Nitrate: from Farm to Faucet?

A Commentary on the Cultural Ecological Critique of 'Industrial Agriculture'

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Heidelberg Appeal Nederland

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This research project was initiated by *HAN*, and was financed by the *Nederlandse Vakbond Varkenshouders* (*NVV*; *Dutch Union of Pig producers*) This report analyses the nitrate issue in relation to ground- and drinking water. Toxicological and environmental issues are - together with sociological deliberations on the cautious society- discussed. An independent scientific committee was consulted during the preparation of this document. The results presented below are the intellectual property of *HAN*.

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EXECUTIVE SUMMARY (NEDERLANDS)

Inleiding

Is nitraat een alom tegenwoordig gezondheidsrisico voor de mens? In hoeverre is de volksgezondheid meetbaar gediend met de nitraatnorm van 50 mg NO_3^-/l? Of is deze vraag te beperkt aangezien de nitraatnorm in de *Nitraatrichtlijn* ook ingezet wordt om de milieukwaliteit van grond- en oppervlaktewater te waarborgen? In deze studie zal ik nagaan in hoeverre de nitraatnorm voor drinkwater, grondwater en oppervlaktewater als riskmanagement instrument functioneert overeenkomstig het uitgangspunt dat risicoreductie strategieën alleen zinvol zijn indien een meetbaar rendement wordt behaald tegen een kosteneffectieve investering.

De vigerende politieke visie op de nitraatthematiek gaat uit van feitelijk voorkomende volksgezondheidsrisico's in bevolkingsgroepen die worden blootgesteld aan nitraat afkomstig uit de landbouw. Daarnaast draagt de aanwezigheid van nitraat bij aan de verslechtering van de kwaliteit van het oppervlaktewater. Voor beide typen risico's stelt de *Nitraatrichtlijn* een maatregel voor die het probleem bij de bron zou aanpakken uitgaande van het niet te overschrijden nitraatmaximum van 50 mg NO_3^-/l: een beperking van de toepassing van dierlijke mest op het niveau van 170 kg N/hectare. Uitgangspunt bij deze visie is dat bepaalde hoeveelheden nitraat, nadat het gedeeltelijk opgenomen is door planten en gedeeltelijk is omgezet in andere stikstofverbindingen in de grond en bodemvocht, doorsijpelen naar het grondwater dat uiteindelijk zal worden gebruikt als drinkwater. Het beeld van een 'vervuilende nitraatdeken' over Nederland doemt hier op.

De nitraatnorm van 50 mg NO_3^-/l kent een humaan toxicologische (medische) geschiedenis. Om die reden kan oppervlaktewaterkwaliteit -in termen van eutrofiëring- per definitie niet worden gerelateerd aan de handhaving van deze norm. Daarom zal ik in deze studie de norm van 50 mg NO_3^-/l alleen inhoudelijk beoordelen op grond van humaan-toxicologische en farmacologische overwegingen. Omdat in Nederland drinkwater wordt bereid uit grondwater heb ik tevens de uitspoelingsthematiek onder de loep genomen.

Ruwweg de laatste twaalf jaar is veel nieuw wetenschappelijk materiaal verschenen dat de toxicologie van nitraat in een ander daglicht plaatst dan tot dan toe gebruikelijk. Deze nieuwe inzichten zullen in deze studie aan de orde worden gesteld. Blijkens dit onderzoek hebben organisaties zoals de *WHO* en *decision-makers* in Brussel en Den Haag deze nieuwe inzichten nog geen plaats gegeven in zowel normstelling als nieuw beleid.

Samenvatting

Wetenschappelijk onderzoek staat nooit los van de maatschappelijke implicaties van de resultaten daarvan. Dat geldt in het bijzonder voor onderzoek naar milieu- en volksgezondheidsconsequenties van de aanwezigheid van landbouw in Nederland. Zeker in het huidige tijdsgewricht waar sprake is van een zogenaamde voorzorgscultuur (*cautious culture*).[1] Bij voorzorgdenken staat de vuistregel 'bij twijfel, niet doen' centraal. Wetenschappelijke kennis is in de voorzorgcultuur sterk verbonden geraakt met politieke functionaliteit. Een toenemende politisering van de wetenschap is daarmee een feit: de politiek stuurt in toenemende mate het onderzoeksprogramma van de wetenschappelijke wereld en onderzoeksresultaten behoren in toenemende mate aan te sluiten bij de politiek-beleidsmatige wereld. De grenzen tussen wetenschap en politiek vervagen daarmee en krijgen steeds minder respect. Beleid vraagt dus in toenemende mate om geselecteerde feitenkennis, en wetenschappelijke instituten worden in toenemende mate gevraagd die selectie te genereren. De wijze waarop in beleid wordt omgegaan met de nitraatkwestie is een uitstaand voorbeeld van de voorzorgcultuur. Wanneer wetenschappelijke kennis er wel en er niet toe doet wordt duidelijk wanneer de *risks* en *benefits* van nitraatblootstelling onder de loep worden genomen.

Risks-benefits: risks

De meest besproken en bestudeerde volksgezondheidsaspecten van nitraat zijn het *acuut-toxische risico* voor zuigelingen op het *blauwbaby syndroom* (*methemoglobinemie*; het cyanotisch worden van jonge kinderen als gevolg van een verminderde zuurstofopname door de *nitriet* geïnduceerde oxidatie van hemoglobine (Fe^{2+}) tot methemoglobine (Fe^{3+})) en het *chronisch-toxische risico* op kanker. Acute toxiciteit betreft die symptomen die ‘direct’ na toediening van het vergift zichtbaar worden zoals in dit geval ademhalingsproblemen. Chronische toxiciteit betreft die symptomen die na langdurige blootstelling van het betreffende vergift zich openbaren zoals in dit geval kanker. De nitraatnorm is overigens alleen in gebruik ter bescherming van zuigelingen tegen het blauwbaby syndroom.

Gezien de wetenschappelijke kennis die de afgelopen honderd jaar is opgedaan over nitraat kan worden geconcludeerd dat beide risico's verwaarloosbaar zijn of een andere achtergrond hebben. Het blauwbaby syndroom heeft een oorzaak die los staat van de inname van nitraat via voeding; vooral infecties van maag en darmen spelen een overheersende rol. Daarnaast is gebleken dat een verhoogde blootstelling aan nitraat -zoals het geval bij kunstmestfabriekarbeiders- niet resulteert in meer gevallen van kanker in vergelijking met een populatie die een gemiddelde nitraatblootstelling ondergaat. Samenvattend:

NITRAAT VORMT GEEN VOLKSGEZONDHEIDSRISICO. DE NITRAATNORM VAN 50MG NO_3^-/L DRAAGT NIET BIJ TOT ENIGE VORM VAN VOLKSGEZONDHEIDSBESCHERMING OF -VERBETERING. DE NITRAATNORM VOOR GROND- EN DRINKWATER IS GEZIEN RECENTE WETENSCHAPPELIJKE ONTWIKKELINGEN ACHTERHAALD EN DAARMEE OVERBODIG GEWORDEN.

Risks-benefits: benefits

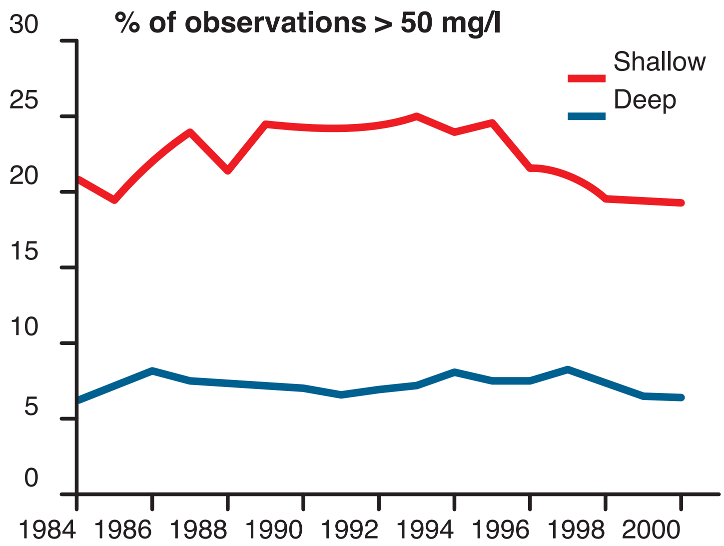
Nitraat speelt een interessante en belangrijke rol in de humane fysiologie. Nitraat, actief opgenomen in de darmen en uitgescheiden in het speeksel, draagt indirect bij aan het verlagen van de infectiedruk op maag en darmen via een anti-microbiële werking van nitraatomzettingsproducten. Nitriet, micro-biologisch gevormd uit nitraat in de mondholte, kan onder zure condities in de maag worden omgezet in een aantal stikstofverbindingen met een sterke antibiotische werking. Pathogene micro-organismen -immer aanwezig in voedsel- krijgen als gevolg van het aanwezige nitraat in het speeksel niet de kans om maag en darmen te infecteren. Samenvattend:

NITRAAT VORMT NIET ALLEEN *GEEN* VOLKSGEZONDHEIDSRISICO MAAR DRAAGT INDIRECT BIJ AAN DE VOLKSGEZONDHEID DOOR DE INFECTIEDRUK OP MAAG EN DARMEN TE VERLAGEN.

Grondwater

Uitgaande van het gegeven dat de wetenschappelijke literatuur geen aanleiding geeft tot de handhaving van de 50 mg NO_3^-/l norm, komt het vraagstuk van de nitraatuitspoeling naar het grondwater in beeld. Immers, bij het ontbreken van deze norm komt in politieke en bestuurlijke zin de beperking van stikstofapplicatie door de landbouw in het gedrang. Gezien het huidige beeld van nitraat als 'vervuilende deken' lijkt dat geen goede ontwikkeling. Nitraatbelasting van grondwater wordt bijvoorbeeld weergegeven zoals in onderstaande figuur gepubliceerd door het *RIVM*:[2]

Figuur 1 Voorbeeld van bewerking van *Landelijk Meetnet Grondwaterkwaliteit* door het *RIVM*

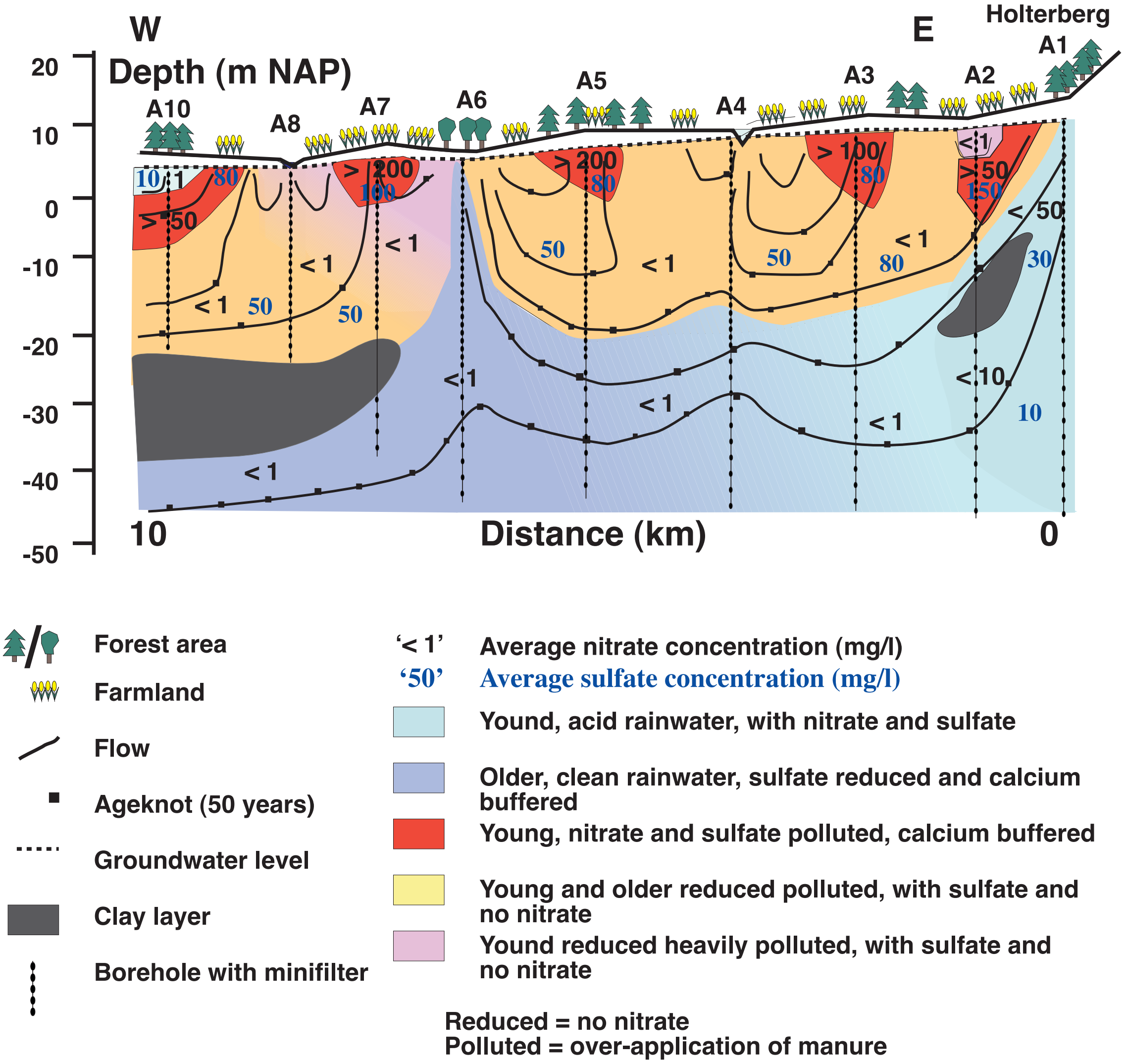


Bovenstaande figuur schetst een generiek beeld van nitraat in grondwater in ondiepe (ongeveer 10 meter onder maaiveld) en diepe meetfilters (ongeveer 25 m onder maaiveld). Het kengetal dat wordt gebruikt is het relatieve aantal meetwaarden boven de norm van 50 mg NO_3^-/l per meetjaar over de periode 1984 tot en met 2000. *Niet in deze figuur vermeld is de selectie van de meetlocaties: alleen vermeld is het gegeven dat de locaties op zandgrond mét landbouw zijn gebruikt. De aantallen meetfilters waar dit percentage op gebaseerd is wordt echter niet genoemd.* De reikwijdte en de betekenis van deze figuur is dus aanzienlijk beperkter dan wordt gesuggereerd.

Uit bovenstaande figuur blijkt dat er in ondiep grondwater meer normoverschrijdingen zijn dan in diep grondwater, maar dit gegeven alleen is onvoldoende. Hoewel ongeveer 20% van de ondiepe meetfilters een normoverschrijding vertoont, een percentage dat ogenschijnlijk stabiel blijft over 16 jaar, betekent dit dat 80% van de meetfilters geen normoverschrijding vertoont. Een nader onderzoek laat zelfs zien dat veel van de meetfilters die tot deze 80% normonderschrijdingen behoort, nitraat onder de detectiegrens meet. *Het is specifiek voor nitraat belangrijk om te melden hoeveel detectielimietwaarden zijn gemeten.* Nitraat vertoont vaak een aan/uit gedrag in water: het zit er in relatief hoge concentraties in of is juist onder de detectielimiet. Dit wordt veroorzaakt door efficiënte denitrificatieprocessen in bodem en grondwater, bijvoorbeeld door chemische reactie met organische stof en pyriet. Een hoog aantal detectielimietwaarnemingen, bijvoorbeeld meer dan 25% van alle waarnemingen, maakt het gebruik van bepaalde kengetallen zoals gemiddelden, onbruikbaar.[3]

In de zogenaamde Salland Sectie is goed naar voren gekomen dat nitraat zich *niet* als een 'vervuilende deken' gedraagt. Nitraat –als gevolg van de reactiviteit in de ondergrond- heeft een beperkte *directe* invloed op grondwater. De Salland Sectie loopt vanaf de Holterberg ongeveer 10 kilometer westwaarts en omvat een tiental boringen met minifilters (van circa 15 cm) op iedere meter tot zo'n 50 meter diepte (vanaf 20 meter is om de 2 meter diepte een minifilter geplaatst). Deze sectie is eind jaren tachtig door *TNO* in opdracht van *RIZA* opgezet en in 1989 bemonsterd en geanalyseerd op onder andere nitraat. In 1996 en 2002 is deze sectie herbemonsterd om een beeld van de dynamiek van de watersamenstelling in de ondergrond te krijgen. Onderstaande figuur geeft een beeld van de nitraatuitspoeling, op basis van de meetgegevens uit 1989:[4]

Figuur 2 Nitraatuitspoeling in de 'Salland Sectie'



In de kleuren rood, geel en paars wordt agrarisch beïnvloed water weergeven. Echter alleen de rode kleur geeft agrarisch beïnvloed grondwater weer dat nitraat bevat. *Het nitraathoudende grondwater vormt 'zakjes'; nitraat vormt dus geen diffuse deken van verontreiniging in grondwater*. Dit beeld verandert niet noemenswaardig in 1996 na herbemonstering.[5] Verklaring hiervoor is dat grondwaterstromingspatronen en denitrificatieprocessen de verspreiding van nitraat in de ondergrond beperken na uitspoeling. Verder is het interessant op te merken dat het 'natuurlijke' water in de Holterberg stuwwal ook nitraat bevat.

Nitraatconcentraties in grondwater blijken sterk te variëren zowel binnen percelen, tussen percelen als op regionale en landelijke schaal én in de diepte. De huidige meetnetten en meetprojecten bevatten te weinig meetlocaties in ruimte, tijd en diepte om een verantwoord, gebiedsdekkend beeld van de nitraatsituatie weer te geven of te volgen.[6] Samenvattend:

NITRAAT VORMT GEEN DIFFUSE DEKEN VAN VERONTREINIGING IN GRONDWATER. UITSPOELING LIJKT BEPERKT TOT KLEINE, VRIJ ONDIEPE *POCKETS*.

Het is wel zo dat als gevolg van nitraatreductie sulfaat kan vrijkomen als er pyriet in het spel is. In bovenstaande figuur zijn in blauw de verschillende waargenomen sulfaatconcentraties vermeld. Indirect kan nitraat dus het grondwater op grotere afstand via sulfaat beïnvloeden. Het gele gedeelte in de figuur geeft een indruk van de afstand waarover nitraat via reductie invloed heeft op het grondwater. Denitrificatie door pyriet is in principe niet erg verzurend en hoeft dus niet te worden gebufferd door kalk:[7]

$$11\ FeS_2 + 30\ NO_3^- + 10\ H_2O \rightarrow 4\ Fe(OH)_3 + 7\ Fe^{2+} + 22\ SO_4^{2-} + 15\ N_2$$

In hoeverre sulfaat daadwerkelijk als 'vervuilend' kan worden aangemerkt is veeleer een juridische dan een humaan- en eco-toxicologische dan wel een geochemische kwestie.[8] De humaan-toxicologische norm die bestaat voor sulfaat in drinkwater is een 'smaaknorm'. Boven de 500 mg SO_4^{2-}/l verandert de smaak van drinkwater. Wat betreft het natuurlijk voorkomen van sulfaat in oppervlakte- en grondwater is het zo dat het in zeer uiteenlopende concentraties wordt aangetroffen. In het Nederlandse oppervlaktewater worden waarden gevonden van beneden de detectielimiet tot meer dan 1000 mg SO_4^{2-}/l. Ook het zoete oppervlaktewater vertoont variaties tot ongeveer 300 mg/l sulfaat. Het sulfaatgehalte in grondwater vertoont nog grotere variaties dan in oppervlaktewater. Het grondwater in Nederland kan zeer zout zijn en sulfaatconcentraties kunnen oplopen tot meer dan 2 000 mg/l. De vrijgekomen hoeveelheden sulfaat als gevolg van denitrificatie moeten milieutechnisch worden beoordeeld binnen de context van genoemde natuurlijke achtergrondconcentraties.

Sulfaat is allerminst een conservatief element. Met andere woorden, sulfaat is reactief in de (anaerobe) ondergrond. Grondwater in organische rijke sedimenten, zoals veen en klei, bevat niet of nauwelijks sulfaat en het wordt zeer snel (binnen meters transport) gereduceerd. In zandige sedimenten kan sulfaat zich verder verplaatsen, en het kan over maximaal enkele kilometers worden getransporteerd in de ondergrond, maar zal uiteindelijk ook tot sulfide gereduceerd en vastgelegd worden. De Salland Sectie laat zien dat op een diepte van zo'n 20 meter het sulfaat gereduceerd –en dus verdwenen- is.

De vele nieuwe inzichten die het laatste decennium van de vorige eeuw ten aanzien van nitraat en aanverwante stikstofverbindingen zijn verworven hebben tot nu toe niet geleid tot enige herziening van de nitraatnorm en daarmee de *Nitraatrichtlijn*. In deze kwestie is het evident dat wetenschappelijke kennis onderschikt is gemaakt aan de koers die reeds vele jaren geleden ten aanzien van het landbouwbeleid is ingezet. Een aantal overwegingen om deze koers wel te wijzigen zijn:

- Beperken van nitraatinname via drinkwater vraagt om investeringen die niet resulteren in de bescherming of verbetering van de volksgezondheid, zeker gezien het feit dat een bepaalde nitraatinname via voeding functioneel is. Investeringen om die beperking van nitraatblootstelling te bewerkstelligen onttrekken onnodig gelden aan economische en bestuurlijke activiteiten ten koste van andere zaken. Een evidente negatieve *tradeoff*
- Handhaving van de huidige nitraatnorm voor grond- en drinkwater continueert de gedachte dat exogene nitraatbelasting nadelig is voor de volksgezondheid, in het bijzonder voor jonge kinderen. Een misconceptie
- Het ontstaan van het blauwbaby syndroom blijft onduidelijk voor publiek, politiek, beleidsmakers indien de huidige nitraatnorm wordt gehandhaafd. Een vorm van obscurantisme

- Aangezien groente eveneens nitraat kan bevatten, kan de focus op nitraat in drinkwater leiden tot een afzien van de gezondheidsbevorderende consumptie van groente.[9] De nitraatnorm draagt in die zin indirect bij aan negatieve beeldvorming van groente, met mogelijke nadelige consequenties voor de volksgezondheid bij verminderde groenteconsumptie
- Nitraatuitspoeling vanuit landbouwpercelen is aanzienlijk minder diffuus dan wordt aangenomen. Gedetailleerde empirische kennis van nutriëntenstromen uit landbouwpercelen is nodig om de feitelijke belasting van grondwater vanuit de landbouw in kaart te brengen en effectief te reguleren.[10]

De eindconclusie van deze studie luidt:

GEZIEN DE BEPERKTE UITSPOELING VAN NITRAAT UIT LANDBOUWGRONDEN DIE NIET DÍE DIEPTEN BEREIKEN VAN WAARUIT GRONDWATER WORDT OPGEPOMPT VOOR DE DRINKWATERVOORZIENING, GEKOPPELD AAN DE AFWEZIGHEID VAN NADELIGE VOLKSGEZONDHEIDSEFFECTEN MAAKT DAT DE HUIDIGE NITRAATNORM VAN 50 MG NO_3^-/L GEEN FUNCTIE VAN BETEKENIS HEEFT. BINNEN DE CONTEXT VAN EEN EFFECTIEF MINERALENMANAGEMENT EN DE BESCHERMING VAN DE VOLKSGEZONDHEID -ZEKER GEZIEN DE POSITIEVE FYSIOLOGISCHE FUNCTIE VAN NITRAAT- KAN DEZE NORM DAN OOK WORDEN AFGESCHAFT.

EXECUTIVE SUMMARY (ENGLISH)

The nitrate standard revisited: observations and conclusions

Nitrate has -through the history of scientific research- revealed two faces: *risks and benefits*. The risks have been under severe scrutiny the last 50 years. Through the discovery of the physiological role of $NO^{\bullet}$ in the late 1980s and early 1990s, the beneficial aspects of exogenous nitrate exposure were unearthed.

The Comly paper, though anecdotal in nature, still forms the basis of the present nitrate standard in drinking (ground) water.[11] The link between dietary nitrate and infant methaemoglobinaemia shall for convenience be called 'the Comly paradigm'. The potential relation between nitrate exposure and cancer is not part of the nitrate drinking water standard, and therefore will not be discussed here. The Walton paper published in 1951 is the only survey on infant methaemoglobinaemia the *WHO* does refer to, and delivered the epidemiological no-observed-effect-level criterion for the nitrate standard in drinking water.[12] Looking at the *WHO* defence of the nitrate standard, however, it is obvious that crucial scientific findings have been omitted, or discussed in an obscure fashion.

The Walton paper is partly based on the Bosch *et al.* paper, which reviewed 139 methaemoglobinaemia cases -reported between 1947 and 1949- in Minnesota.[13] The survey included the 'Comly limit' as a diagnostic criterion, so only cases within the Comly paradigm -that is to say above the range of more than 10-20 mg NO_3^--N/l- were included.[14] Obviously, this approach by definition generated results suggesting a no-observed-effect-level of 10 mg NO_3^--N/l, that is to say the Comly limit. This artefact is carried over to the Walton paper yielding therefore similar results.[15]

However, the Bosch *et al.* paper unintentionally foreshadowed the actual aetiology (branch of the medical sciences concerned with the causes of diseases) of infant methaemoglobinaemia, namely gastro-intestinal infections resulting from the intake of bacteriological polluted well-water.[16] The presence of nitrate in the wells investigated namely is consequently an indicator for the seriousness of the bacteriological pollution. The more elevated the nitrate concentrations, the higher the bacteriological pollution, generating a higher risk of inducing gastro-intestinal infections at consumption. And indeed, this is exactly what the Walton paper implicitly shows. Therefore, the Walton paper is not an epidemiological representation of infant methaemoglobinaemia in relation to nitrate in drinking water but clearly hints at the micro-biological cause of the ailment which -from a physiological point of view- was not understood at that time. However, already in the period of the publication of the Walton paper, severe doubts were raised concerning the Comly paradigm.

It is now clear that exogenous nitrate is not related to infant methaemoglobinaemia. In 1982 for instance, Hegesh and Shiloah attribute blue-baby syndrome to gastro-intestinal infections.[17] The mechanism of this phenomenon was laid bare in the 1990s when $NO^{\bullet}$ was discovered as playing a crucial role in -among others- the immune response; nitrate being the metabolic end product of $NO^{\bullet}$. The original hypothesis postulated by Comly, that dietary nitrate in drinking water is the primary cause of infant methaemoglobinaemia, is untenable on other grounds as well:[18]

- Cases of methaemoglobinaemia are almost solely observed in children suffering from gastro-intestinal disorders

- When drinking water is involved it contained more than 100 mg NO_3^-/l, strongly indicating decomposing organic wastes due to bacterial activity in the polluted wells[19]
- The direct exogenous exposure of young infants to high nitrate doses in an experimental setting did not result in the disorder[20]
- Several studies in different countries show that despite high nitrate in drinking water -in the absence of bacteria- the disorder was not observed in young infants[21]
- The elucidation of endogenous nitrate production in relation to an augmented immune response resulted in a compelling explanation of infant methaemoglobinaemia as a result of infectious diseases, in particular of the gastro-intestinal tract

As research efforts continued, especially in the last decade, it became more evident that nitrate serves a physiological purpose in humans.[22] The active excretion of nitrate in the saliva has a substantial physiological role formerly obscured by the fact that this was regarded as a risk factor in relation to gastric cancer. Nitrite synthesised from excreted nitrate by micro-organisms present in the mouth-cavity, under acidic conditions, has bactericidal capabilities. Nitrite, therefore, greatly enhances the micro-biocidal effect of acidic conditions found in gastric juice and the mouth cavity where plaque accumulate. Addition of nitrite achieves kill of pathogenic micro-organisms potentially present in foodstuff where acid alone in the stomach allows growth to continue. Nitrate is therefore to be regarded as an essential reservoir for a number of nitrogen oxides with health-promoting capabilities. These scientific results have placed the nitrate issue in a wholly different light, not presently considered in relation to the nitrate standard. *Not only the risks commonly associated with nitrate exposure have proven to be absent, under normal physiological conditions nitrate exposure adds to human health.*

Tradeoffs of a precautionary approach of the nitrate issue -continuing the nitrate drinking water standard with its health and environmental protecting aura- are obvious:

- Limiting nitrate exposure through drinking water is not a cost-effective means of protecting public health, guiding governmental and economic funding in the wrong direction[23]
- The existence of the nitrate standard for drinking water sustains and strengthens the widespread misconception that exogenous nitrate *is* a primary source of infant methaemoglobinaemia, which nowadays is altogether virtually non-existent
- Nitrate containing vegetables are also included in this perpetuated misconception
- The aetiology of clinically diagnosed infant methaemoglobinaemia remains obscured when the nitrate standard for drinking water is perpetuated
- The general public might veer away from heath promoting diets for their children containing vegetables

Considering the above, the following main conclusion can be drawn:

THE PRESENT NITRATE STANDARD FOR DRINKING WATER IS OBSOLETE AND NEEDS TO BE RECONSIDERED. IT DOES NOT CARRY ANY HEALTH PROTECTING CAPACITY AS IT IS ONLY IN USE FOR INFANT METHAEMOGLOBINAEMIA, WHICH, IS NOT RELATED TO DIETARY NITRATE. DISCONTINUANCE OF THE NITRATE DRINKING WATER STANDARD IS THEREFORE THE LOGICAL STEP TOWARDS RATIONALISATION OF PART OF THE ENVIRONMENTAL AGRICULTURAL REGULATION.

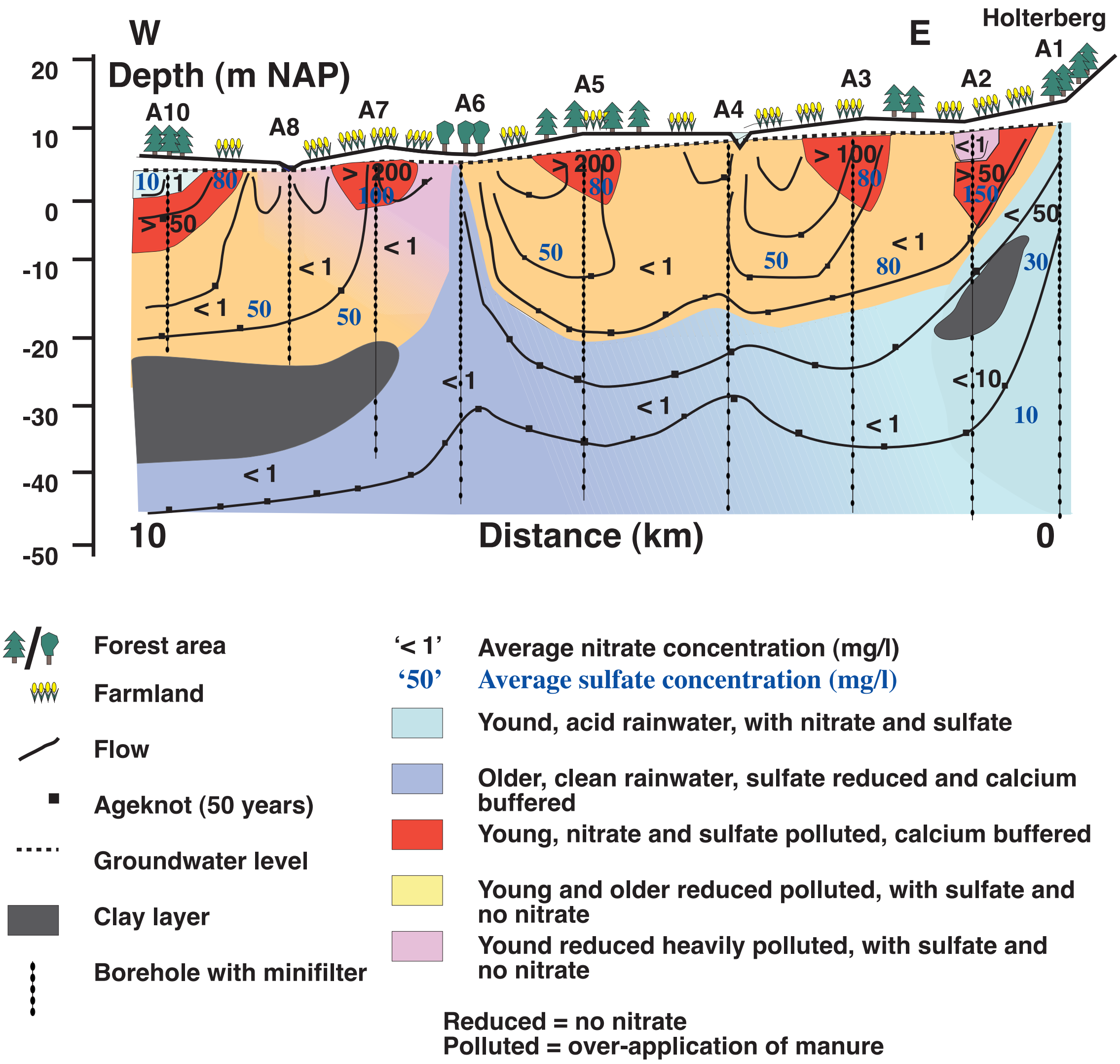
Groundwater

Reviewing scientific data on the nitrate issue it is clear that the nitrate drinking water standard -also functioning for ground- and surface water in relation to human and environmental health- has become obsolete. Moreover, the 50 mg NO_3^-/l standard does not fit the environmental bill as ecological quality of surface waters cannot be related to this standard, considering its medical history.

When indeed the nitrate standard of 50 mg NO_3^-/l is done away with, where does that leave us considering the environmental issues? In other words, what is the environmental impact of nitrate from agricultural practices, and can we evaluate nitrate leaching from farming? As the entirety of the Netherlands is considered as vulnerable to nitrate leaching, the image of a polluting nitrate-blanket as a result of agricultural activities is invoked. Ground- and surface waters are therefore throughout the Netherlands regarded as in danger of nitrate pollution due to agricultural activities.

However, detailed monitoring of nitrate leaching in a part of the sandy area in the Netherlands propounds quite a different image:[24]

Figure 2 Nitrate leaching in the 'Salland Sectie'



Detailed monitoring west from the Holterberg with mini-filters (15 cm in length) every metre up to 50 metres, in an area covering 10 kilometres in which some 10 drill holes reach to a depth of 50 m, gives the picture illustrated above. The sampling was carried out in 1989. In the colours red, yellow and purple water influenced by agricultural activities is depicted. However, only the red pockets denote nitrate-containing groundwater. Nitrate is therefore, as this scheme clearly shows, not spread as a polluting blanket over the Netherlands. This image does not change visibly after sampling was carried out again in 1996. Explanations for this not so well known nitrate behaviour in groundwater are hydrological flow patterns and denitrification, which limit spread considerably of nitrate. Moreover, it is interesting to note that undisturbed water flowing from the Holterberg nevertheless contains nitrate.

Through oxidation of pyrite, nitrate does extend its geochemical reach into the groundwater further than its mere physical presence. Sulphate is generated by this reduction of nitrate, and indeed is found in the yellow zones below the nitrate containing pockets in the Salland Section. Whether that represents a polluting presence, one needs to look at the natural occurrence of sulphate in surface- and groundwater. As groundwater is involved the toxicology of sulphate also needs to be considered. The *WHO* proposed no health-based guideline for sulphate. Sulphate does at most change the taste of drinking water above certain concentrations (± > 500 mg SO_4^{2-}/l). The 150 mg SO_4^{2-}/l drinking water standard is therefore to be regarded as a 'flavour' standard; a safeguard against flavour variations.

The natural occurrence of sulphate in Dutch surface- and groundwater varies wildly. Surface waters contain natural concentrations up to 1 000 mg SO_4^{2-}/l starting below the limit of detection. Groundwater concentrations vary even more: up to 2 000 mg SO_4^{2-}/l have been monitored in brine groundwater. Taking these concentrations into consideration, the formation of sulphate from pyrite oxidation needs to be seen in light of these natural occurring concentration ranges. Moreover, once sulphate has been generated through nitrate reduction, sulphate will be transported and again be reduced, as the Salland Section shows. By no means will sulphate be transported unrestricted.

When indeed the nitrate standard for ground- and drinking water would be abolished this would certainly not lead to a massive spread of nitrate within Dutch groundwater. Detailed monitoring of farmland would insure optimisation of manure application in relation to nitrate losses in farmland, therefore protecting ground- and surface waters from the infusion of nitrate and related compounds.

The cautious tradition: empowering bureaucracy

Whether or not the presence of nitrate can be linked to agricultural practices within a certain geographical, hydro-geochemical and temporal frame is more or less irrelevant within the legal context of the *Nitrate Directive*. Moreover, the foreseeable abolition of the 50 mg NO_3^-/l standard would pose an immediate regulatory problem, as the policy-target would become equivalent to the proposed regulation: the 170 kg N/hectare regulation would become the policy-target in itself. However, on what grounds would such a nutrient restriction be based?

The need for the continuance of the nitrate standard in drinking water, therefore, needs to be looked at in a different light, considering the fact that scientific data do not supply any substantial foundation for this standard. My contention is that perpetuating the nitrate standard primarily serves a bureaucratic and a political prerequisite for exerting political power with a 'green' content. Science does matter merely when results and data concur with the specific bureaucratic needs. As consent is grossly lacking in which direction European agriculture should be progressing, perpetuating the nitrate standard -albeit using outdated and incomplete scientific data- keeps a seemingly non-contested scientific opinion on this matter in place. Opening the scientific debate on the nitrate standard might make the search for political and public consent on the future of agriculture even more problematic. Therefore, the newly gained insights into not only the nitrate toxicology but also the hydrogeochemical behaviour of nitrate are at best discussed only within the scientific community or at worst ignored altogether for the sake of political conformity.

1 CONTEMPORARY AGRICULTURE: IMAGES OF ENVIRONMENTAL MALADIES

1.1 Preamble: Heidelberg Appeal Nederland

The *HAN* foundation (Stichting Heidelberg Appeal Nederland, *HAN*) was established within the Dutch scientific community in 1993. The *HAN* foundation is an independent alliance of scientists and science supporters. Its aim is to ensure that scientific debates within the public and political arena on e.g. environmental, agricultural, biotechnological and foodsafety issues are properly aired, and that decisions which are taken and action that is proposed are founded on sound scientific principles. Members are accepted from all walks of life and all branches of science. At present it has over 1000 donors, including almost 200 professors. Our primary role is to contribute to the scientific debate itself. Our second role is to provide an independent voice to the media, the general public and the educators, and by doing so, it aims to provide a balance on scientific issues. One of the activities of the *HAN* Foundation is to conduct scientific research at the request of third parties. Such research is performed by *HAN*, and supported by an independent scientific supervisory committee. To ensure that the study is executed in an independent fashion the *HAN* foundation has the right to publication regardless of the outcome of the research.[25]

1.2 Introduction

The *HAN* Foundation published studies on the toxicology and related public and environmental health aspects of nitrate in 1997, 1998 and 1999.[26] In these studies it was shown that nitrate, as an omnipresent molecule in foodstuffs and the environment, presents no specific threat to human heath, both on an acute and a chronic level. The nitrate standard of drinking water was, however, not evaluated in these studies. The Dutch *Water-Supply System Decree* defines the maximum acceptable concentrations of substances in drinking water.[27] The *WHO* set the nitrate standard for drinking water at 50 mg NO_3^-/l.[28] Recent scientific literature, however, gives rise to a renewed investigation into the nitrate issue on a toxicological and a normative level. The following issues are under scrutiny in this study:

- Nitrate standard (50 mg NO_3^-/l)
- Physiology and toxicology of nitrate, and related nitrogen compounds
- Risk management in the precautionary culture

As the Netherlands is a gross user of groundwater for its drinking water production, the fate of nitrate in groundwater is studied as well. The physio-chemical fate of nitrate and its impact on the local soil chemistry is briefly discussed. Both the human health and the environment themes on nitrate will result in an overall perspective on agricultural activities and its impact on the local, regional, national and international environment. The transition from relatively simple target-risk definitions, as now chosen in the environmental lawmaking such as the *Nitrate Directive*, towards a more integrated *risk superior* approach such as defined by Graham *et al.*, will be discussed in this study.[29]

In relation to the nitrate issue my contention is that the nitrate standard and the *Nitrate Directive* –notwithstanding the drastically altering scientific perspective- are upheld in order to impart regulatory power to national and European bureaucracy. This is typical for the cautious culture with its specific cultural ecological critique. As consent on the future of European agriculture is grossly lacking, opening the scientific debate on the nitrate issue would seriously hamper the process of consensus forming. Therefore, in relation to the nitrate issue one would find a selective use of scientific knowledge -of the outdated kind- in support of the implemented regulation. This, indeed, proves to be the case. This requires, however, an intimate relation between science and politics, which is indeed an essential part of the cautious culture.

In this chapter I will delve in the toxicological literature, which generated a remarkable shift –yet unobserved by the decision-makers and public alike- in the perspective on nitrate. Furthermore, I will highlight some aspects of the rise of the cultural ecological critique, which, in my view, adds to the understanding of the focus on the environmental and human health risks of nitrates, despite the abounding scientific knowledge on this subject. In the second chapter of this study I will look into the decisional intricacies surrounding the nitrate issue, with added discussion on the relationship between science and politics.

1.3 The rise of the cultural ecological critique and the cautious culture

Exposure to the nitrate molecule (NO_3^-) is a life-long experience that cannot be evaded. Nitrate is ubiquitous in the environment and our food. As food is the primary condition of life for any living organism, human beings included, one of the factors that determine human health is the quality of this food. Water is an essential element of man's diet. To be suitable for human consumption, drinking water must meet a number of requirements.

Although humans are routinely exposed to many substances, including a wide range of (natural) toxic compounds, it is important to keep exposure to such toxic compounds in check. Many toxic substances, however, are natural ingredients of our diet and as such cannot be, or only marginally, controlled. Nitrate and nitrite are present in our food, partly as natural components and partly as food additives.

Nitrate and nitrite, through the centuries, did not generate concern in relation to human health; on the contrary. Nitrate has a long-standing medical history dating back to the 12th century and reaching its zenith in the 19th century.[30] Nineteenth-century pharmacies for instance sold nitre-based powders -10 g of nitre in 150 g of excipient (powder consisting of a mixture of Arabic gum, marshmallow, liquorice and lactose)- as treatment against incipient gonorrhoea.[31] In the twentieth century, salts of nitrate were still used as medication. A pharmacological handbook states that 30 000 to 60 000 mg $NaNO_3$ (21 870 - 43 740 mg NO_3^-) per day can be administered to patients as a diuretic for a period of 2 months.[32] In more recent times, 268 persons were treated with daily doses of 2 000 - 9 000 mg NH_4NO_3 (1 550 - 6 975 mg NO_3^-) for a period ranging from 2 weeks to 2 years as part of medical research into the formation and prevention of kidney stones.[33]

Despite these recent academic exercises, nowadays nitrate is of considerable concern to the public and policy-makers. These concerns mainly originate in the middle of the twentieth century. Two scientific reports can be identified in relation to this change of view. Comly reported on methaemoglobinaemia in infants observed after ingestion of nitrate-rich well-water, and Magee and Barnes demonstrated the carcinogenesis of several nitrosamines in animals.[34,]

However, there is more to this change of view of such chemicals than just these two technical reports, which were and are available and intelligible only to specialists. This change of perspective is best explained by the rise of the cautious culture, which mainly revolves around environmental and human health issues in relation to science and technology. The cautious culture, in other words, has a specific green content.[35] Bramwell, in her study on the ecological movement in the twentieth century, probes the development of green thinking and its impact on the Western society.[36] She shows how two distinct strands of ecology merged in the early 1970s. First, there is the classic strand, which arose in the late nineteenth century and is 'an anti-mechanistic, holistic approach to biology', deriving from the German zoologist, Ernst Haeckel. The second strand was a new approach to economics called energy economics. This focused on the problem of scarce and non-renewable resources. In her own words:[37]

> 'The distinctive qualities of ecologism arose in the late nineteenth century, and consisted of two distinct strands. One was an anti-mechanistic, holistic approach to biology, deriving from the German zoologist, Ernst Haeckel. The second strand was a new approach to economics called energy economics. This focused on the problem of scarce and non-renewable resources. These two strands fused together in the 1970s. The scientific element in energy economics gave impetus to the biologically based ecological movement, which had lost its credibility because of its links with Germany. The two categories, biological and economic, had a certain degree of cross-membership. … *It is the combination of the intensely conservative moral and cultural ecological critique with the full apparatus of quantitative argument that has rendered ecologism the powerful force it is today.*'

Here I use 'ecology' and 'ecological' in the normative political sense, which has become part and parcel of the mental furniture of most people in the Western world. It encompasses the belief that a man-induced drastic change within the environment is wrong and should be amended. Ecology is therefore associated with conservation, sustainability and precaution.[38] Green thinking on the one hand postulates 'wrongness' about Western industrialised society in for instance its use of finite resources and its pollution potential and on the other hand sees part of the solution in a reorganised society in which these resources could be used more efficiently whereby environmental contamination could be curbed. Green thinking paradoxally combines pessimism about human nature –in relation to the freedom of doing scientific research and the free marker concept- with optimism of the human possibilities to change the future.

Veldman furthermore, points out that this vision of the reshaping of society –as part of green thought- holds a 'romantic' component.[39] By that she neither refers to a historical period nor an artistic stand, but rather to a world-view. By and large this 'romantic' outlook on life, history and society is centred on the conviction that modern science with all its statistical and explanatory potential cannot depict or grasp all of reality, which is experienced beyond the reach of the physical senses. Within this vision, a rejection of the materialistic technological and scientific character of modern-day society is supplanted by a focus on the past, which is regarded as a guide to the future. The 'right relations' between individuals and the community, humanity and nature, humanity and technology and so on, overcoming the deep felt fragmentation of modern society, are projected on this envisioned past. Indeed, the bureaucratic interest in organic farming is a prime example of the romantic vision of the future of European agriculture, which at the same time is a basis for criticism of the growth potential of modern agricultural techniques such as pesticides, genetically modified organisms and of course fertilisers.

Bramwell notes how two influential international reports gave ecologism intellectual and political status. First, in 1972 Barbara Ward and Rene Dubos presented a report to the *United Nations World Conference on the Human Environment*. It argued that man had to replace family or national loyalties with a sense of allegiance to the planet. It preached imminent doom through man's technological capacity. Second, the *Club of Rome* produced its first report in 1972. It too projected imminent global catastrophe, unless resource use was curbed, and resources shared. These two reports coincided in time with the oil crisis of the early 1970s, which gave them economic credence and social repute. *The fusion of green values with resource fears had taken place*:[40]

> '… *In the early 1970s the finite resource arguments fused with the biological argument.* Today it is thought that the oil crisis of the early 1970s seemed to prove the economic ecologist argument beyond doubt. The West's dependence on this finite resource seemed very clear when an abrupt rise in price created shortages and economic depression. The long-term implications of a shortage of mineral resources could be impressed clearly on the public mind.
>
> However, the emergence of finite resources as a global issue predated the oil crisis. In 1972 a report was presented to the United Nations World Conference on the Human Environment by Barbara Ward and Rene Dubos. It argued that man had to replace family or national loyalties with a sense of allegiance to the planet. It preached imminent doom through man's technological capacity. The book prophesied that children alive then would see the global crisis take inescapable shape. The Club of Rome was also founded in 1972. It too prophesied imminent global catastrophe, unless resource use was curbed, and resources shared.
>
> The ideal of global planning of resources had emerged well before the Second World War. Later bodies that embodied this ideal, like the United Nations and its subsidiaries, had begun the post-war era full of hope. Yet their scope had grown in almost direct proportion to their increasing powerlessness over Third World countries. Fears of their over-population increased in the 1960s. Theories of increasing immiserisation continued in parallel with increasing population growth and prosperity. The stage was set for academic arguments about inter-generational allocation of resources to affect the public. To do this the media had to present ecological issues seriously. It was helped to do so now by well-organised, massively-financed conferences, conference reports and press releases from authoritative-sounding bodies. *The mixture of vague alarm about forthcoming doom and convincing statistics extrapolated from current experience proved irresistible. …, the media now dealt with intellectuals who spoke and understood the jargon of growth, but turned it on its head.* Those who absorbed economic ecologism did so because of their values, their love of countryside and animals. They found in economic ecologism a legitimation of these values, which were no longer presented as a selfish, middle-class luxury. Here were scientifically backed and quantified arguments. Instead of feeling guilty for wanting to preserve nature, the desire was a means to save the world from catastrophe. The oil crisis of 1972-4 seemed a rapid vindication of economic ecologism. *The fusion of green values with resource fears had taken place.*'

Bramwell's contention that the combination of the conservative moral and cultural *ecological critique* en lieu with *quantitative scientific imagery* has rendered ecologism -since the 1970s- the powerful force it is today, is shown by the fact that the precautionary culture is largely shaped around health and environmental (ecological) themes related to human activities. *Principle 15* of the *Rio Declaration* on the precautionary principle makes this clear.

Indeed, ecological risks both in relation to nature and human health are at the centre of the precautionary culture. These ecological risks need to be presented of being on a global scale. This is simply because the local cause of the handicapped or of the unemployment of the Arab minority in Dutch suburbia is not so formidable, damage not so irreversible or so grand in scale as to warrant beseeching general doom.[41] Moreover, cultural ecological critique of the affluent Western society must relate to the whole of mankind as the precautionary approach is closely linked to the intergenerational theme of sustainability.[42] Precaution and sustainability are both sides of the same medallion and have by the very nature of their semantics global implications. The need for rules or principles of management is inherent to the intergenerational aspects of the vision of sustainability. Irreversible environmental loss or damage and uncertainty about future needs requires a 'safe minimum standard of natural capital', or to establish a precautionary principle, according to which the overall stock of environmental resources and carrying capacity should not be allowed to diminish over time.[43]

All this is best served with the image of the pollution of nature as a whole.[44] Pollution upholds -apart from the strict technical sense, as when we speak of river or air pollution, when the physical putrefaction of an earlier state can be precisely measured- conceptual categories dividing the moral from the immoral and sustain the vision of the good society. Impurities in the physical world or chemical carcinogens in the human body are in this sense directly traced to immoral forms of economic and political power. In more abstract wording, physical nature and its (perceived) pollution proves to be the best substitute for the divine, amongst other things that nature is powerful, 'eternal' relative towards the human life span, unfathomable and requires purity. Ecological values and its ensuing critique have the force of a religion.[45] However, there is no reason why religion should not be subjected to critical analysis like any other belief. One can sympathise with people's values without believing that cultural relativism prevents an examination of the implications of their credo.[46]

In *Risk and Culture* Douglas and Wildavsky add some explanations for the question why green thinking gained so much support during the 1960s and 1970s (in the US). They point out that religious sectarianism has always been a prominent feature of American culture. They also stress the importance of the civil rights movement. The economic and educational boom together produced a cohort of articulate, critical people with no commitment to commerce and industry. Because the more the means of production are ideas rather than things, the less the hierarchical organisation of production appears essential. Douglas and Wildavsky end on a gloomy note, which goes well with the historical analysis delivered by Bramwell:[47]

> '[Technological r]isk, like worldliness, is an ideal target for criticism. It is immeasurable and its unacceptability is unlimited. … Since the sources of risk are virtually infinite in number, subject only to the fertility of the mind, there is no limit on what can be spent on eliminating them.'

The nitrate issue is a prime example in the context of this discussion. Indeed, use of nutrients such as nitrate has made the Netherlands as one of the primary producers of agricultural products in the world with the ensuing affluence for the Dutch. This makes the agricultural economic sector especially prone to the ecological critique and a prime objective for the sustainability agenda where biological and ecological agriculture is regarded as the future 'solution' of the 'ecological degradation' and threats to human health.[48] Nitrate fills this bill quite well regarding its reputation as the supplier of carcinogens in the human body and its notoriety as a potential 'baby-killer'. *Reviewing the science of nitrate it is clear that morality as opposed to scientific knowledge stands at the centre of regulatory initiatives in relation to the nitrate issue*. Scientific data, to put it in a different way, are chosen on the basis of the moral potential it generates for bureaucracy.

1.4 The case against nitrate: methaemoglobinaemia and cancer

1.4.1 Methaemoglobinaemia (blue-baby syndrome): introducing the nitrate standard

As said, the history of legislation of nitrate-standards in drinking water goes back to the paper of Comly in 1945.[49] He was the first to report two cases of cyanosis in infants receiving well-water containing among other things high amounts of nitrate. He summarised his observations as follows:[50]

> 'Although no define statement can be made, it would seem advisable to recommend that well water used in infant feeding possess a nitrate content no higher than 10, or at the most 20 parts per million.'

With this article the nitrate health-issue in relation to drinking water was born. Although the alleged association between nitrate intake (mostly through drinking water) and methaemoglobinaemia was based on no more than anecdotal evidence, his article has determined the direction of later research. Many cases of well-water methaemoglobinaemia reported in the literature were attributed only to the nitrate concentration in drinking water. Other possible causes of the observed methaemoglobinaemia remained undiscussed.

Nitrate itself is not responsible for the cyanotic condition reported. Indeed, nitrate is not very toxic at all. In the scientific literature experiments are described in which doses of 150 mg NH_4NO_3 per kgbw (kilogram bodyweight; 116.3 mg NO_3^-/kgbw; the total dose was between 5 425 and 8 137 mg NO_3^-) were orally administered to 12 volunteers *without* any direct adverse effects.[51] The same article reports that 12 volunteers were intravenously administered 9 500 mg $NaNO_3$ (6 929.5 mg NO_3^-) without this having any observable toxic effects.

In vivo reduction of nitrate (NO_3^-) to nitrite (NO_2^-) is a necessary prerequisite for the condition of methaemoglobinaemia. *Obviously, when exogenous nitrite is involved, methaemoglobinaemia can be readily induced both in infants and adults*. Oxygen transport by haemoglobin is hampered by the presence of nitrite. Haemoglobin, the oxygen-carrying protein that is present in large amounts in red blood cells, contains iron in its second oxidation state: $\mathbf{Fe^{2+}}$. This haemoglobin is also called ferro-oxyhaemoglobin.[52] With iron in this oxidation state, haemoglobin is capable of binding and releasing oxygen. Nitrite can take the iron to a higher oxidation state: $\mathbf{Fe^{3+}}$; Fe^{2+} is oxidised to form Fe^{3+}. In this state the so-called (ferri) methaemoglobin is not able to bind oxygen and liberate it in organ tissue. Above a certain concentration level the organism may be harmed by oxygen deficiency. In the most serious cases this leads to death -occuring at methaemoglobin formation levels of between 45% and 60%.[53] Lethal nitrite poisoning is assumed to take place at 60% methaemoglobin formation. Fatal nitrate poisoning -as e.g. described by Amundsen- is to be attributed to this mechanism.[54] He describes that the victims consumed food that had erroneously been salted with sodium nitrate. It was noted that the meal consumed promoted slow absorption, so that reduction to *nitrite* could take place in the gastro-intestinal tract, and as a consequence the victims died of methaemoglobinaemia.

Methaemoglobinaemia is clinically diagnosed at a methaemoglobin concentration of 10%. Normal methaemoglobin levels in blood vary from 0.5 to 2%.[55] New-borns have a higher methaemoglobin level in their blood (1-2%) because their methaemoglobin reductase enzyme system is still not fully functional. This makes infants more susceptible to nitrite poisoning. Other reasons are:

- The foetal haemoglobin (the so-called *F-haemoglobin*) that is still present in the blood of new-borns, is more sensitive to oxidation than A(dult) haemoglobin. F(oetal) haemoglobin has a higher affinity for oxygen, which is necessary if an oxygen exchange benefiting the foetus is to take place in the placenta between the mother's A(dult) haemoglobin and the foetus' F(oetal) haemoglobin
- Nitrate reduction in the gastro-intestinal tract due to bacterial colonisation in the stomach. The stomach is usually virtually sterile. Nitrate cannot be reduced there. Presumably the pH of the stomach of new-borns is not yet low enough to prevent the (temporary) presence of bacteria, hardly any gastric juice being excreted yet

In the US the *Public Health Service* recommended a limit of nitrate of 45 mg NO_3^-/l in accordance with Comly's findings and on the basis of the reports of Bosch *et al*. and Walton.[56] These two articles still are part and parcel of the epidemiological basis for today's nitrate standard. Indeed, the Walton paper is still referred to in the *WHO* guidelines for drinking-water quality.[57] The *WHO* states in her drinking-water guidelines that:[58]

> 'In summary, the epidemiological evidence for an association between dietary nitrate and cancer is insufficient, *and the guideline value for nitrate in drinking-water is established solely to prevent methaemoglobinaemia, which depends on the conversion of nitrate to nitrite. …*
>
> Extensive epidemiological data support the current guideline value for nitrate-nitrogen of 10 mg/litre. However, this value should not be expressed in terms of nitrate-nitrogen but as nitrate itself which is the chemical entity of health concern, and the guideline value for nitrate is therefore 50 mg/litre.'

Until today the recommendations of Comly -translated into the *WHO* guideline value of 50 mg NO_3^-/l- thus remains in place.

Experiments and field studies have attempted to provide clarity with respect to the exact relationship between nitrate intake and infant methaemoglobinaemia. Cornblath and Hartmann for instance -in an unethical experiment- studied children who were administered controlled nitrate doses via their food in order to test the Comly hypothesis.[59] The methaemoglobin content of their blood was determined and adequate treatment was provided if cyanosis was diagnosed. Four infants aged between 11 days and 11 months, which were administered 50 mg NO_3^-/kgbw per day for 2 - 18 days, were found to have a maximum of 5.3% methaemoglobin in their blood; a doubling of the normal background concentration. The dose was then doubled to 100 mg NO_3^-/kgbw per day; four infants aged from 2 days to 6 months were given this dose for 6 - 9 days. The authors report as follows:

> 'The only noteworthy level of methaemoglobin, 7.5% of total haemoglobin, was obtained in an infant 10 days of age 8 days after the nitrate solution was added to his formula.'

The doses studied in the experiments by Cornblath and Hartmann correspond to a nitrate concentration in water of 330 and 660 mg NO_3^-/l, respectively, for a normal liquid intake of 150 ml/kgbw per day. These experiments cast serious doubt on a simple causal relationship between nitrate intake and methaemoglobinaemia. Donahoe described the problem of the enigmatic aetiology of well-water methaemoglobinaemia as follows:[60]

> 'It is difficult to explain why only an occasional infant develops cyanosis, why the nitrate content of the water (associated with the cases) varies so greatly and why it is not always the water with the highest nitrate concentration which causes cyanosis in the infant.'

Moreover, the US standard for nitrate concentrations in drinking water, which roughly equals the *WHO* standard, was strongly criticised by Parsons who pointed to the high bacterial content of the implicated well-waters as a probable, and presumably even necessary prerequisite, of the reported infantile methaemoglobinaemia cases.[61] He concluded that the set standard of nitrate was inconsistent with the facts already known at that time.

Sattelmacher -in a world-wide survey- and Simon *et al*. -in a survey of German hospitals- have reviewed the relation between nitrate concentrations in drinking water and the relative number of infantile methaemoglobinaemia cases.[62] Both reviews show that the majority of cases are reported above a nitrate concentration of 100 mg NO_3^-/l:

Table 1.4.1.1 Distribution of reported infantile methaemoglobinaemia in relation to nitrate concentrations in well-water

	Sattelmacher (1962)		Simon *et al.* (1964)	
	Number	**Percentage**	**Number**	**Percentage**
Reported cases	1060	100	745	100
Deaths	83	7.8	64	8.6
Nitrate concentrations in Water (mg NO_3^-/l)				
Unknown	593	56.0	496	66.5
Known	467	44.0	249	33.5
0 - 40	14	3.0[a]	-	-
0 - 50	-	-	11	4.4[a]
41 - 80	16	3.4[a]	-	-
50 - 100	-	-	29	11.8[a]
81 - 100	19	4.1[a]	-	-
> 100	418	89.5[a]	209	83.8[a]

[a]Percentage of cases with known nitrate concentrations in water.

These studies, among other things, resulted in a transient shift in the nitrate standard. The *WHO* stated in 1970 that a nitrate concentration of less than 50 mg NO_3^-/l is satisfactory, concentrations up to a 100 mg NO_3^-/l acceptable, and concentrations beyond 100 mg NO_3^-/l not recommendable.[63] However, in 1971 the *WHO* reverted to its original standpoint concerning the nitrate standard, and the 1970 recommendation was abandoned.[64] In 1980, the EU members drafted a *Council Directive* in order to harmonise the drinking water standards.[65] The maximum admissible concentration for nitrate was set, not surprisingly, at 50 mg NO_3^-/l and a guideline was set at 25 mg NO_3^-/l. The EU gave no legal or scientific underpinning of the nitrate guideline. Both the nitrate standard and the guideline were taken over by the Dutch government in 1984.[66]

1.4.2 Cancer

Apart from the methaemoglobinaemia topic, cancer as a result of exposure to nitrate via drinking water also became an issue, even though the present nitrate standard does not reflect this risk. An association between gastric cancer -thought to be the prime target organ in relation to nitrate exposure- and nitrate intake was made by Correa *et al*.[67] Nitrate itself does not show any direct carcinogenic activity.[68] Chronic toxicity studies are focused mainly on the potential 'indirect' carcinogenicity of nitrate via N-nitroso compounds, nitrate being capable of generating such compounds in organisms via a number of biochemical reactions. Magee and Barnes demonstrated the carcinogenesis of several nitrosamines in animals.[69] The *in vivo* formation of N-nitroso compounds proceeds via nitrite. The suspect N-nitroso compounds (NOCs) themselves are also present in our food, but will not be discussed further in the framework of the present analysis.[70] The chemical process involved in the formation of N-nitroso compounds under acidic conditions is the following (in a simplified form):

$$R_2NH \text{ (secondary amine)} + HNO_2 \rightarrow \rightarrow R_2N\text{-}NO \text{ (nitrosamine)} + H_2O$$

The stomach is regarded as the *in vivo* reaction vessel in which most of the NOCs are formed from dietary nitrate and ingested food.[71]

Nitrite is formed in the saliva from the nitrate secreted by the salivary glands. A certain amount of the nitrate consumed with food finds its way to the salivary glands. (The same holds true for the nitrate resulting from *endogenous de novo* formation (see below).) Saliva is the major source of nitrite formed by nitrate reduction; the mouth cavity contains bacteria that are capable of reducing nitrate to nitrite.[72] Approximately 25% of the nitrate present in the human body are secreted by the salivary glands. And of this secreted nitrate 20% is reduced to nitrite in the mouth cavity. In total, therefore, 5% of the exogenous and endogenous nitrate is reduced to nitrite.[73] At an average daily nitrate intake of 143 mg NO_3^- this amounts to 7.2 mg NO_2^- per person per day (see below).

The carcinogenicity of this category of compounds resides in the so-called alkylating capacity of, for instance, DNA.[74] Under the influence of nitrosamines the DNA therefore undergoes a chemical change. This may result in all kinds of DNA 'translation mistakes' that may give rise to the formation of carcinoma.

Nitrite, as formed in the mouth-cavity, is transported to the stomach. Nitrite is reactive under acidic conditions. It can decompose into nitric oxide ($NO^\bullet$) and other nitrogen oxides react with vitamin C (ascorbic acid), and it can react with a host of organic compounds in food present in the stomach to form N-nitroso compounds. The formation of N-nitroso compounds might potentially be harmful. The vitamins C and E, however, inhibit the formation of N-nitroso compounds.[75] However, taking into account the average daily intake of those vitamins it is unlikely that formation of N-nitroso compounds is totally inhibited. On the contrary, because of the endogenous production of nitric oxide, N-nitroso compounds are produced irrespective of the dietary nitrate exposure.[76]

1.5 Sources of nitrate and related compounds

1.5.1 Exogenous sources

Nitrate is found in numerous exogenous sources such as drinking water, vegetables, meats and etceteras. Two tables are given to give some idea of the presence of nitrate and nitrite in meats and vegetables:[77]

Table 1.5.1.1 Average nitrate and nitrite concentrations in a number of meat products (mg NO_3^- and NO_2^- per kg)

Meat products	Nitrate (mg NO_3^-/kg)	Nitrite (mg NO_2^-/kg)
Bacon	56 - 171	27 - 60
Corned beef	44 - 51	10 - 15
Ham (boiled)	944	15
Ham (raw)	149 - 343	14 - 21
Ham (canned)	201	15
Sausage	14 - 488	0 - 64

Table 1.5.1.2 Average nitrate and nitrite concentrations in vegetables (mg NO_3^- and NO_2^- per kg of fresh product)

Vegetables	Nitrate (mg NO_3^-/kg)	Nitrite (mg NO_3^-/kg)
Beans (green)	340	0.6
Blanched celery	2297	0.5
Broccoli	739	1.0
Cauliflower	480	1.1
Cucumber	110	0.5
Endive	1298	0.5
Kale	799	1.0
Kohlrabi (leaves)	6590	2.3
Kohlrabi (root)	390	-
Leek	510	-
Lettuce	1699	0.4
Melon	3595	-
Mushrooms	160	0.5
Peas	29	0.6
Potato	109	0.6
Red beet	2397	4.0
Rhubarb	2114	-
Spinach	1800	2.5

In the Netherlands the average nitrate exposure is estimated to be 131.2 mg NO_3^- per person per day (excluding drinking water), the exposure range being 18.2 - 574 mg NO_3^- per person per day.[78] The same authors estimate the average nitrite intake in the Netherlands at 5.1 mg NO_2^- per person per day, the range being 1.3 - 40.2 mg NO_2^- per person per day. According to Corre and Breimer the daily nitrate intake is 137 mg NO_3^- per person, drinking water again being excluded.[79]

The contributions of the various food products to the overall nitrate and nitrite intake have also been studied. Gangolli *et al*. discuss the study by van Loon and van Klaveren for the Netherlands.[80] Information on food consumption was collected on the basis of a two-day diet status of 5 898 persons aged between 1 and 74. The study covered a full year: the period from April 1987 to March 1988. The average nitrate intake of the Dutch population was estimated to be 98.6 mg NO_3^-/day, of which:

- 68% originates from vegetables
- 19% originates from other sources
- 9% originates from potatoes
- 4% originates from drinking water

Nitrate losses on boiling were taken into account. The exogenous nitrate intake is strongly dependent on individual eating patterns and food preparation methods (cooking, blanching, etc.), among other factors. Cooking, for instance, reduces the amount of nitrate in food. However, evaporation of cooking broth that is not poured off again may increase the nitrate concentration. In terms of the average nitrate consumption per unit of time, the biggest contribution comes from vegetables. Vegetarians, for instance, will therefore have a substantially higher nitrate intake than non-vegetarians. Another factor to be taken into account is the cultivation method, which can have a substantial effect on the nitrate concentration per kilogram fresh produce. The above mentioned factors may cause the exogenous nitrate intake to fluctuate strongly.

To give an impression of the contribution of drinking water to the overall nitrate intake, in the following table average values -based on an average diet and average water consumption- are presented:[81]

Table 1.5.1.3 Average contribution to the total nitrate intake from drinking water

NO_3^- concentration (mg/l water)	Contribution to total intake (%)
10	20
50	55
75	65
100	71
150	79

1.5.2 Endogenous sources

Apart from the well-known exogenous sources it has long been common knowledge that mammals produce nitrate *de novo*, meaning that humans and other mammals have an internal source of nitrate.[82] Infections yield the most striking instance of biosynthesis of nitrate. Mayerhofer already observed this in 1913.[83] In urine passed by healthy, breastfed babies no nitrate was found, but in urine from breastfed babies having a mild gastro-intestinal infection nitrate was found to be present. Twenty years later, however, Catel and Thunger did find small amounts of nitrate in the urine produced by healthy, breastfed babies.[84] Accurate quantification was not yet possible at that time, but it was by then clear that endogenous *de novo* synthesis of nitrate does take place in humans.

In fact, in 1916, Mitchell *et al.* published an article, which described research on the origin of nitrate in urine.[85] This study showed that nitrate continued to be eliminated in urine in the absence of exogenous nitrate sources in the diet. In the early years of the twentieth century therefore, the outlines of a nitrate metabolism were drawn. More than half a century later the subject was revived and by now it is firmly established that nitrate is an endogenous metabolite.

Nitric oxide ($NO^{\bullet}$) is the key molecule in the story of *endogenous* production of nitrate, but also nitrite, numerous nitrogen oxides and N-nitroso compounds. The scientific history of nitric oxide is still very young, so that the endogenous production of nitrate and cognate compounds remained elusive for decades. The *ECETOC* study published in 1988, for instance, does not yet discuss the central role of $NO^{\bullet}$ in human physiology and its concomitant effects on nitrate excretion. Nitrogen oxides, which enter the earth's atmosphere as a result of combustion and other processes, were known only as air pollutants up to that time. Its important pharmacological role earned $NO^{\bullet}$ the title of *Molecule of the Year* in 1992. In 1998, Robert F. Furchgott, Louis J. Ignarro and Ferid Murad were honoured with the Nobel Prize in Physiology and Medicine for their findings concerning nitric oxide as signalling molecule in the cardiovascular system. $NO^{\bullet}$ put the nitrate molecule and related compounds -as molecular parts of the human physiology- in a whole different light, as will be shown below.

$NO^{\bullet}$ is a molecule that is produced by various types of cell, examples being macrophages (defence cells), endothelial cells, neurones, and etceteras.[86] This implies that the substance is therefore involved in a wide range of biochemical processes: blood pressure regulation, neurotransmission, prevention of blood platelet aggregation, immune response to invading pathogenic organism and etceteras.[87] In high concentrations $NO^{\bullet}$ and its oxides are cytotoxic and mutagenic.[88]

NO's *constitutive* aspect is to be found in the area of cardiovascular regulation. Nitric oxide stimulates relaxation of blood vessels. Therefore $NO^{\bullet}$, before its discovery, was referred to as the *endothelium-derived relaxing factor* (*EDRF*). It has been found that constitutive $NO^{\bullet}$ production is higher during pregnancy.[89] This is bound up with the need for the blood pressure in the foetus, the umbilical cord and the placenta to be kept low so as to ensure good blood circulation.

The daily production of $NO^{\bullet}$ in healthy human beings is derived from the daily excretion of nitrate in urine, being the metabolic 'end-product' of nitric oxide. Gangolli *et al.* estimate the normal endogenous *de novo* nitrate synthesis at 1 mg NO_3^-/kgbw per day, corresponding to a total daily production of 60 - 70 mg NO_3^-.[90] This relates to a daily nitric oxide production of about 20 - 30 mg $NO^{\bullet}$. Sakinis *et al.* come to somewhat lower daily nitrate excretion figures -namely 38 - 45 mg NO_3^-- using an $^{18}O_2$ inhalation approach.[91] This relates to a daily nitric oxide production of 18 - 21 mg $NO^{\bullet}$.

Quite a few pathological conditions -but certainly not all- results in an increase of nitrate concentrations in the blood plasma. L'hirondel presents an extensive list of pathological conditions which show an increase of nitrate concentrations in plasma.[92] It has been found that activated macrophages produce $NO^{\bullet}$. $NO^{\bullet}$ is an important factor in the defence mechanism of the immune system as it -together with other nitrogen oxides- has cytotoxic (cell-killing) properties. This $NO^{\bullet}$ production is much more important than the constitutive $NO^{\bullet}$ production, for the amount of $NO^{\bullet}$ that can be released upon macrophage activation are many times higher. This in turn explains the high nitrate plasma concentrations during infections. Increased levels have been shown in neonatal and paediatric sepsis,[93] in adult septic shock,[94] and in infant and adult gastro-enteritis.[95]

Hegesh and Shiloah describe the case of 58 children admitted into hospital suffering from acute diarrhoea.[96] Their blood was examined to determine the nitrate, nitrite and methaemoglobin concentrations. In addition, the amount of nitrate excreted in the urine was measured. The control group was comprised of 130 people -including 30 children- *without* gastro-intestinal disorders. Both groups were put on a diet poor in nitrate (2 - 7 mg nitrate per child per day). The nitrate concentrations measured in the blood of the sick children were 7 times as high as the levels found in the healthy control group. The nitrate concentrations found in the urine of the sick children were even 15 times as high as those found for the control group. The *ECETOC* expert panel calculated the nitrate excretion of the healthy children to be 1 mg NO_3^-/kgbw per day; for the sick children a value of 15 mg NO_3^-/kgbw was found.[97] Twelve of the sick children had a methaemoglobin level higher than 8% (at 10% cyanosis occurs: the lips and cuticles turn blue) and a nitrate concentration in the blood of 37 mg NO_3^-/l.

Gangolli *et al*. estimate the *infectious* endogenous *de novo* nitrate synthesis at some 7 - 15 mg NO_3^-/kgbw per day.[98] As already discussed, part of the nitrate secreted by the salivary glands is converted into nitrite in the mouth cavity. Under normal conditions 0.05 mg NO_2^- /kgbw is produced in the mouth cavity as a result of endogenous $NO^•$ synthesis. In case of infection this increases to some 0.35 - 0.75 mg NO_2^-/kgbw per day. For an individual with a weight of 70 kg the following estimates are assumed:

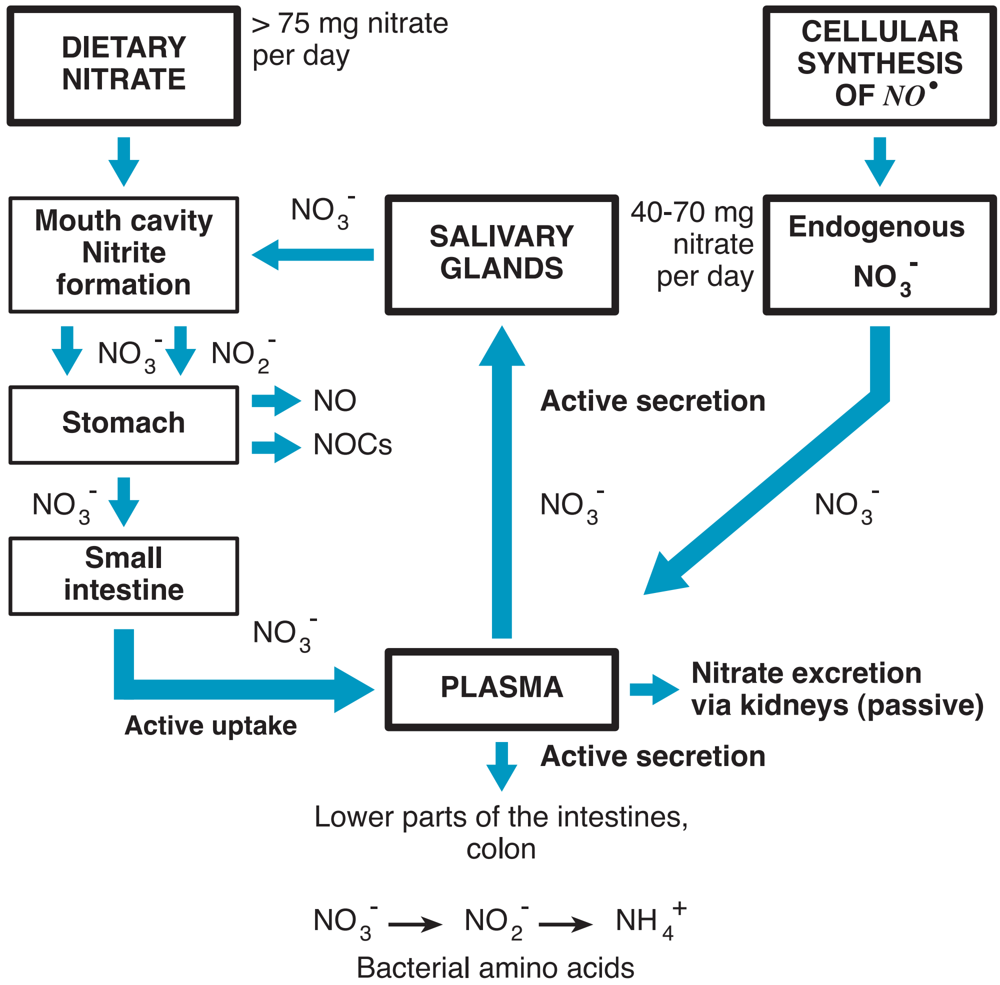
- Normal endogenous *de novo* nitrate synthesis: *70* mg NO_3^-
- 5% Reduction to nitrate (in the mouth cavity): *3.5* mg NO_2^-

- Total infectious endogenous *de novo* nitrate synthesis: *490 - 1050* mg NO_3^-
- 5% Reduction to nitrate (in the mouth cavity): *24.5 - 52.5* mg NO_2^-

Comparing the exogenous nitrate burden and the endogenous synthesis of nitrate and related compounds it is obvious that the endogenous part is much more the variable component. Infectious diseases can result in a massive nitrate production and excretion, greatly exceeding the exogenous nitrate intake. This could pose a health problem to the patient suffering from such a condition. In the next paragraph I want to examine the health impacts from both sources in relation to the risk of methaemoglobinaemia and cancer.

In conclusion of this paragraph I will give an overview of the 'nitrate-cycle' of the human body both including exogenous and endogenous sources:[99]

Figure 1.5.2.1 The human nitrate cycle



1.6 Nitrate and human health: the balance of facts

1.6.1 Methaemoglobinaemia and nitrate in drinking water

The omnipresence of nitrate makes it a prime target for policymaking. Humans need to be exposed as little as possible, is the common response. The Dutch *Consumer Organisation* (*Consumentenbond*) calls it the 'shadow-side of vegetable consumption': the otherwise healthy consumption of vegetables (vitamins, anti-oxidants), in the light of the possibility of 'to high a nitrate exposure', needs to be monitored carefully, especially concerning young children.[100] The Dutch *Consumer Organisation* even recommends that fresh vegetables should not be given to young children because of the possibility of methaemoglobinaemia.

Infantile methaemoglobinaemia is a rare disorder. When exogenous nitrate is indeed the culprit then young infants need to have the capability to convert nitrate into nitrite, possible in the gastro-intestinal tract. In 1985 the WHO, in agreement with Comly's observation, assumed that well-water methaemoglobinaemia is caused by:[101]

> '... low gastric acidity in infants [permitting] the growth of nitrate-reducing bacteria in the upper gastro-intestinal tract, allowing ingested nitrate to be reduced to nitrite.'

This conjecture made by the *WHO* contradicts, however, published observations. Agunod *et al.* for instance examined 12 babies (aged from 12 hours to 3 months) and found only one baby with achlorhydria, meaning that colonisation of the stomach with bacteria (possibly with nitrate-reducing capabilities) is doubtful.[102] The next step would be that dietary nitrate is reduced to nitrite in the intestinal tract. Dietary nitrate, however, will -for the most part- not reach those parts of the intestine where colonisation of nitrate-reducing bacteria could take place. Exogenous nitrate is rapidly and almost instantaneously absorbed in the upper small intestine (the *duodenum* and the *jejunum*), from which it is passed to the blood-stream.[103]

Indeed, the 1996 discussion by the *WHO* of this issue is much more cautious, yet obscure and still erroneous:[104]

> 'Cases of methaemoglobinaemia related to low nitrate intake appear to be restricted to infants. In studies in which a possible association between clinical cases of infant methaemoglobinaemia or subclinically increased methaemoglobin levels and nitrate concentrations in drinking-water was investigated, a significant relationship was usually found, most clinical cases occurring at nitrate levels of 50 mg/litre and above, and almost exclusively in infants under 3 months of age (). In most of these studies, no account was taken of the additional intake of nitrate or nitrite from other sources or of infections, which may increase endogenous synthesis; infections in which nitrate-reducing bacteria are involved result in massive endogenous nitrite production. Some cases of infant methaemoglobinaemia have indeed been described in which increased endogenous nitrite synthesis as a result of gastrointestinal infection appeared to be the only causative factor. *As most cases of infant methaemoglobinaemia reported in the literature have been associated with the consumption of private and often bacterially contaminated well-water, the involvement of infections is highly probable.* Most of these studies may therefore be less suitable from the point of view of the quantitative assessment of the risk of nitrate intake for healthy infants. On the other hand, bottle-fed infants have a high probability of developing gastrointestinal infections because of their low gastric acidity; this is an additional reason to treat them as a special risk group.'

Again, the *WHO* reverts in the last sentence of the above quotation to the low gastric acidity argument as a risk factor in relation to methaemoglobinaemia, which has been falsified to some extent. Furthermore, it is stated that a relationship was found between clinical cases of infant methaemoglobinaemia and levels beyond 50 mg NO_3^-/l. However, the subsequent remarks obscure this statement. Cause and effect of infant methaemoglobinaemia are not represented properly. Does e.g. the remark '... infections in which nitrate-reducing bacteria are involved result in massive endogenous nitrite production' mean that *dietary* (*exogenous*) nitrate is reduced to nitrite *or* that *endogenously* produced nitrate is converted to nitrite by the pathogenic bacteria? As discussed above it is improbable that exogenous nitrate will reach the nitrate-reducing pathogenic bacteria. Indeed, the *WHO* states that with most cases of infant methaemoglobinaemia 'involvement of infections is highly probable' meaning that the primary cause of the disorder is related to endogenous nitrate production as a result from the immune response. This puts the statement of a relationship between clinical cases of the disorder and levels beyond 50 mg NO_3^-/l in a wholly different light.

Experiments and field studies have attempted to provide clarity with respect to the exact relationship between nitrate intake and methaemoglobinaemia. The study of Cornblath and Hartmann is already mentioned (see above). No methaemoglobinaemia could be induced in the young subjects despite elevated nitrate concentrations in the feeding.

Craun *et al*. studied 102 children of ages varying between 1 and 8 years that used water with nitrate concentrations of 97 - 492 mg NO_3^-/l.[105] In these cases *no* abnormal methaemoglobin levels were measured in the blood. All values found were within the normal range.

Looking at different studies around the world which focus on methaemoglobinaemia it is clear that exogenous nitrate present in drinking water cannot be regarded as causative for the disorder. Borneff reports that in the period 1961-1986 no cases of well-water methaemoglobinaemia have been reported in the Mainz area, even though some of the wells used produce water containing up to 400 mg NO_3^-/l.[106] Acheson, in Great Britain, found no cases of food-induced infant methaemoglobinaemia between 1972 and 1985.[107] A French review surveyed occurrence of methaemoglobinaemia between 1989-1992.[108] The primary research parameter was whether the 50 mg NO_3^-/l standard was exceeded, which proved to be the case for 894 communes. Withín those communes it was established that none of the 9 500 infants below the age of 1 year fell victim to methaemoglobinaemia within the chosen timeframe.

The study of Hegesh and Shiloah, also discussed previously, indicates that gastric and intestinal infections may lead to strongly increased nitrate concentrations in the blood.[109] The researchers formulate this as follows:

> 'Infantile methaemoglobinaenemia is of much more frequent occurrence among hospitalized newborns and young infants than is generally appreciated. When present, acute diarrhoea of different etiologies is almost exclusively the cause of hospitalization. *No correlation between this condition and ingestion of food and water containing high concentrations of nitrates or nitrites was found.* This study demonstrates for the first time that high blood nitrates are a regular part of the syndrome. *The evidence presented is interpreted as indicating that diarrhoea results in endogenous, de novo synthesis of nitrites, and this is the principal cause of infantile methaemoglobinaenemia.*'

What Hegesh and Shiloah demonstrate here is that methaemoglobinaemia in infants they observed is caused primarily by *de novo* nitrite synthesis in the body (*vide supra*), which leads to the disorder. The researchers had not found a relationship between nitrate/nitrite intake from food and the disorder as the patients were given a diet containing low levels of nitrate. This study clearly shows that gastro-enteritis may lead to methaemoglobinaemia in young children and infants. The authors thus state that high plasma nitrate concentrations due to gastro-enteritis ánd methaemoglobinaemia go hand in hand.

A similar study was conducted 12 years later.[110] Of 43 infants less than 6 months old, hospitalised due to diarrhoea (without vomiting) that had lasted at least 24 hours, 64% had a methaemoglobin level higher than 1.5. Thirty-one percent (31%) of these children were cyanotic. The mean and the maximum methaemoglobin levels reported were 10.5% and 45%, respectively. Hanukoglu *et al*. estimate that in the authors' hospital about one third of the children hospitalised with severe diarrhoea and acidosis suffered from methaemoglobinaemia.[111]

Reviewing the above, it is clear that the exogenous nitrate source drinking water is not related to infant methaemoglobinaemia. Therefore, the original hypothesis postulated by Comly is flawed. The following observations make this conclusion inexorable:

- Cases of methaemoglobinaemia are mostly observed in children suffering from gastro-intestinal disorders

- When drinking water is involved it contained more than 100 mg NO_3^-/l, strongly indicating decomposing organic wastes due to bacterial activity in the polluted wells
- The direct exogenous exposure of young infants to high nitrate doses in an experimental setting did not result in the disorder
- Several studies in different countries show that despite high nitrate in drinking water -in the absence of bacteria- the disorder was not observed in young infants
- The elucidation of endogenous nitrate production in relation to an augmented immune response resulted in a compelling explanation of methaemoglobinaemia as a result of infectious diseases especially of the gastro-intestinal tract

1.6.2 Nitrate and cancer

Knowledge concerning *N*-nitroso compounds (NOCs) has accumulated greatly the past 3 decades.[112] It is clear that NOCs form in the human body when nitrates and amines are given simultaneously.[113] Nevertheless, whether or not endogenous formation of NOCs pose a risk to humans remains ambiguous. The *WHO* recognises this and states the following in relation to the carcinogenic potential of endogenously formed NOCs:[114]

> 'Several reviews of epidemiological studies have been published, most of which are geographical correlation studies relating estimated nitrate intake to gastric cancer risk. The US National Research Council found some suggestion of an association between high nitrate intake and gastric and/or oesophageal cancer (). However, individual exposure data were lacking and several other plausible causes of gastric cancer were present. In a later WHO review (), some of the earlier associations appeared to be weakened following the introduction of individual exposure or after adjustment for socioeconomic factors. No convincing evidence was found of an association between gastric cancer and the consumption of drinking-water in which nitrate concentrations of up to 45 mg/litre were present. No firm evidence was found at higher levels either, but an association could not be excluded because of the inadequacy of the data available. More recent geographical correlation and occupational exposure studies also failed to demonstrate a clear relationship between nitrate intake and gastric cancer risk; …'

This issue is complicated because of the endogenous $NO^{\bullet}$ metabolism. From this endogenous metabolism, NOCs can be formed. Moreover, as humans are routinely exposed to nitrate through excretion in the salivary glands, after which nitrite is formed in the mouth cavity, and transported to the stomach, the question whether formation of NOCs in the stomach has toxicological relevance is an appropriate one.

It is important to note that nitrate sources themselves (vegetables, water, tobacco, etc.) can strongly influence the relationship between nitrate consumption and the incidence of gastro-intestinal cancer. Vegetables are the major source of nitrate for humans. On average, 85% of the total daily nitrate intake is derived from vegetable consumption, when nitrate concentrations in drinking water are below 10 mg NO_3^-/l.[115] An above-average consumption of vegetables, however, reduces the risk of cancer, especially that of gastric cancer.[116] It would seem that the potential consequences of a higher nitrate intake due to an increased consumption of vegetables are more than offset by a number of substances in the vegetables that protect against cancer. Møller states the following on this subject:[117]

> 'The results of studies based on estimated dietary intake of nitrate vary from no association to a significantly negative association between nitrate intake and gastric cancer risk. Negative associations are most likely due to the fact that vegetables are the main source of nitrate in the study populations and that the estimated nitrate intake therefore is an index of vegetable consumption. It is a consistent epidemiological finding that a diet rich in vegetables and fruits reduces the risk of gastric cancer.'

Be that as it may, inhibition of NOC formation in the stomach by e.g. vitamin C is far from complete. Kyrtopoulos *et al.* reported an inhibition of approximately 50-60%.[118]

Another way to find out whether there is a relationship between nitrate intake and the onset of certain types of cancer is to study groups of individuals with a (strongly) increased professional exposure to nitrate compounds. In this case workers in, for instance, fertiliser production units, whose professional exposure is many times higher than can be expected in an average population, classify. L'hirondel summarises 7 cohort studies dealing with fertiliser workers (several hundreds or several thousands) in comparison with the general public.[119] None of the studies observed an increased risk of gastric cancer despite exposure of substantial amounts of nitrate.

NOCs are part and parcel of human daily exposure to innumerable exogenous and endogenous carcinogenic compounds. However, the question remains why the possible enhanced formation of NOCs in gastric juice resulting from nitrate intake does not consistently translate in to observable increases of various types of cancer as for instance is shown by the above mentioned cohort studies. For the largest part NOCs are formed *in vivo*. To what extent NOCs are made in the stomach in comparison with other *in vivo* sites remains unclear. Chronic infections, as Mirvish already noticed, could contribute to carcinogenesis.[120] Bladder cancer that is observed in bilharzia patients, colon cancer succeeding ulcerative colitis and gastric cancer resulting from a *Helicobacter pylori* infection could be due to chronic exposure to nitric oxide and other nitrogen oxides at the infection site. Whether or not NOCs are the mediating carcinogenic compounds remains to be seen. Vermeer showed both for *H. pylori* and intestinal inflammation that NOCs are produced at very low levels (or could not be detected) so that it is unlikely that they play a major role in carcinogenesis at infection sites.[121]

It is more likely that nitrogen oxides themselves are directly responsible for the formation of tumour cells. Infection and inflammation of the gastric mucosa with *H. pylori* is likely to be the elementary precursor of gastric cancer.[122]

The inference drawn in 1994 by Gangolli *et al.*, that dietary nitrate does not constitute a human health hazard, is holding until now. Their main conclusion reads as follows:[123]

> 'Epidemiological studies thus far have failed to provide evidence of a causal association between nitrate exposure and human cancer risk. Similarly, intense efforts directed at establishing a causal link between N-nitroso compounds, ..., and the incidence of human cancers have so far been unsuccessful in generating clear and unequivocal evidence. On the other hand, there is convincing evidence showing that the consumption of vegetables is associated with a reduced cancer risk in humans. Vegetables in addition to being a major contributor of dietary nitrate are also an important source of essential micronutrients and antioxidants such as ascorbic acid, tocopherols, carotenoids, and flavonoids. These compounds have been found to afford protection against the toxicity of nitrite ... and prevent the formation of N-nitroso compounds in the body.
>
> *Thus, there is no firm scientific evidence to support the conclusion that dietary nitrate, …, constitutes a health hazard to man.'*

On the contrary, nitrate seems to play a positive role in human health. This aspect has not been elucidated until recently and will be discussed below.

1.6.3 The physiological importance of (dietary) nitrate: a concise overview

The main research enterprise related to dietary nitrate has gone into clarifying the potential link between nitrate and methaemoglobinaemia and carcinogenesis. These lines of inquiry did result in elucidating the true nature of infant methaemoglobinaemia, which is primarily related to infections of the gastro-intestinal tract and *not* to dietary nitrate. NOCs, as the historical prime suspect in relation to nitrate intake and cancer, are a fact of human life, but -until now- do not seem to be intimately related to human carcinogenesis.

However, all this research effort has not been in vain. Since the discovery of $NO^{\bullet}$ as a primary molecule in a host of biological processes, nitrate proved to have a remarkable role in human physiology. It has been known that nitrate is excreted by the salivary glands. This was primary regarded as a risk factor.

However, the active excretion of nitrate in the saliva has a substantial physiological role. Nitrite synthesised from excreted nitrate by micro-organisms present in the mouth cavity, under acidic conditions, has bactericidal capabilities. Nitrite, therefore, greatly enhances the micro-biocidal effect of acidic conditions found e.g. in gastric juice and the mouth cavity where plaque accumulate. Addition of nitrite achieves kill of micro-organisms where acid alone (in gastric surroundings) allows growth to continue.[124] Nitrite itself is unstable under acidic conditions and is converted via nitrous acid (HNO_2) into nitric oxide ($NO^{\bullet}$).[125] Further reaction (with superoxide) yields peroxynitrite ($ONOO^-$).[126] Peroxynitrite is known to be an antimicrobial agent. As other nitrogen oxides are involved such as dinitrogentrioxide and dinitrogentetroxide, for convenience, I will refer to 'acidified nitrite' when discussing this topic.

Several micro-organisms were exposed to acidified nitrite in order to establish antimicrobial activity namely: *Salmonella typhimurium, Salmonella enteritidis, Yersinia enterocolitica, Shigella sonnei, Escherichia coli*, and *Helicobacter pylori*.[127] These micro-organisms were not killed by gastric juice alone. Added nitrite proved to result in a bactericidal mixture; the higher the concentration of nitrite ions, the higher the bactericidal effect was observed at a higher pH. Dykhuizen *et al*. showed that *H. pylori* is effectively killed *in vitro* when adding potassium nitrite to an acid solution (pH2) containing the organism.[128] As *H. pylori* is regarded as an important precursor to gastric cancer, nitrate -through indirect action via acidified nitrite- could play a protective role by reducing or eliminating *H. pylori* from gastric mucosa. As remarked by McKnight *et al*.:[129]

> 'Doubtless, gastric cancer is of multifactorial aetiology but a protective, rather than a detrimental, role for nitrate, by suppression of *H. pylori*, is possible.'

Gastrointestinal infections, as I have already shown, greatly increase the nitrate concentration in plasma because of induced $NO^{\bullet}$ production. This will reinforce the gastrointestinal defences against re-infection. The augmented plasma concentrations translate into higher nitrate excretion levels in the saliva resulting in higher nitrite concentrations in the mouth cavity and the gastrointestinal tract. Higher acidified nitrite concentrations are protective against re-infection with the pathogens concerned. Travellers' diarrhoea for instance seems to be effectively tackled by ingestion of a daily dose of nitrate (124 mg NO_3^-/day) as an exogenous fortification of the internal physiological processes.[130]

The above cited research efforts did elucidate the role of nitrate excretion in saliva as an important mechanism to reduce risk of infection through foodstuff. As is known for quite some time, food is the main carrier of pathogenic micro-organisms that are potentially health threatening.[131] The above does, however, not singularly translate into a recommend daily dose of nitrate through the diet.[132] *Therefore, the appropriate daily intake of nitrate still remains unknown.* It is important to state that the commonly endorsed adagium for e.g. vitamins 'if some is good, then more is better' is false for any type of food ingredient or any other chemical for that matter -be it natural or man made. Nitrate is no exception, even if health-improving effects have been uncovered. The Paracelsus adagium *dosis sola facit venemum* ('the dose makes the poison') should always be kept in mind.

1.7 Nitrate and (ground)water: from farm to faucet?[133]

1.7.1 Monitoring grids

Reviewing scientific data on the nitrate issue it is clear that the nitrate drinking water standard -also functioning for ground- and surface water in relation to human and environmental health- has become obsolete. The 50 mg NO_3^-/l standard does not fit the environmental bill as ecological quality of surface waters cannot be related to this standard considering its medical history.

When indeed the nitrate standard of 50 mg NO_3^-/l is done away with, where does that leave us considering the environmental issues? In other words, what is the environmental impact of nitrate from agricultural practices, and can we evaluate nitrate leaching from farming?

In effect, two systems are in use in the Netherlands that monitor nitrate concentrations (apart from other compounds) in groundwater: *Het Landelijk Meetnet Grondwaterkwaliteit* (*LMG; Dutch National Groundwater Quality Monitoring Network*) and *Het Landelijk Meetnet Effecten Mestbeleid* (*LMM; Dutch National Monitoring Network on Nutrient Policy*).

LMG was set up between 1979 and 1984. The monitoring grid comprises of 400 locations and is positioned at the most prevalent combinations of soil type and soil uses. The *LMM*, however, is directed towards farming activities in relation to policy trends within the agro-environmental field. The monitoring grid shall be fully operational in 2003. Different farms on various soil types will alternatively be monitored for a number of years. Summing up the different aspects of the grids (including the monitoring grid on county level):

Table 1.7.1.1 Dutch efforts on nitrate monitoring in groundwater

Grid	Scale	Number of locations	Parameters	Depth (m)	Frequency	Target
LMG	National	400	Macro-ions (incl. nitrate, ammonium and phosphate), metals	10 and 25	1/year	General picture groundwater and nitrate leaching (drinking water)
PMG[134]	County	A few dozen[135]	Macro-ions (incl. nitrate, ammonium and phosphate), metals	(5), 10 en 25	1/year	'Meso' picture directed at environmental issues
LMM	National	3*27 'sand farms' 55 'clay farms' 3*12 'peat farms' Total 172 farms with 16 sample locations/farm	Phosphate, nitrate, ammonium, metals	Up to 1	3/7 year	Monitoring of nutrient leaching

1.7.2 Dilemmas

The monitoring grids have in common that a relation is postulated between surpluses of nutrients such as nitrate and leaching towards ground- and surface waters. Nitrate is in that sense regarded as a conservative element in effect not interacting with and within the soil/groundwater matrix. The monitoring networks and its data output do not include bio-chemical soil processes influencing the presence and amount of nitrate (mineralisation, de-nitrification).

Monitoring nitrate at depth (10 m below ground level and lower) is, however, not easily correlated with nutrient exposure (through manure) at field levels. The sampled groundwater is usually several years old (the average infiltration speed in the Netherlands is about 1 m per year). It is not possible to ascertain the exact *origin* of the sampled ground water. Ground water movements are both vertically as well as horizontally. Depending on the inclination (slope), ground water moves between a few to several hundred metres per year. The inspected groundwater could well originate from a farm (or any other location in the relative vicinity) up to a few kilometres away from the sample point. No relation can therefore be drawn between use of nutrients and the presence of nitrate in the drawn sample. Other sources than agriculture might contribute to the presence of nitrate as well, adding to the already blurred picture.

Another complicating factor is the fact that the length of the used sample filters in the monitoring grid results in a nitrate concentration spanning several years. Referring to the infiltration speed of 1 metre per year, a sample filter of 2 metres in length will sample nitrate over a period of 2 years. Nitrate is therefore also sampled at times when no manure is added to the specific field.

The reactivity of the soil will influence the nitrate concentration continually. Nitrate has usually disappeared within a few dozen metres because of dissolved organic carbon or pyrite. Exceptions are less reactive soil types such as sand.

It is moreover not clear to what extent the representation of the various monitoring grids is. In other words: what will the nitrate concentration be a hundred metres from the sample tube. *Statistics are, as normal procedure, used in order to generate an image of nitrate leaching at places where no sampling will take place.*

Measuring at deep levels will only produce a general picture of the presence of nitrate. Correlation with use of manure is difficult to elucidate because of the issues raised above. Shallow sampling will of course result in a more direct correlation with use of manure, but the length of the sample tube will complicate matters considerably. The answer whether or not nitrate measured in shallow groundwater will penetrate the soil to greater depths remains unanswered, depending on numerous aspects such soil reactivity, precipitation, ground water levels and etceteras.

The following questions therefore are of prime concern if a monitoring grid will live up to its expectations and will result in a picture with reliable characteristics:

- Amount of locations?
- Number of samples within a certain time frame?
- Which depth(s)?

Variations of nitrate concentrations are dependent on a number of factors, which are:[136]

- Amount/homogeneity of nitrogen application
- Precipitation surplus
- Depth of the unsaturated zone
- Denitrification capacity
- Uptake by crops
- Inhomogeneity of the porosity of the soil
- Mineralization of the organic nitrogen capacity in the soil
- Precipitation of other nitrogen sources (traffic)
- Drainage
- Flow pattern of ground water
- Others?

These aspects play a crucial role on several scales. Not just a nitrate source such as manure determines the presence and concentration-levels of nitrate in groundwater at several depths. On the contrary, hydro-geochemical parameters are important determining factors when considering nitrate. For instance, with an increasing unsaturated zone, oxygen enters the soil capable of breaking done organic material resulting in among other things nitrate. This nitrate will subsequently leech to deeper groundwater. A deepening of local or regional hydrology, with a subsequent introduction of oxygen, will result in nitrate leaching not related to manure application.[137]

If the number of samples within a monitoring grid is too small both in a geographical and a temporal time frame, this will greatly affect the quality of the generated image of nitrate leaching ('casino effect') from manure application.

1.7.3 the statistics of a monitoring grid

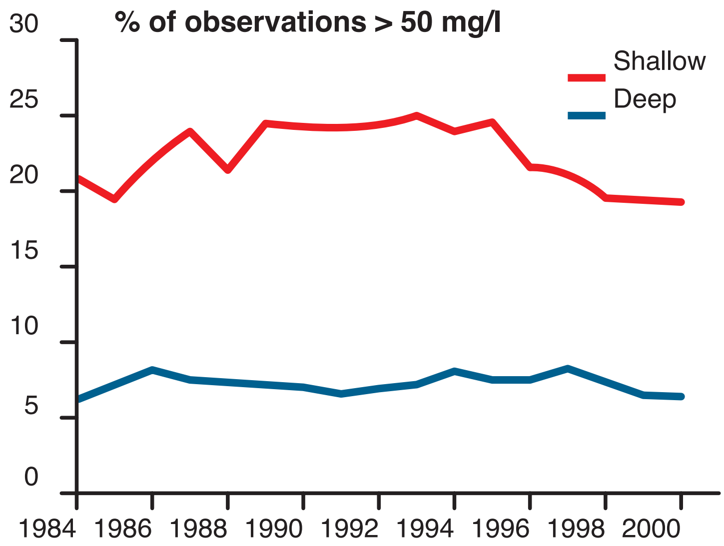
Data generated from monitoring grids need to be processed in order to generate a picture of the status of groundwater quality. A central theme in this processing is that from a data set generated from a limited number of sampling locations and depths a general picture needs to be created over the whole of a region or even nation-wide. This means in effect that nitrate concentrations are calculated for locations that were *not* sampled. The actual situation and trends need to be generated from this limited data set. This normal procedure is a complicating factor in interpreting data sets.

Summarising large data sets is usually done with the publication of an average nitrate concentration in rural (farming) areas, a trend, the percentage of observations above the nitrate standard, the number of sample locations above the nitrate standard related to the total amount of sample locations and so forth. These are usually published without any background information such as the actual data sets (or a selection therefrom). This information is however of overarching importance in order to appreciate the quality of such publications. The following issues to be considered are of crucial importance:

- Which data sets and what kind of selection criteria (if any) were used?
- Why was the specific parameter chosen?
- What is the number of Lodes (limit of detection)?
- What is the statistic distribution of the data set?

The calculation of a parameter implies a representative data set generated from a monitoring grid. This is most evident when an average nitrate concentration in groundwater is calculated. *However, what is Dutch groundwater; to what depth does groundwater extend; delivers the monitoring grid a representative data set?* When one focuses on the relative number of sample locations exceeding the nitrate standard in relation to the total amount of sample locations this problem is circumvented. Consequently, such a representation leaves much to be desired and it is questionable whether such an approach will give a reliable picture of the situation. The following illustrates this predicament:[138]

Figure 1.7.3.1 Processing example of one of the national monitoring grids



This figure published by the *RIVM* (*Dutch National Institute of Public Health and Environment*) does not depict the selection of sample locations. The actual locations used for this figure were all situated in the sandy area in the Netherlands. Other locations were not incorporated in this representation. The number of sample filters is also not mentioned.

Shallow sample locations exceed the nitrate standard more often than the deep sample locations. Both sample depths show a rather stable trend throughout the depicted time frame. Even for the sandy area, which is represented in the above figure, around 80% of the shallow sample locations remain below the nitrate standard. Moreover, a considerable portion of the sample locations is below the LOD. If a large number of sample locations are below the LOD -say between 25-50%- averages cannot be representative.

Again, it needs to be reiterated that with statistics nitrate concentrations are calculated for locations that were not sampled. Logically, this is a normal procedure as it would be impossible to sample 'all' locations. A number of different interpolations are used in the Netherlands. *Rigging* is one of those methods that interpolates directly from acquired data sets. With this method of interpolation it also possible to generate the error of interpolation, that is to say that it is possible with this method to calculate the error of the nitrate concentration in locations, which have not been sampled. Plebes, in his thesis, shows that for the 1991 ground water quality data set -using *rigging*- the error for nitrate concentrations were in the range of several dozen milligrams.[139]

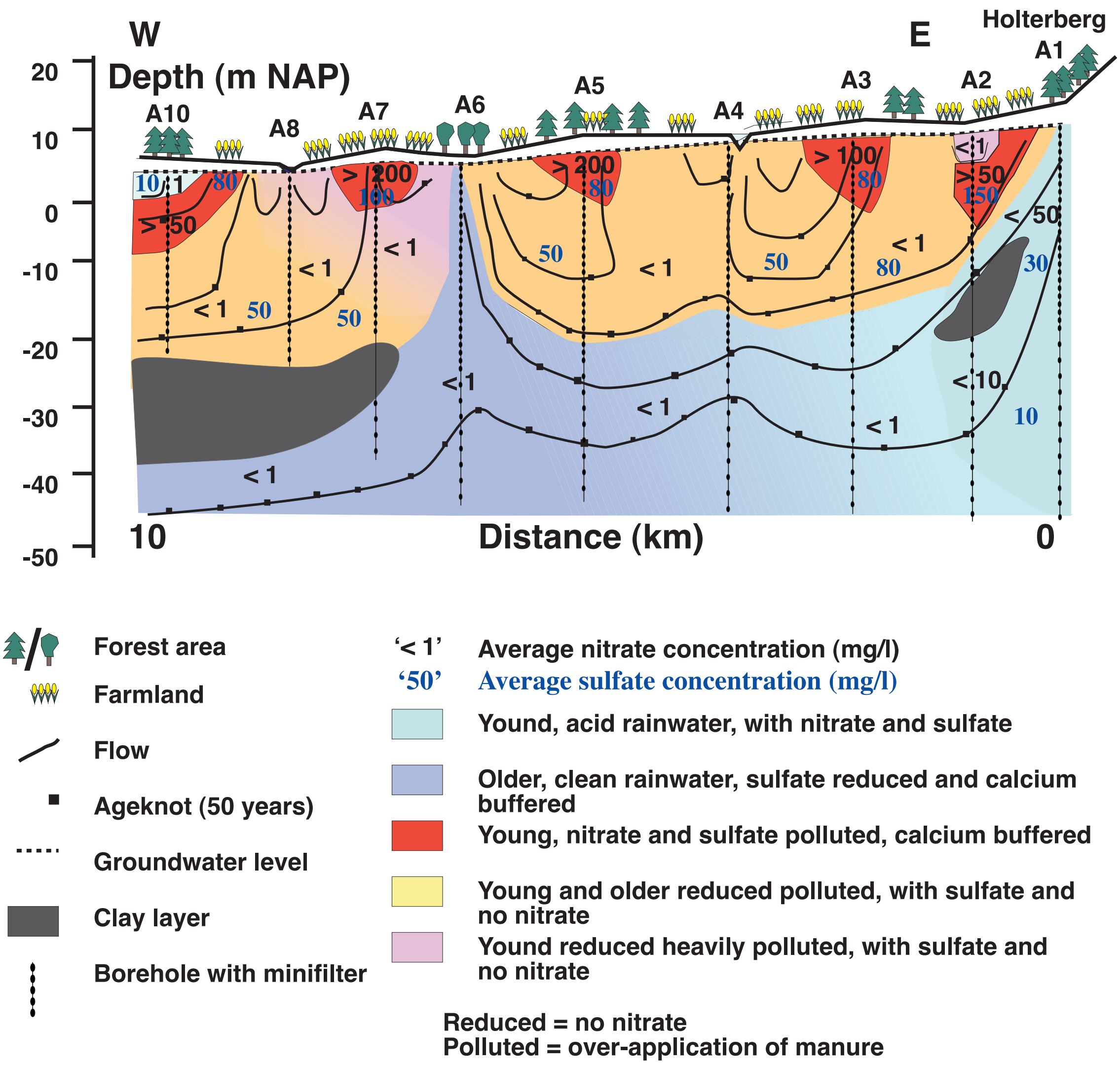
Another interpolation method brings local and regional information such as soil types, groundwater levels, soil uses like farming or the presence of cities and the like in relation to nitrate concentrations. The assumption is that when these different types of information are available, nitrate concentrations can be made available. Using homogenous areas -areas with a unique combination of soil type and use- the assumption is that this will result in a unique bandwidth of nitrate concentrations. However, Rapport *et al.* showed that such an approach is highly problematic as the deciding hydro-geochemical aspects -the reactivity of the soil matrix in combination with groundwater present- are not taken into account.[140]

A third method uses calculating models. Nitrate concentrations are calculated on the basis of variables such as groundwater levels, soil types, manure application, nitrogen mineralization capacity, precipitation surpluses and etceteras. The model will then calculate on the basis of the input variables the nitrate concentrations, which will be validated with monitoring data. It will be difficult to decide which model within this range will be the best representation of reality as validation proves to be extremely difficult.

1.7.4 A spatial image of nitrate in groundwater: the 'Salland Section'

Reviewing the above discussion, it remains unclear whether or not nitrate is to be regarded as a 'polluting blanket'. Generated images e.g. published by the *RIVM* do suggest such a notion.[141] The scheme below, however, propounds a completely different view of the nitrate issue:[142]

Figure 1.7.4.1 Nitrate leaching in the 'Salland Section'



Detailed monitoring west from the Holterberg with mini-filters (15 cm in length) every metre up to 50 metres, in an area covering 10 kilometres in which some 10 drill holes reach to a depth of 50 m, gives the picture illustrated above. The sampling was carried out in 1989. In the colours red, yellow and purple water influenced by agricultural activities is depicted. However, only the red pockets denote nitrate-containing groundwater. Nitrate is therefore, as this scheme clearly shows, not spread as a polluting blanket over the Netherlands. This image does not change visibly after sampling was carried out again in 1996.[143] Explanations for this not so well known nitrate behaviour in groundwater are hydrological flow patterns and denitrification, which limit spread considerably of nitrate. Moreover, it is interesting to note that undisturbed water flowing from the Holterberg contains nitrate.

Through oxidation of pyrite, nitrate does extend its geochemical reach into the groundwater further than its mere physical presence. Sulphate is generated by this reduction of nitrate, and indeed is found in the yellow zones below the nitrate containing pockets in the Salland Section. Whether that represents a polluting presence, one needs to look at the natural occurrence of sulphate in surface- and groundwater. As groundwater is involved the toxicology of sulphate also needs to be considered. The *WHO* proposed no health-based guideline for sulphate.[144] Sulphate does at most change the taste of drinking water above certain concentrations (± > 500 mg SO_4^{2-}/l). The 150 mg SO_4^{2-}/l drinking water standard is therefore to be regarded as a 'flavour' standard; a safeguard against flavour variations.

The natural occurrence of sulphate in Dutch surface- and groundwater varies wildly. Surface waters contain natural concentrations up to 1 000 mg SO_4^{2-}/l starting below the limit of detection. Groundwater concentrations vary even more: up to 2 000 mg SO_4^{2-}/l have been monitored in brine groundwater.[145] Taking these concentrations into consideration, the formation of sulphate from pyrite oxidation needs to be seen in light of these natural occurring concentration ranges. Moreover, once sulphate has been generated through nitrate reduction, sulphate will be transported and again be reduced, as the Salland Section shows. By no means will sulphate be transported unrestricted.

The inference from this research is that the national monitoring grids do not contain resolution capacity needed for a detailed description of the spread of nitrate as a result of agricultural activity. Too few sample locations from a spatial and temporal point are currently present in the Netherlands. Used statistics to calculate nitrate concentrations at non-sampled points are off the mark. Representation of data generated from the limited capacity of the monitoring grids therefore is rather limited.

When indeed the nitrate standard for ground- and drinking water would be abolished this would certainly not lead to a massive spread of nitrate within Dutch groundwater. Detailed monitoring of farmland -as proposed in the 'Yardstick' approach developed by Frapporti *et al*.- would insure optimisation of manure application in relation to nitrate losses in farmland, therefore protecting groundwater from the infusion of nitrate and related compounds.[146] This would form a transition between a legalistic precautionary approach of environmental regulatory efforts on agricultural themes towards a realistic and empirical approach.

2 THE NITRATE ISSUE IN A CAUTIOUS PERSPECTIVE; A CRITIQUE

2.1 *Target risk* management versus the *risk superior* alternative

Nitrate is neither a public health threat (on the contrary) nor ubiquitous because of agricultural activities. Undeniably however, in the Netherlands agricultural activities throughout the centuries drastically changed the countryside. Indeed, the principal spatial human activity with all its related consequences is agriculture. Grübler notes that:[147]

> 'Reference to technology's impact on land use usually conjures up images of land covered by city skylines, sprawling suburbs, factories, roads, dams, pipelines, and other human artefacts. In reality, although detailed statistics are lacking, the area covered by such technological artefacts is most likely less than 1% of the earth's total land area. In contrast, the percentage of the total global land area that is used for agricultural and pasture is close to 40% …. Technological changes in agriculture therefore directly affect much larger areas than other technological changes. …'

Risk management of agriculture therefore is a complicated issue. Physical and chemical alterations because of agricultural activities concern large masses of land with global environmental, social and economic implications. Moreover, food-production is one of the most elementary activities for any society. The *Nitrate Directive*, however, only takes care of a specific agricultural issue related to the environment and public health:[148]

> 'The Directive seeks to reduce pollution caused by nitrates from agricultural sources and to prevent further pollution. This it seeks to achieve by requiring Member States to implement action programs in areas identified as being vulnerable to pollution by nitrates from agricultural sources (these areas are designated on the basis of their exceeding, or being likely to exceed in the future, the 50 mg/l of nitrates limit, and/or the existence, or likely existence in the near future, of eutrophication induced by nitrates). Among its measures is a limitation of the application of livestock manures to 170 kg N/ha by 2003.
>
> Higher levels of nitrate in drinking water is a public health problem because nitrate rapidly reduces to nitrite in the body. Environmentally, the inputs of nitrate from Member States are particularly significant in causing increased algae growth, which lead to the detriment of ecosystems and eutrophication.'

Two central aspects concerning nitrate from agricultural sources are mentioned in the *EC Directive*:

- *Human health* in relation to nitrate exposure via drinking water
- *Eutrophication of surface waters* as a result of the presence of nitrates (as a nutrient for algae)

The seemingly appropriate response is formulated in terms of a prohibitive risk management instrument. The 50 mg NO_3^-/l standard is used both for the human health as the environmental part of the *Directive*. The limitation of the application of livestock manure to 170 kg N/ha by the year 2003 is the means by which this target is attained. Both human health and environmental quality –in the *Directive*- are related to the nitrate standard.

The case that I want to make here is that -in general- prohibitive risk management instruments within the realm of environmental policies are counterproductive as a result of the probability of the introduction of countervailing risks or tradeoffs. Graham *et al*. define this notion as follows:[149]

'Though the term "risk tradeoff" may not be familiar to many people, the phenomenon is commonplace in human decisionmaking, reflected in such familiar adages as "out of the frying pan and into the fire" and "the cure is worse than the disease". The general problem is that efforts to combat "target risk" can unintentionally foster increases in "countervailing risks". Many kinds of countervailing risks are commonly known by the terms "side effects" (medicine), "collateral damage (military tactics), or "unintentionally consequences" (public policy*). Unless decisionmakers consider the full set of outcomes associated with each effort to reduce risk, they will systematically invite such risk tradeoffs*. ...'

Graham *et al.* show that implemented risk reduction strategies concerned with only one or a limited set of target risks result in the introduction of other related risks. Risks of a certain activity carry a number of intricate interactions seldom acknowledged by decision-makers.[150] These interactions are, however, quite relevant in the formulation of risk reduction strategies by policymakers.

Most policy making, however, regards risk tradeoffs -countervailing risks arising from target risk management- as irrelevant externalities. A number or reasons can be identified why that is so:

- *Tunnel vision*: The many ministries and research centres, which the Western world is endowed with, have a specific core business resulting in the fragmentation of decision-making into specialised roles with bounded oversight responsibilities. This results in a fragmented mono-thematic approach of all kinds of policy themes. Integration of different themes has therefore a low priority. Media attention, political importance, current scientific funding may result in the over-exaggeration of certain risks. It is therefore not surprising that different policies concerned with one issue differ wildly in cost effectiveness. Tengs *et al.* e.g. showed that the cost per life-year saved (a 'life-year' saved is a statistical measure of how much a lifesaving program increases the life span of a target population) for the median toxin control program in the US lies a factor 150 higher than the median medical program.[151] Put in other words, median environmental policies concerned with environmental toxin control are a factor 150 less effective per life-year saved than the median medical program. Spending $ 100 million per year on control of benzene emissions at rubber tire manufacturing plants might save one life-year over a 200-year period (i.e. $ 20 000 billion per life-year saved). The same $ 100 million, if invested in automobile airbag technology, is expected to save 2 000 life-years every year (or $ 50 000 per life-year saved).
- *The omitted voice*: The absence or even ignoring stakeholders during policymaking could lead to a disproportionate attention to well-organised lobby-groups (NGOs of environmental organisations, industries, and etceteras). Moreover, in a democracy the constituency of the particular decision-maker largely defines the development of specific policies concerning a certain target risk.[152] The advantages of a reductionist policy solution directed at the specific democratic backbone of the concerned decision-maker by far outweigh the costs involved in a full-scale analysis of the issue. The introduction of countervailing risks as a result of the proposed target risk reduction strategy is regarded as non-relevant externalities.[153] For society as a whole, however, a full-scale analysis of the specific issue ís relevant. Chances are that in such a set-up all the relevant stakeholders are involved during policy-making. However, when all the countervailing risks of a certain reductionist policy are spread over a large number of different sub-populations within a given society, chances are that only the well organised lobby-groups will have a say in the matter as the countervailing risks will remain invisible for decision-makers.
- *Public perception*: If a high percentage of the general public regards a certain issue as dangerous to their health, democratic decision-makers will be inclined to do something about it.[154] Whether or not the perceived risks are factually and measurably detrimental to public health is a far less important question. The decision-makers response is primarily driven by the 'democratic content' of the perceived risks.
- *Heuristics*: Heuristics are relatively primitive and simple decisional strategies in order tot reduce complex mental tasks to orderly proportions. Another words for this is problem-sizing.[155]

When one is confronted with an overwhelming amount of information some sort of condensation process takes place resulting in prioritisation of information. The issue is downsized into mentally digestible chunks. This downsizing is more or less a subconscious process and frequently (but not always) results in a misinterpretation of reality.[156] The *Delaney Clause*, a policy devised to regulate the risks of synthetic food-additives in relation to carcinogenesis is an example of a heuristic approach of reality. Resulting research efforts concentrate primarily on carcinogenic characteristics of synthetic compounds in foodstuffs. The overwhelming amount of natural carcinogenic compounds in foodstuffs is ignored.[157] Other non-carcinogenic toxicological effects of compounds are also disregarded. Another heuristic is the precautionary principle (PP).[158] The *Nitrate Directive* is also to be regarded as a heuristic tool of environmental and human health impacts of nitrate.

Despite the fact that considerations about risk tradeoffs are not part of the policy-making tradition, the reality thereof stands out quite unmistakably. A target risk approach is therefore a seldom-effective method of dealing with risks especially in the environmental arena. This has to do -among other things- with the inter-relatedness of environmental issues especially when dealing with agriculture.[159] Wiener shows that optimal regulation in the face of a target risk (TR) and countervailing risks (CR) *both* need to be taken seriously, not just the target risk.[160] *Uncertainty is not the crucial dilemma here; tradeoffs are*. Even risks with a high probability of occurrence would not justify regulatory action if CR > TR (such that regulating TR would yield negative net benefits). Meanwhile, standard advice to 'muddle through' by 'ignoring side effects' (ignore CR) is too lax; it will yield more net harm (because of neglected CR) than maximizing (TR - CR) whenever CR is positive and CR can be reduced at less than equal increases in TR.

In order to attain a risk superior approach of the nitrate issue, a number of agricultural and environmental themes need to be connected. Empirical knowledge of nitrate leaching from farmland is the first prerequisite in the risk superior approach of nutrient management. The Salland Section is an example of the possibilities this empirical approach holds. Next, the potential risk management options should be considered in the light of economical sustainability of the agricultural activities, as too stringent risk management strategies could result in a geographical displacement of the activities to areas with less stringent environmental risk management policies.[161] Furthermore, it should be kept in mind that apart from the different risk management strategies, food production is a fundamental requirement. Any global risk management strategy needs to take that into account. Stringent environmental policies will not diminish the demand –or indeed production- of food.

Apart from the abovementioned decisional characteristics surrounding the continuance of the *Nitrate Directive* and the role it plays in the bureaucratic cultural ecological critique, the ensuing selection of scientific data needs to be scrutinised in more detail. Data selection is obvious in the nitrate issue. The previous chapter gives undisputable evidence of that. Of course, to err on the side of safety is deeply rooted in the democratic policy-making tradition. Simply put: it is attractive for a decision-maker to opt for a so-called 'zero-risk' policy in environmental legislation as choosing for a certain (acceptable) risk-level is choosing for the complementary exposure level. This requires an intimate relation between science and politics, as the science of nitrate offers noticeably more than is factually used in the decision-making process.

2.2 Late modern relativism: the interdependence of knowledge and power

Post-modernity as a theory about the nature of late modern society is clearly the most relativistic position about the value of scientific knowledge in the early modern sense.[162] However, even ignoring this theoretical position and sticking to the more classical epistemological points of view of e.g. Popper it becomes clear that all knowledge nowadays is regarded as a product of social processes, the scientific method being one of them.[163] The belief in the possibility of objective knowledge, which is eternally true, is discarded. Today, the belief of an inter-subjective knowledge under constant scrutiny, discussion and revision is held. What we hold to be true today can (and probably will) be revised tomorrow. According to Gellner this epistemological position -the possibility of revision of scientific standpoints- has always been present in modern culture and accounts for its success, although he makes it quite clear that 'serious knowledge is not subject to relativism'.[164] Modern man in Western society has to forego the possibility of believing in any eternal truth.[165] As Gellner puts it:[166]

> '… It [the cognitive ethic of the Enlightenment; *authors*] requires the breakup of data into their constituent parts, and their *impartial* confrontation with any candidate explanatory theories. It shares with monotheistic exclusive scriptural religion the belief in the existence of a unique truth, instead of an endless plurality of meaning-systems; …. It shares with hermeneutic relativism the repudiation of the claim that a *substantive*, final and definitive version of the truth is available. It is, however, separated from it by refusing to endorse, as equally valid, each pre-Enlightenment, socially enmeshed, cognitive cocoon of meanings. Only a *procedure*, but no substantive ideas, is absolutized. …'[167]

Searle makes the useful distinction between purely natural phenomena (e.g. a stone), artefacts (e.g. a knife) and social institutions (e.g. marriage).[168] The historical trend in the development of human society is that artefacts and institutions have become more and more important for the fate of humans whereas natural phenomena have become less important. More and more it is social reality which dominates our human existence. This social reality is constantly (re)constructed and in this construction *knowledge* –moral, political, legal or scientific– is the central feature. Today the artefacts and institutions created by humans in the interest of humans present the most visible risks to humans, albeit arguably not the most important. Therefore, risks have to be understood as *created* as well. They normally involve natural phenomena (e.g. snow), artefacts (e.g. ski slopes) and institutions (e.g. 'avalanche watchers'). Even the most natural of dangers like storms, floods and earthquakes are no longer seen as 'just' natural phenomena. They are considered to fall under human scrutiny and prediction if seldom under human control. In this sense our human environment is almost entirely considered to be social, whether or not that is justifiable. It is in this socialised environment that knowledge and power come together.

The production and application of knowledge is never free from social relationships. This is an old sociological theme that is directly relevant for the way people respond to dangers and damage. In this sense we may speak of the politics of danger, which is a prominent theme in the work of Mary Douglas. In her essay on *Risk and Justice* she writes:[169]

> 'Cultural theory starts by assuming that a culture is a system of persons holding one another mutually accountable. … From this angle, culture is fraught with the political implications of mutual accountability'

That is why every culture needs -as Douglas states- a common forensic vocabulary with which to hold persons accountable. It is this vocabulary, which allows certain claims of justice and danger as rhetorical resources for all parties. On this fulcrum concepts of liability and tort are continuously at stake.

According to Douglas the discourse of risk is our modern, rational and technical variant of such a forensic language in which politics and knowledge are very much intertwined. Together with Aaron Wildavsky she developed a conceptual schema of four ideal types to elaborate on the cultural nature of risks.[170] In order to know what we hold to be most dangerous we have to ask what we hold to be most precious. The ultimate evil is that which threatens the ultimate good most. Douglas and Wildavsky suggest that we should view discussions about risks as political struggles between adherents of the different cultural points of view. This is also known as *Cultural Theory*, which I have discussed elsewhere.[171]

To put matters into perspective, risk should be seen as a joint product of *knowledge* about the future and *consent* about the most desired prospects.[172] When *knowledge* is *certain* and *consent comprehensive* -societal objectives are agreed upon and alternatives are known together with the relative probability of occurrence- then a problem within this frame is of a technical nature and solutions are found in calculations. In the situation where *knowledge* is *certain* but *consent* is *contested* -different ideas exist concerning the way to go within society- then the solution is more discussion (e.g. the 'polder model' so much revered in the Netherlands). When this proves to be unworkable, coercion in the form of e.g. legally binding legislation is the other option. In the case where *complete consent is hampered by a lack of knowledge*, the problem of risk is defined as a deficit of information. The solution to this specific risk problem is scientific research. Douglas and Wildavsky describe the situation -where consensus is wanting on both knowledge and consent- as follows:[173]

> 'The last situation, in which knowledge is uncertain and consent is contested, is precisely how any informed person would characterise the contemporary dilemma of risk assessment.'

Within this specific risk-problem-frame science and politics are closely interwoven, as both are in need of each other in the search for solutions. This makes the scientific community vulnerable for political opportunism resulting in a politicisation of science. Rip has analysed the relation between science and politics in discussions about risks. His work leads him to two conclusions. Firstly and not surprisingly he finds that scientific agreement is more likely among participants who adhere to similar normative views. His second conclusion is more interesting. He claims that scientific agreement is more 'robust' when it has been reached by discussion between participants who represent more diverse normative points of view. The more robust the scientific knowledge, the more difficult it is for newcomers to the discussion to break the consensus and renew the struggle about facts and explanations. Rip speaks of 'empirically controlled normativity'. His research into the development of science leads him to the conclusion that the construction of scientific facts and the authoritative application of values are two consequences of one process: increasing robustness. It is this goal that guides scientific experts in their everyday practices.[174]

Rip presents two other important points. First of all, acceptance of a certain construction of scientific facts does not have to be based on consensus. For different reasons opponents may give up the fight against a dominant view. One reason why industry sometimes accepts governmental norms based on disputed science is that at least the case is settled officially and uniform standards are in place for everyone. Predictability of governmental decisions and equality of treatment are valuable to captains of industry who might care less about scientific accuracy. Rip's second point is that wherever the same parties meet each other time and again in similar discussions, 'second order robustness' is likely to arise. By this he means the institutionalisation of the struggle that facilitates the creation of first order robustness: the agreement on facts and values.[175] All kinds of legally regulated procedures can be regarded in this sense as politically generated second order robustness.

This view that questions about scientific fact are related to questions of normative agreement goes squarely against the early modern idea of the separation of science and politics, which just like the separation of law and politics was one of the basic tenets of the Enlightenment. Both ideas have been criticised from the outset, but it was only during the twentieth century and especially in the second half that they came under increasing attack. Of course lawyers as well as scientists try to salvage as much of the separation as possible, because only then can they feel secure in their own discipline. But as soon as the public takes an active interest, professionals are fighting a losing battle. With the erosion of the separation of science and society we witness erosion of the authority of science and scientists as well as government and industry as far as they are dependent on science. By now famous cases like smoking and asbestos have taught the public that scientists can make wrong ascertains and that government and industry have strong interests in denying established adverse effects of products that are important to them. The recent cases of BSE in the United Kingdom and the contamination of blood in France have added scandal to scepticism. Under these circumstances it is relatively easy for pressure groups to qualify some activity or product as a huge risk, especially when there is much unknown and *ipso facto* uncertain. In such cases the predicted actual damage will typically only come about in the distant future -if at all-, which renders these predictions impossible to falsify. For scientists this means an easy disqualification. For policymakers, however, such disqualification is less easy to do, because they have to cope with public opinion. And for the public, unfalsifiable threats are unrefuted (actual) treats!

Consent in which direction European agriculture should be progressing is lacking. One would expect therefore a vivid discussion in Europe as to what the future of farming should be. Indeed, this seems to be the case when viewing for instance the discussion on organic farming. On the knowledge side, the *WHO* maintains the nitrate standard -albeit using outdated and incomplete scientific data- therefore upholding a seemingly non-contested scientific opinion on this matter. It seems to me that as consent is lacking, opening the scientific debate on the nitrate standard might make the search for political and public consent even more problematic. Therefore, the newly gained insights into nitrate toxicology are ignored for the sake of political conformity. On those grounds alone the *Nitrate Directive* may be kept in place.

2.3 The cautious tradition: empowering bureaucracy

Reviewing the science of nitrate toxicology -as was be done in the previous chapter- it is quite clear that the nitrate drinking water standard has become irrelevant. The toxicological data, gathered in the past hundred years, do not leave much room to doubt. However, the cautious tradition in environmental legislation, such as the *Nitrate Directive*, results in a choice of scientific material politically deemed appropriate.

To err on the side of safety has until now resulted in the obvious selection of scientific facts. In other words: *precaution empowers bureaucracy*.[176] Science in the context of policymaking is dependent of policy-driven questions. A politicisation of science is a result of this: politics have become a strong steering mechanism in scientific research, and scientific results need to be incorporated into policymaking. *This has, among other things, resulted in a Nitrate Directive not concerned with human and environmental risks per se but in a regulatory instrument with a predominant legislative quality separating law-abiding economic activities from the rest*. Pollution is therefore not used in the technical sense but in the moral sense.[177]

> '... Pollution, defilement, contagion, or impurity implies some harmful interference with natural processes. It assumes something about normality because it implies an abnormal intrusion of foreign elements, mixing, or destruction. It is used in two senses. … The technical sense of pollution is not morally loaded but depends upon measure of change. The other sense of pollution is a contagious state, harmful, caused by outside interference, but mysterious in origin. *This nontechnical idea of pollution is particularly useful in political argument because it carries the idea of moral defect.* ...
>
> ... pollution beliefs uphold conceptual categories dividing the moral from the immoral and sustain the vision of the good society. ...
>
> ... we realize that the critics of our society are using nature in the old primitive way: *impurities in the physical world or chemical carcinogens in the body are directly traced to immoral forms of economic and political power. ...'*

Whether or not the *Nitrate Directive* is truly related to the defined target risks -the putrefaction of ground- and surface waters with nitrate originating from agricultural activities- has become more or less extraneous. This is for instance shown by the fact that abiding by the 170 kg N/ha standard mentioned in the *Nitrate Directive* is regarded as a sufficient measure in relation to 50 mg NO_3^-/l in groundwater. In that sense the *Nitrate Directive* generates confusion. The 50 mg NO_3^-/l alludes to a (peak) *concentration* in water, which is a clear reference to the medical history of the nitrate standard. The 170 kg N/ha, however, refers to a *nitrogen-flux*. Implementation would by definition be a sufficient measure in relation to 50 mg NO_3^-/l standard. The amount of infiltration water diluting this nitrogen flux and the influence of the *path* (mineralisation, denitrification) on the amount of nitrate reaching the *object* -though crucially relevant from a (eco)toxicological perspective- is beyond the scope of the flux-approach.

In the *source-path-object* route commonly used in environmental discussions the *source-approach* has become predominant in environmental legislation, as this matches best with the increasing legislative (moral) character of environmental issues.[178] Sources of potential and/or perceived environmental and human health risks are of prime concern within the cautious context. *Whether or not the path allows exposure of the object remains out of focus, clearly referring to the 'romantic' view that change is inappropriate*. Within the context of the *Nitrate Directive*, for instance, the *Final Opinion of the Expert Group* on the Dutch request for derogation recommends to the Netherlands and the *EC*:[179]

> 'To exclude peat soils, where N inputs increase inacceptable mineralisation rates and high N_2O emissions.'

N_2O emissions, however, are not a part of the *Nitrate Directive* but belong to the climate change issue. Whether or not that will prove to be relevant is not at stake here, not even considering the fact that for the most part denitrification will produce N_2 and not N_2O (except under very acidic conditions and when nitrite and nitrate concentrations are quite high and the supply of oxygen is not too low).[180] The greenhouse gas issue is, however, misleading here as nitrous oxide (N_2O) contributes little to global warming. On a molecular basis, N_2O has a much greater warming potential than does CO_2 (150 to 1 when CO_2 is set at 1), but its atmospheric concentration is miniscule in comparison.[181]

Indeed, reviewing the above-mentioned final opinion on the Dutch derogation request, the expert group reverts to typical cultural ecological criticism. A few examples from the document will illustrate this:[182]

> 'Moreover, relying on a strong denitrification both from soil and groundwaters to admit high N surpluses is not always and environmental-friendly and sustainable method, as it may significantly increase **N_2O emission for the part occurring at soil level** (greenhouse gas effect), and dissolution of pyrite in groundwaters (oxidised into **sulfate, which can provoke a polluting enrichment**).
>
> 'The **motivation of** the Nl derogation request is mainly **economical** …, rather than driven by technical and ecological reasons.'
>
> 'Further, a majority of members of the experts group … is **not convinced that the Minas** system, reliant only on a Nitrogen balance mechanism, will effectively and simultaneously:
>
> - Ensure a **quick reduction of grazing** for cattle, in farms where this is the preeminent way of fodder management. …
> - Avoid the use of **derogation** possibilities for **pig and poultry manure**, …'
>
> 'Wide ranging **field controls by public authorities** …, are enforced on commercial farmers who are granted derogation.'

No matter what kind of hydro-geochemistry is at work in relation to nitrate, the expert group finds fault with the derogation: either the greenhouse issue is raised or sulphate is regarded as a polluting agent as a result of pyrite oxidation by nitrate. The latter issue is interesting as sulphate is abundantly present in Dutch ground- and surface waters as a natural component. Sulphate concentrations in Dutch surface waters vary between detection-limit up to 1 000 mg SO_4^{2-}/l. In groundwater this variation is even larger: concentrations vary between detection-limit and 2 000 mg SO_4^{2-}/l.[183] Human toxicology is also not at stake here, despite the fact that drinking water quality regulations do include sulphate. The *WHO* recommendation of 150 mg SO_4^{2-}/l is solely based on the taste of water, which changes undesirably above 500 mg SO_4^{2-}/l.[184]

All things considered, the Nitrate Directive advances a moral imperative in the regulation of agricultural activities, separating moral from immoral economic activities. This moral imperative -as is shown by the above-cited quotations- goes hand in hand with a centralist view of upholding law and order.[185] In this, nitrate serves as a moral benchmark. Scientific data only serves the *Nitrate Directive* when it supports this implicit moral imperative. Selection of scientific data is the inevitable consequence of this, as I have shown in this study.

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- Nitraat en volksgezondheid: een Overzicht
- *Nitrate and Public Health: an Overview*
- Fosfaat in Nederland: een Nutriënt in Surplus
- Gewasbescherming: een Toxicologisch Perspectief
- *Emergence of a Debate: AGPs and Public Health*

- Normering en Risico in Wetenschappelijk Perspectief
- Risico's van Preventie: het Voorzorgprincipe Nader Bekeken
- *The Cautious Society? An Essay on the Rise of the Precautionary Culture*
- *From Cautious- to Risk Management of Chloramphenicol in Shrimp: an Introductory Food-Safety Position Paper*

Apart from the above mentioned reports scientific articles were published as well:

- Hanekamp, J.; Bast, A.; Schuiling, R.; Donze, M. *Nitraat Enkele Kanttekeningen. H_2O*, **1999**, *21*, 22-23.
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> 'Ecotoxicology is concerned with *protecting* ecological systems from adverse effects by synthetic chemicals. To do this it attempts to *anticipate* where these substances go in the environment [their *fate*] and what ecological effects they have when they get there.'

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[146] See note 2.
[147] Grübler, A. *Technology and Global Change*. **1998**, International Institute for Applied Systems Analysis Laxenburg, Austria, Cambridge University Press, p. 132.
[148] *Council Directive 91/676/EEC of 12 December 1991 concerning the protection of waters against pollution caused by nitrates from agricultural sources*, **1991**, 91/676/EEC.
[149] See note 23.
[150] See note 23.
A good example is the risk management of pesticides. Graham *et al.* describe the tradeoffs of the abolition of a certain type of pesticide as follows:

> 'When examining the risks and benefits of a pesticide, … revoking the registration of the pesticide will eliminate the associated risks to human health and the environment. However, this would be true only if no pesticide replaced the banned compound and the target pest spontaneously disappeared. In practice, either the pest flourishes, with associated damages to crops and potentially to humans; or a different pesticide or alternative pest-control method, with its own risks and benefits, is used in place of the banned product. Yet the current approach to pesticide regulation has not made it a practice to consider such countervailing risks or to weigh the relative risks of all likely pest control scenarios. …
>
> The use of substitute pesticides can cause countervailing risks in many ways. First, new health risks can occur if the substitute pesticide is itself potentially carcinogenic, or if it has the capacity to cause other adverse health effects …. Second, the pests do not just disappear when a pesticide is banned. The pest itself, if not adequately suppressed by the substitute pesticide, may be responsible for direct risks to human health …. Third, when a substitute pesticide is less effective at controlling the target pest, or acts against fewer pests at a time, farmers may respond by increasing the overall use of pesticidal products (or by selecting plant strains with higher levels of natural pesticides), with potentially adverse implications for human health and wildlife. Finally, restricting pesticides may generate indirect but important risks to the health of farm families and food consumers. If substitute pesticides are less effective or more expensive than the banned products, crop yields may be constrained and the prices of critical foods, especially fruits and vegetables, may rise significantly .... By curtailing the essential nutritional intake of lower-income families, increased food prices can cause health risks that potentially outweigh the health benefits of avoided exposure to pesticides residues.'

[151] Tengs, T.O.; Adams, M.E.; Pliskin, J.S.; Safran, D.G.; Siegel, J.E.; Weinstein, M.C.; Graham, J.D. *Five-Hundred Life-Saving Interventions and Their Cost-Effectiveness. Risk Analysis*, **1995**, *15-3*, 369-389. It is estimated that 60 000 American lives are lost as a result of misdirected environmental toxin control programs.

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152 Sapolsky, H. *The Politics of Risk. Daedalus*, **1990**, *119-4*, 83-96. That is one of the reasons why farmers are seldomly heard properly in policy-making as their numbers are small and therefore not truly relevant for politicians.
153 Sapolsky puts is as follows (note 152):

> 'Government policies add to the confusion of risk. There are contradictory statements about particular risks and inconsistent rankings among them. This is not because agencies lack the capacity to establish coherent programs. Each usually has a long-term policy agenda from which it would prefer not to deviate. Most are closely linked to a profession which has predictable norms and predictable goals. That policies are contradictory within and between jurisdictions, and that they may change as does the calendar, is due to our structure of government and the fact that the agencies are subject to political masters who must respond to public pressures in order to retain office.
>
> Convinced that they must appear willing to alleviate every product or environmental fear as it arises, officials make no effort to pursue consistent, carefully designed policies toward health risks. Whatever the scare of the day, officials stand ready to formulate quickly congressional testimony, briefing papers, news releases, and programs that demonstrate their unsurpassed commitment to protecting the public. Dare they hestitate, and an ambitious congressman armed with staff and a subcommittee will leap forward to take their place in front of the cameras.'

154 *Risk, Media and Stigma. Understanding Public Challenges to Modern Science and Technology*. Flynn, J.; Slovic, P.; Kunreuther, H. (eds.), **2001**, Earthscan Publications Ltd, London and Sterling VA.
The Perception of Risk. Slovic, P. (ed.), **2000**, Earthscan Publications Ltd, London and Sterling VA.
155 Tversky, A.; Kahneman, D. *Availability: A Heuristic for Judging Frequency and Probability. Cognitive Science*, **1973**, *5*, 207-232.
156 *Judgement under Uncertainty: Heuristics and Biases*. Kahneman, D.; Slovic, P.; Tversky, A. (eds.), **1982**, Cambridge University Press, New York.
157 Ames, B.; Gold, L.S. *Paracelsus to parascience: the environmental cancer distraction, Mutation Research*, **2000**, *447*, 3–13.
158 See my study on the Precautionary Principle: Hanekamp, J.C. *Risico's van Preventie: Het Voorzorgprincipe Nader Bekeken*, **2001**, *HAN*, Zoetermeer (*Risks of Prevention: The Precautionary Principle Scrutinised*).
See also note 1.
159 The inter-relatedness of environmental issues can be illustrated by the research done in the field of sustainable development. See e.g.: *Perspectives on Global Change. The TARGETS Approach*. Rotmans, J.; De Vries, B. (eds.), **1997**, Cambridge University Press, UK.
A historic view of environmental issues and its political and ideological backgrounds is delivered by Bramwell; note 36 and 43. See also note 39.
160 Wiener, J.B. *Precaution in a Multi-Risk World. Duke Law School Public Law and Legal Theory Working Paper Series*, **2001** working paper no. 23.
Wiener comments on the Hippocratic Oath 'Do No Harm' (ensure zero CR) as being too stringent as it will yield more net harm because of neglected TR. My contention of the Hippocratic Oath however is different as it seeks to do no harm both in relation to the TR and the CR. Indeed, medical intervention is always focussed on a certain target risk -e.g. infections, cancer, pregnancy and etceteras- which need to be dealt with *considering* any number of known side effects (countervailing risks; CR) -e.g. antibiotics resistance, nosocomial infections, cytostatic toxicity and etceteras- as a result of the chosen intervention.
161 See note 138. The commission of experts specifically underscored this issue in its analysis of the *RIVM* project.
162 For a fundamental critique of the radical relativistic standpoint see: Sokal, A.; Bricmont, J. *Intellectual Impostures. Postmodern philosophers' abuse of science*. **1998**, Profile Books.

[163] Gellner makes it clear that relativism in its logical consequence results in nihilism (Gellner, E. *Post-modernism, Reason and Religion*. **1992**, Routledge, London, UK, p. 49-50):

> 'The author [Clifford Geertz] is impatient with those who, in his view, misunderstand the situation. For instance, he pokes fun at Ian Jarvie's excellent summary of relativism -'all assessments are … relative to some standard … and standards derive from cultures'- notwithstanding the fact that Geertz himself at the end of the essay explicitly embraces relativism precisely in this form, and notwithstanding the fact that Jarvie's derivation of nihilism from this position is altogether lucid and cogent.
> Jarvie's simple and unanswerable point is that if all standards are an expression of culture (and cannot be anything else), then no sense whatever can be ascribed to criticizing cultures as a whole. No standards can then conceivably exist, in terms of which this could ever be done. If standards are inescapable expressions of culture, how could a culture be judged? …
> Relativism does entail nihilism: if standards are inherently and inescapably expressions of something called culture, and can be nothing else, then no culture can be subjected to a standard, because (*ex hypothesi*) there cannot be a trans-cultural standard which would stand in judgement over it. No argument could be simpler or more conclusive. …'

[164] See note 163, p. 95.
[165] Gellner, E. *Conditions of Liberty. Civil Society and its Rivals*. **1996**, Penguin Books, London, UK.
[166] See note 163, p. 84.
[167] Gellner regards relativism as a non-functional pre-Enlightenment approach of reality. Sokal and Bricmont show that relativism has little or no influence on the progress of scientific knowledge in the fields of e.g. physics despite its universal appeal. Moreover, relativism adds little to the scientific method and its efficacy. See note 162 and 163.
[168] Searle, J.R. *The Construction of Social Reality*. **1995**, The Free Press.
[169] This essay is reprinted in: Douglas M. *Risk and Blame*, **1992**, Routledge.
[170] See note 41.
[171] See note 1.
[172] See note 41, p. 5.
[173] See note 41, p. 6.
[174] Rip, A. *Risicocontroverses en verwevenheid van wetenschap en politiek*. In: *Kennis en methode*, **1992**, *16/1*, p. 63-80. [*Risk controversies and the intertwining of science and politics*.]
[175] In fact this is a classical sociological point. See for instance: Dahrendorf, R. *Class and Class Conflict in Industrial Society*, **1959**, Stanford University Press.
[176] Personal communication with Dr. S. Boehmer-Christianson.
[177] See note 41; italics added
[178] In the context of the nitrate issue the source is manure, the path is the (water-containing) soil matrix, and the object is ground- and surface water.
[179] *Grassland Fertisilisation Request for derogation under the 'Nitrates' directive presented by The Netherlands. Final Opinion of the Expert Group*. **2001**, Brussels, ENV.B.1/JD D(2001), p. 6.
[180] Brady, N.C.; Weil, R.R. *The Nature and Properties of Soils. (13th ed.)*, **2002**, Macmillan Publishing Company, New York.
[181] Paul, E.A.; Clarck, F.E. *Soil Microbiology and Biochemistry. (2nd ed.)*, **1996**, Academic Press, San Diego, London, Boston, New York, Sydney, Tokyo, Toronto.
[182] See note 179, p. 2, 3, 5, 7.
[183] See note 8.
[184] See note 8.
[185] Achterhuis, H. *De erfenis van de utopie*. **1998**, Ambo, Amsterdam. [*The legacy of utopia*.]
Hollander, P. *Political Pilgrims. Western Intellectuals in Search of the Good Society*. **1998**, Transaction Publications.