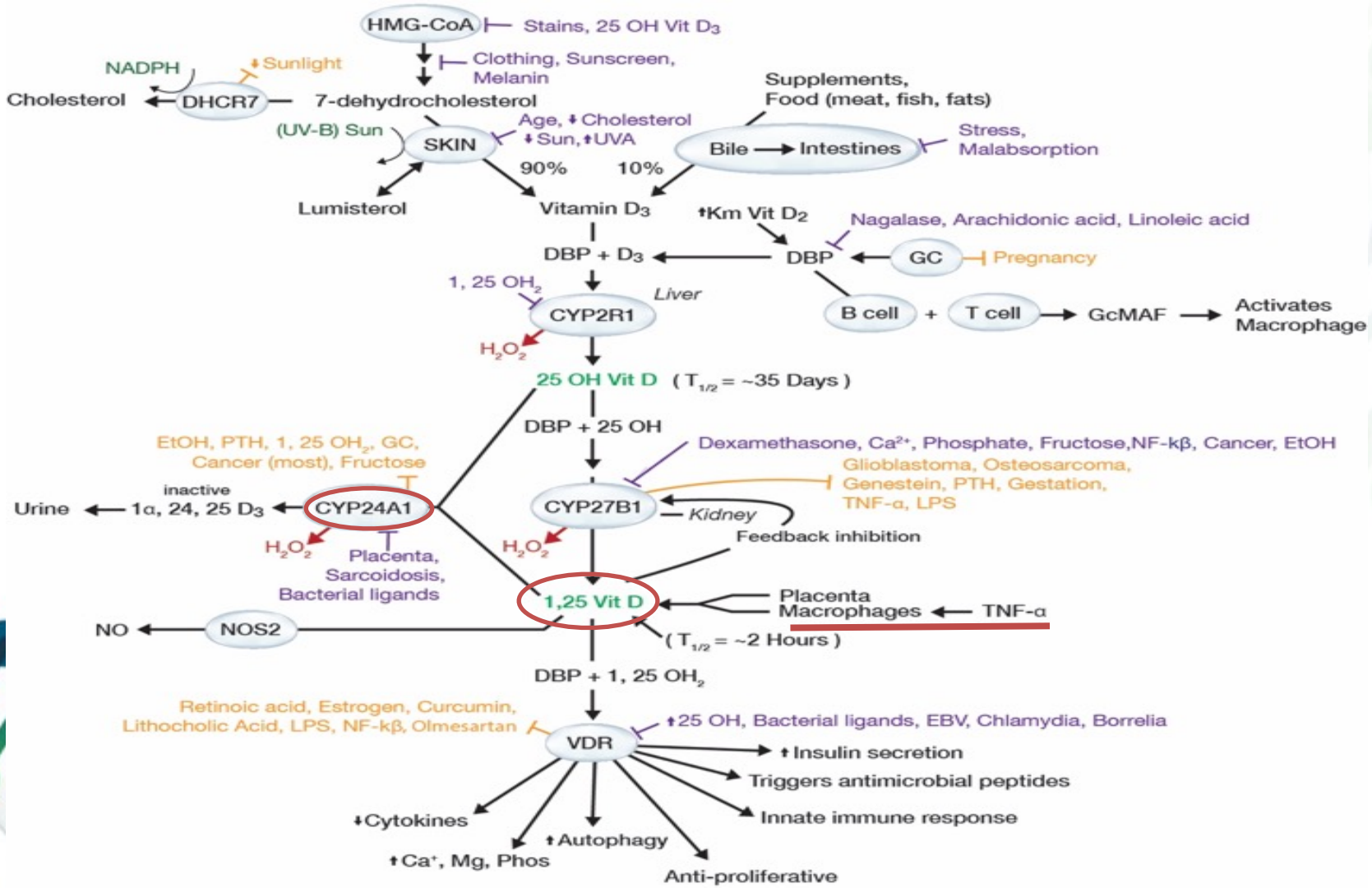
D than expected. Alternatively, regulation of serum 1,25-D by the kidneys may be able to compensate for the production by activated macrophages. Thus, in some tissues, 1,25-D may reach high levels locally, but there may be little or no elevation in serum levels.[7]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Retinoic acid, Estrogen, Curcumin, Lithocholic Acid, LPS, NF-kβ, Olmesartan
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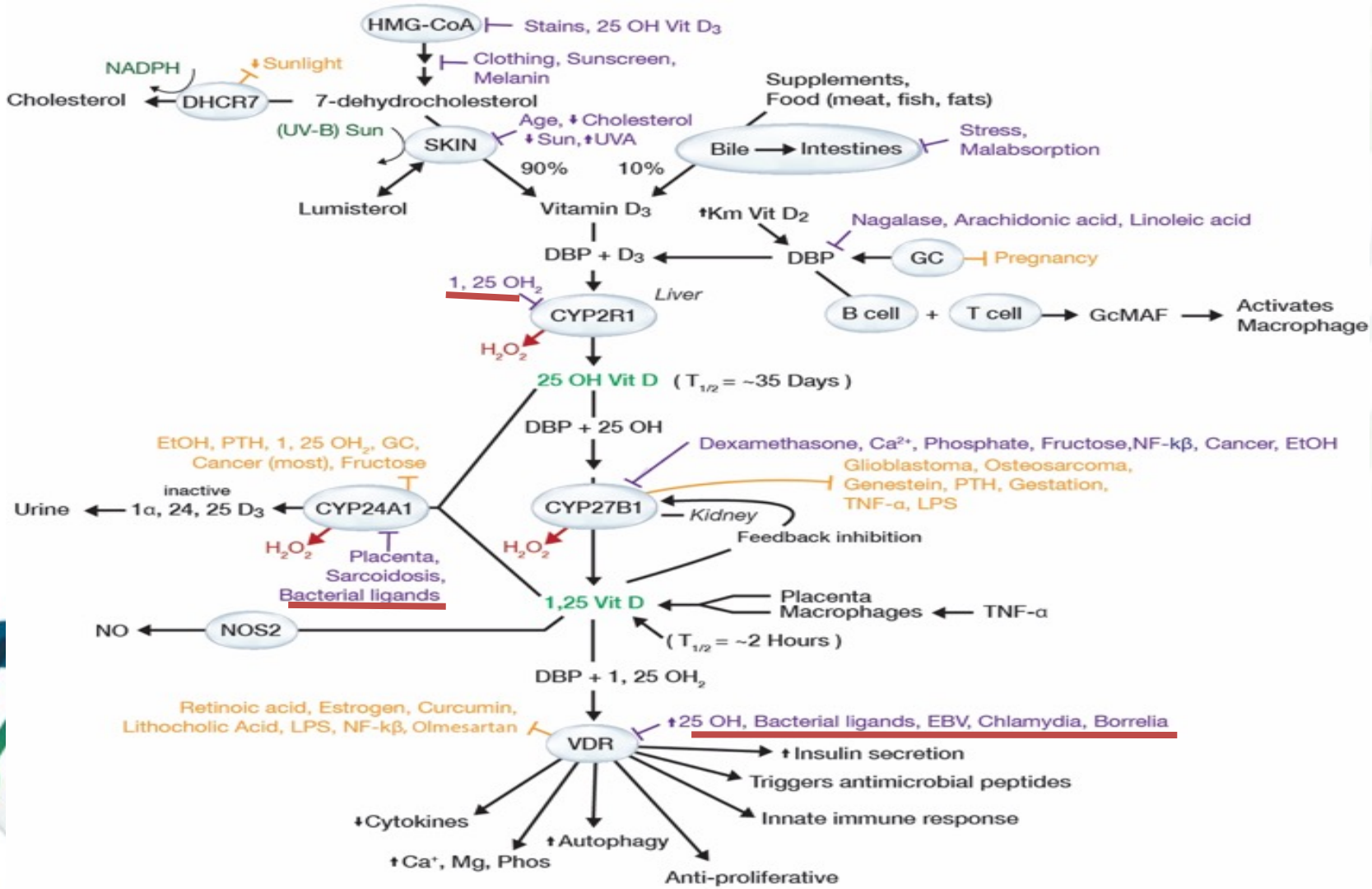
In many cases low 25-D may be a good indicator of disease state because of the feedback mechanism discussed earlier in which blockage of the VDR downregulates the conversion of vitamin D to the 25-D form. In other cases, 25-D is likely to be less diagnostic because of particularly high supplemental/dietary vitamin D ingestion and/or high sun exposure.

Reversing Bacteria-induced Vitamin D Receptor Dysfunction Is Key to Autoimmune Disease


HMG-CoA
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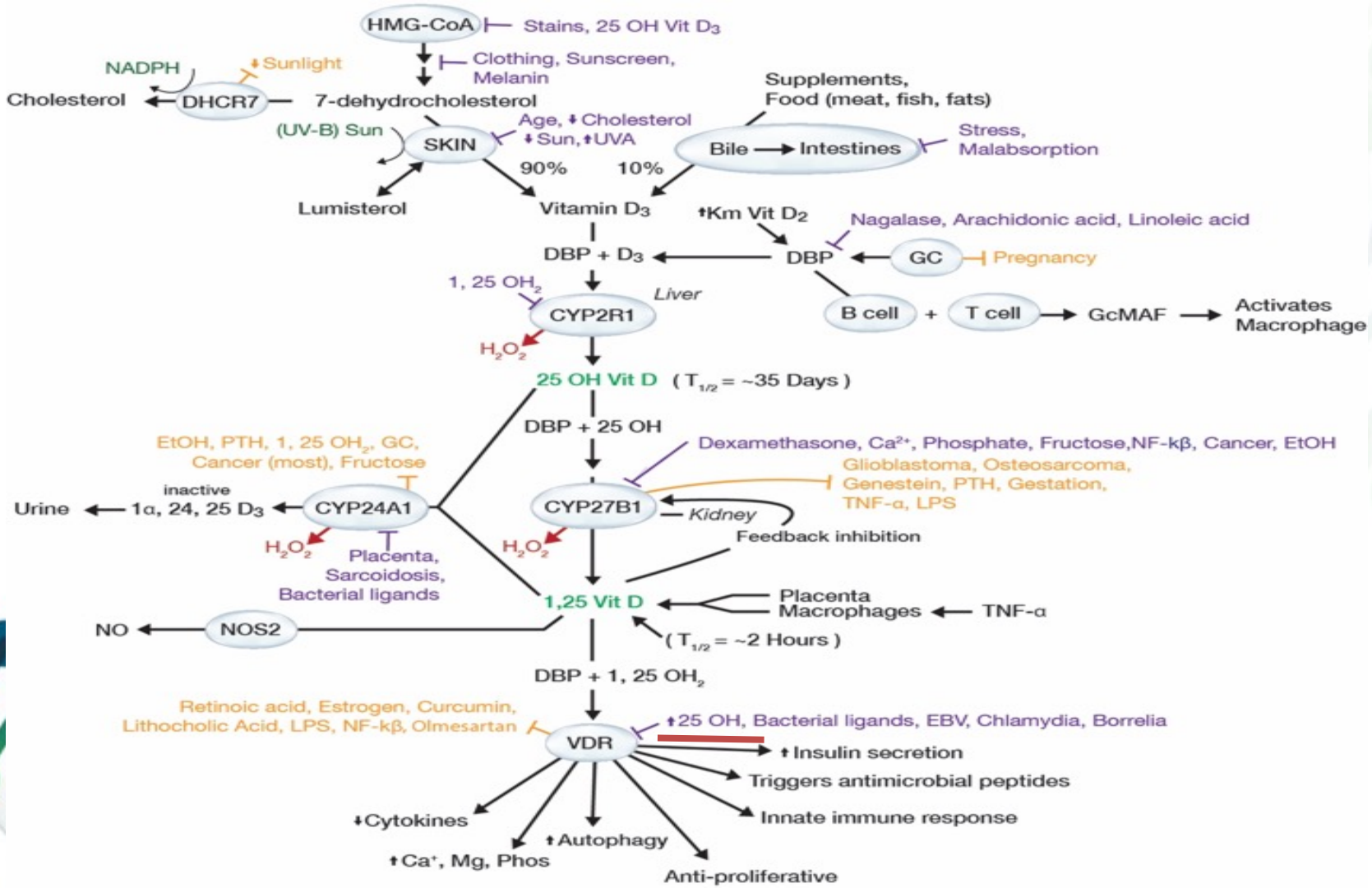
Bacterial Adherence to Mucosal Surfaces. In its simplest form, bacterial adherence or attachment to a eucaryotic cell or tissue surface requires the participation of two factors: a **receptor** and an **ligand**. The receptors so far defined are usually specific carbohydrate or peptide residues on the eucaryotic cell surface. The bacterial ligand, called an **adhesin**, is typically a macromolecular component of the bacterial cell surface which interacts with the host cell receptor.

http://textbookofbacteriology.net/pathogenesis_2.html

VDR dysfunction. In some patients with high 25-D, we have observed the response to the therapeutic probe to be delayed or reduced until their high 25-D levels decline through reducing ingested vitamin D and sun exposure. This further supports the contention that high 25-D levels have the ability to slow the innate immune response in chronically ill patients.

Reversing Bacteria-induced Vitamin D Receptor Dysfunction Is Key to Autoimmune Disease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A Case Study

Practical	Logical	Strategic
Alignment	Plot	Plan
Foundations	Response	Remove
Timeline	Trigger	Restore

11/05/2014

Vitamin D, 25-Hydroxy	49.7	ng/mL	30.0 - 100.0

Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/mL (2).

1. IOM (Institute of Medicine). 2010. Dietary reference intakes for calcium and D. Washington DC: The National Academies Press.

Practical	Logical	Strategic
Alignment	Plot	Plan
Foundations	Response	Remove
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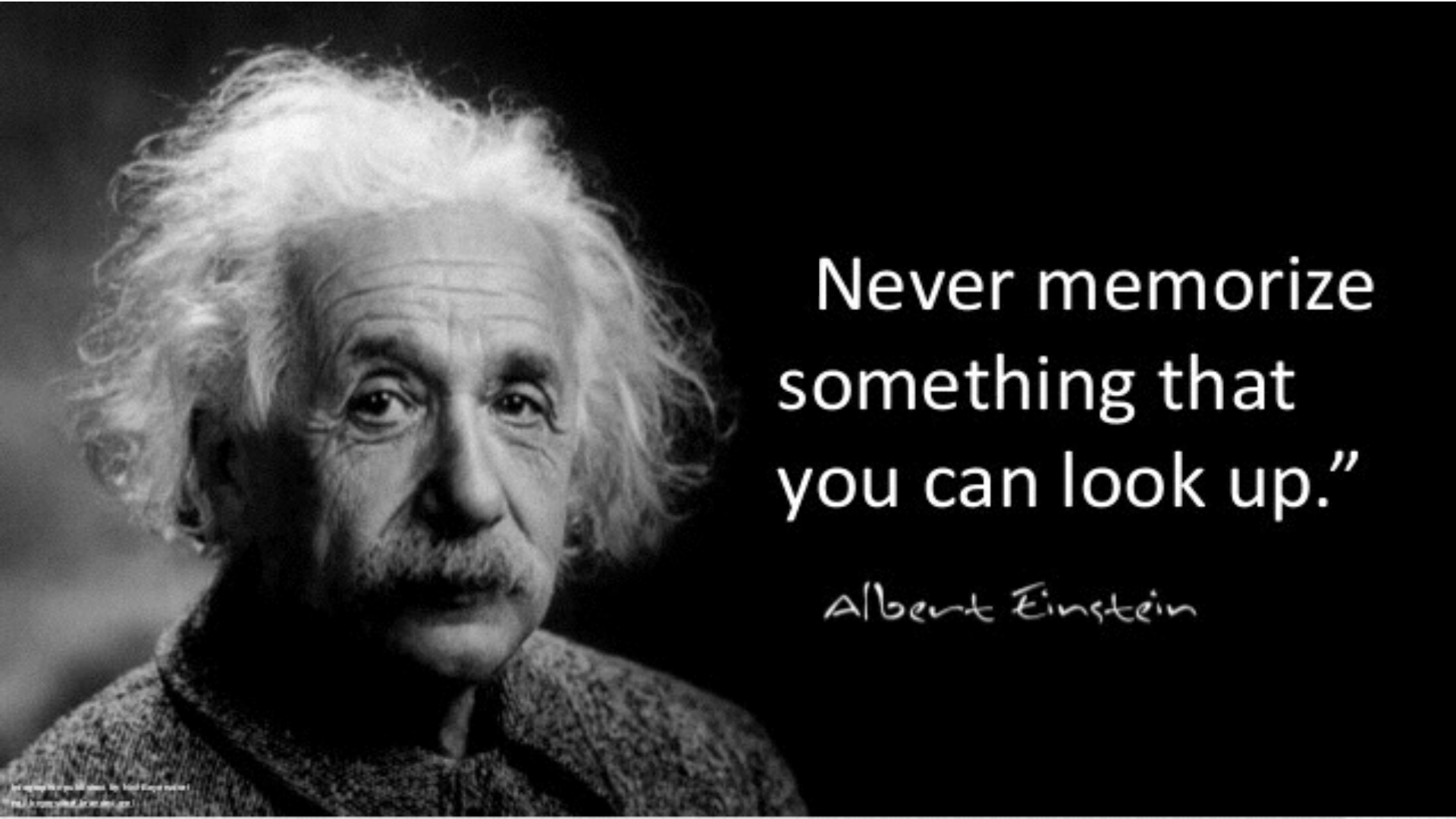
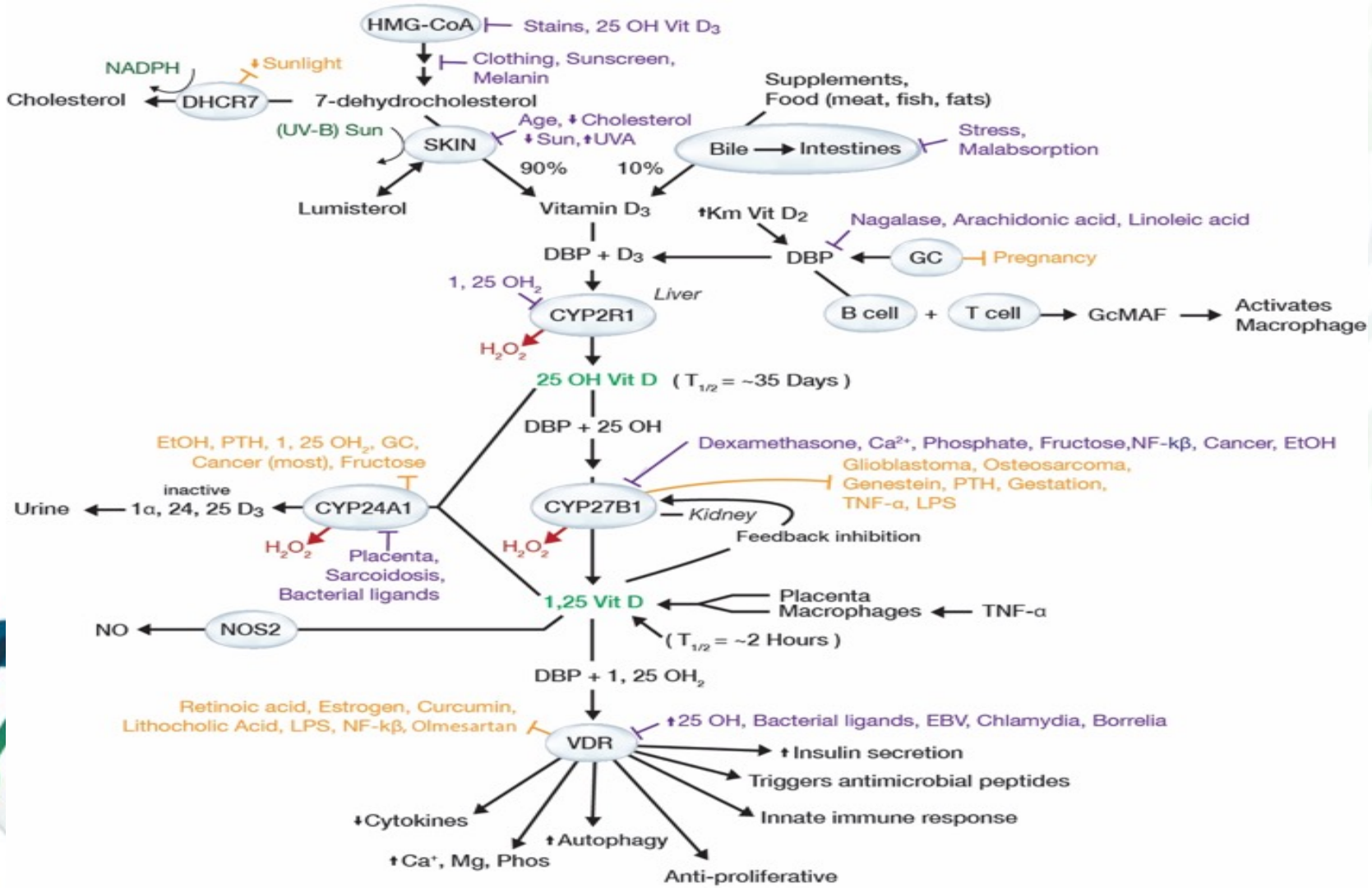
05/20/2015

Calcitriol(1,25 di-OH Vit D)	37.3	pg/mL	19.9 - 79.3
Vitamin D, 25-Hydroxy	41.9	ng/mL	30.0 - 100.0

Vitamin D deficiency has been defined by the Institute of Medicine and an Endocrine Society practice guideline as a level of serum 25-OH vitamin D less than 20 ng/mL (1,2). The Endocrine Society went on to further define vitamin D insufficiency as a level between 21 and 29 ng/mL (2).


Never memorize
something that
you can look up.”
Albert Einstein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(UV-B) Sun
SKIN
Age, Cholesterol Sun, UVA
Bile
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90%
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Vitamin D3
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References

All papers shown in presentation are published in PubMed and cited. References are either at footer presented as a link or is the title of the abstract shown.

All diagrams shown have references organized by pathway and gene.

References may be found here:
https://seekinghealth.org/bibliography/