

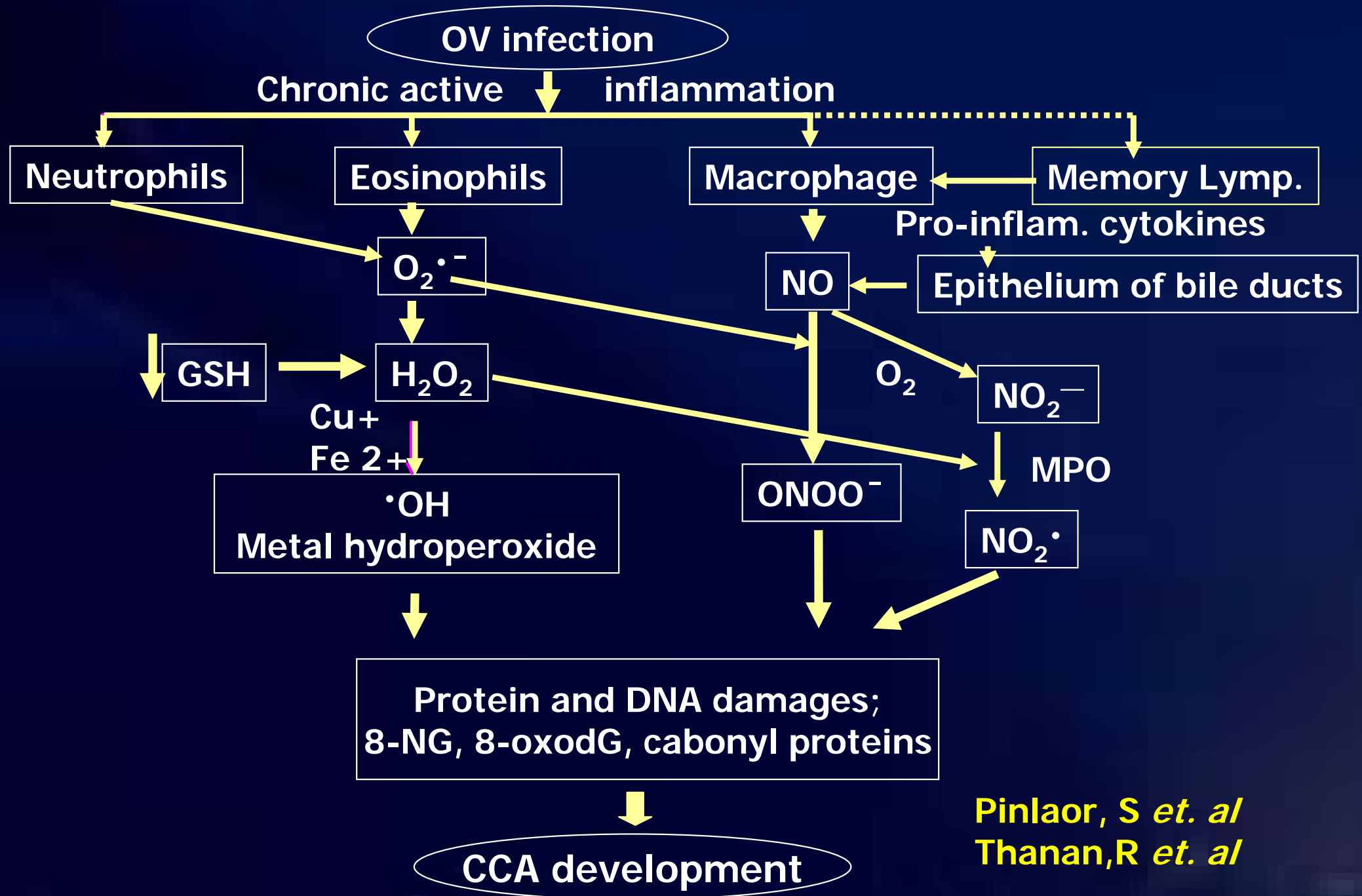


# **Accumulation of Lipid Peroxidation-Derived DNA Lesions in Opisthorchiasis-Associated Cholangiocarcinoma: The Possible Role of Vitamin E and Praziquantel in Chemoprevention**

**Puangrat Yongvanit, Ph.D.**

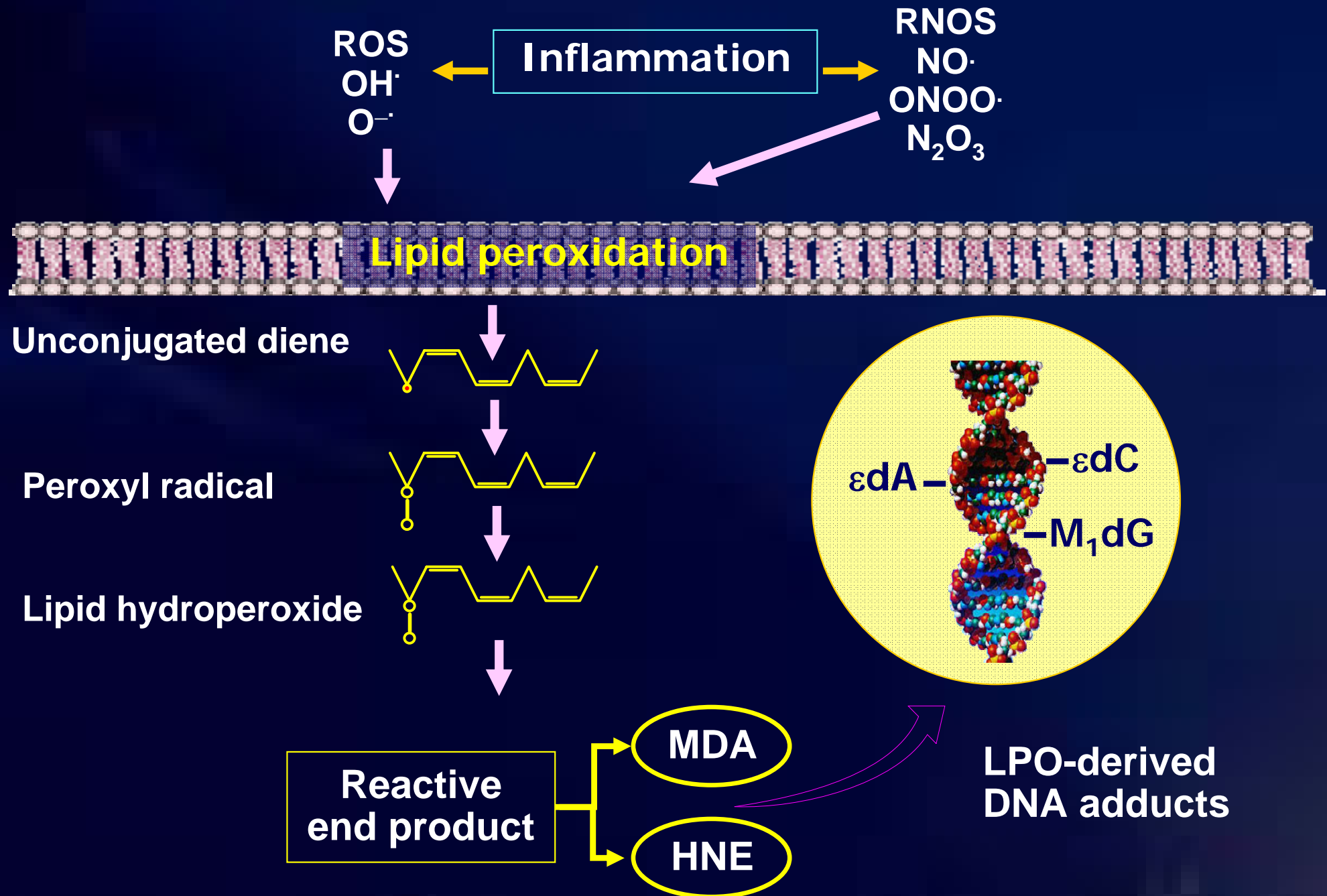
**Department of Biochemistry, Faculty of Medicine  
Liver Fluke and Cholangiocarcinoma Research Center  
Khon Kaen University**

# State of art in inflammation associated CCA



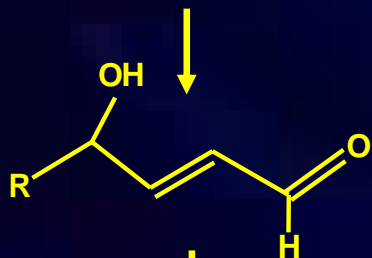
Pinlaor, S *et. al*  
Thanan, R *et. al*

# OV-infection also causes DNA lipid damage



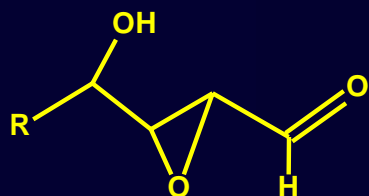
# Endogenous pathways of formation of $\epsilon$ -DNA adducts

Lipid peroxidation

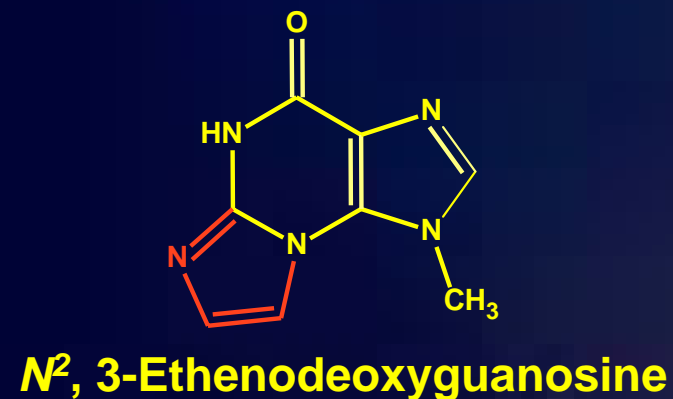
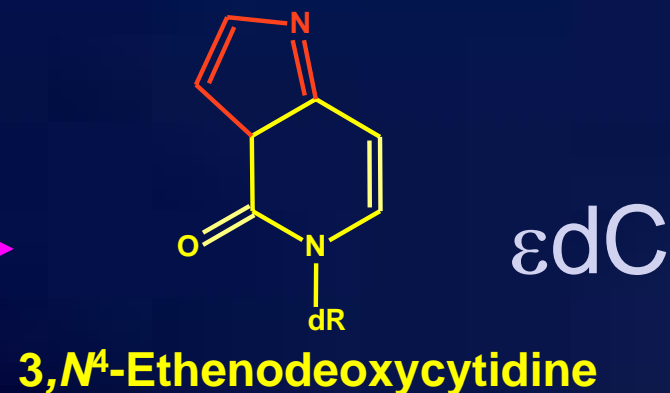
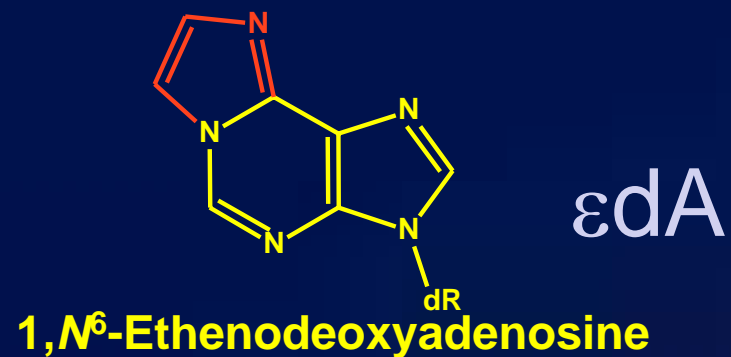


Hydroxy-alkenal (HNE)

$\text{Fe}^{2+}$ , Fatty acid  
hydroperoxides

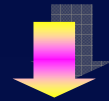


Epoxy-alkanal



## **Animal model**

**LPO-induced DNA damage may play a key role in cholangiocarcinogenesis**

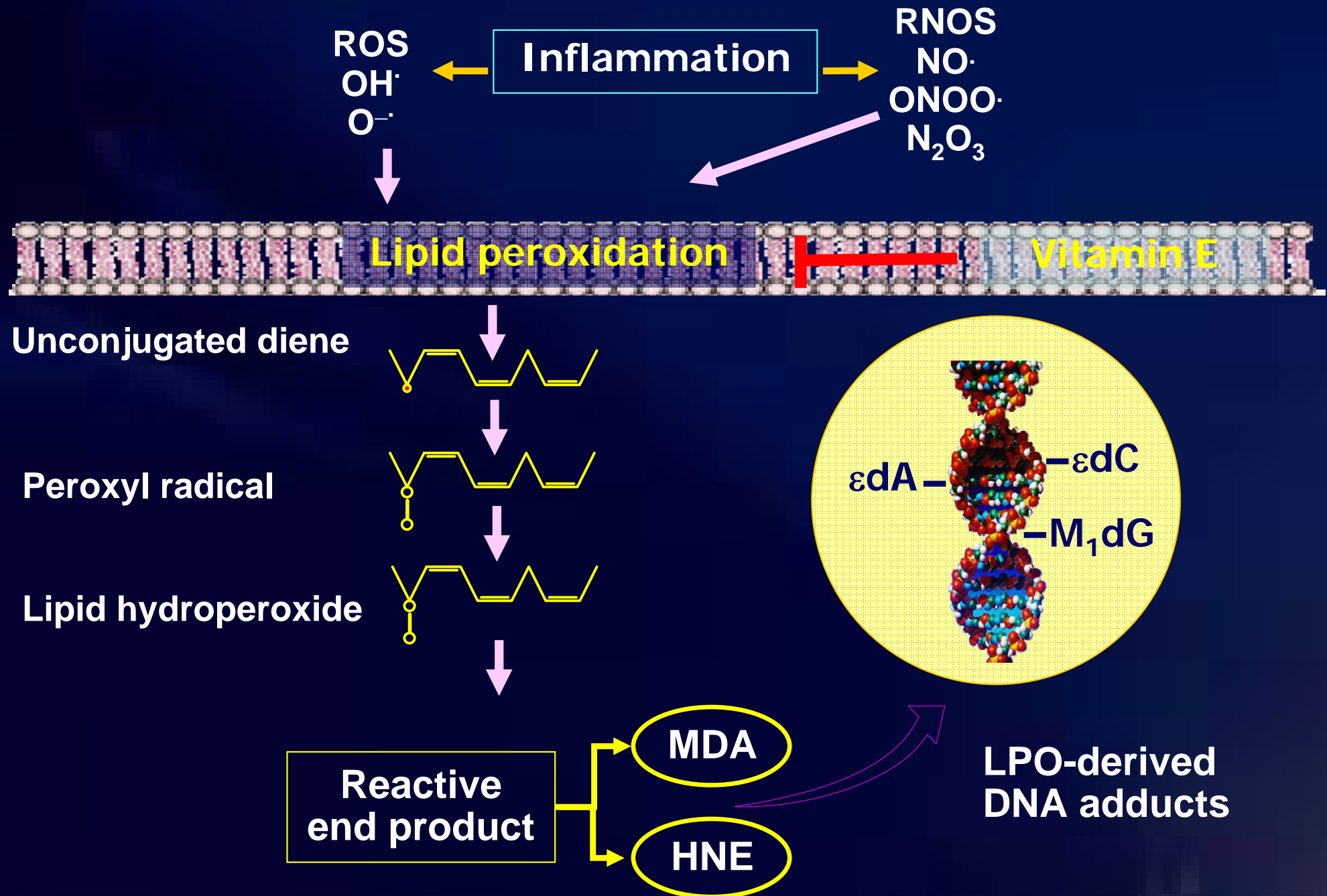


**Verify result in human model**

**Etheno-DNA adduct levels in liver-fluke infected patients**

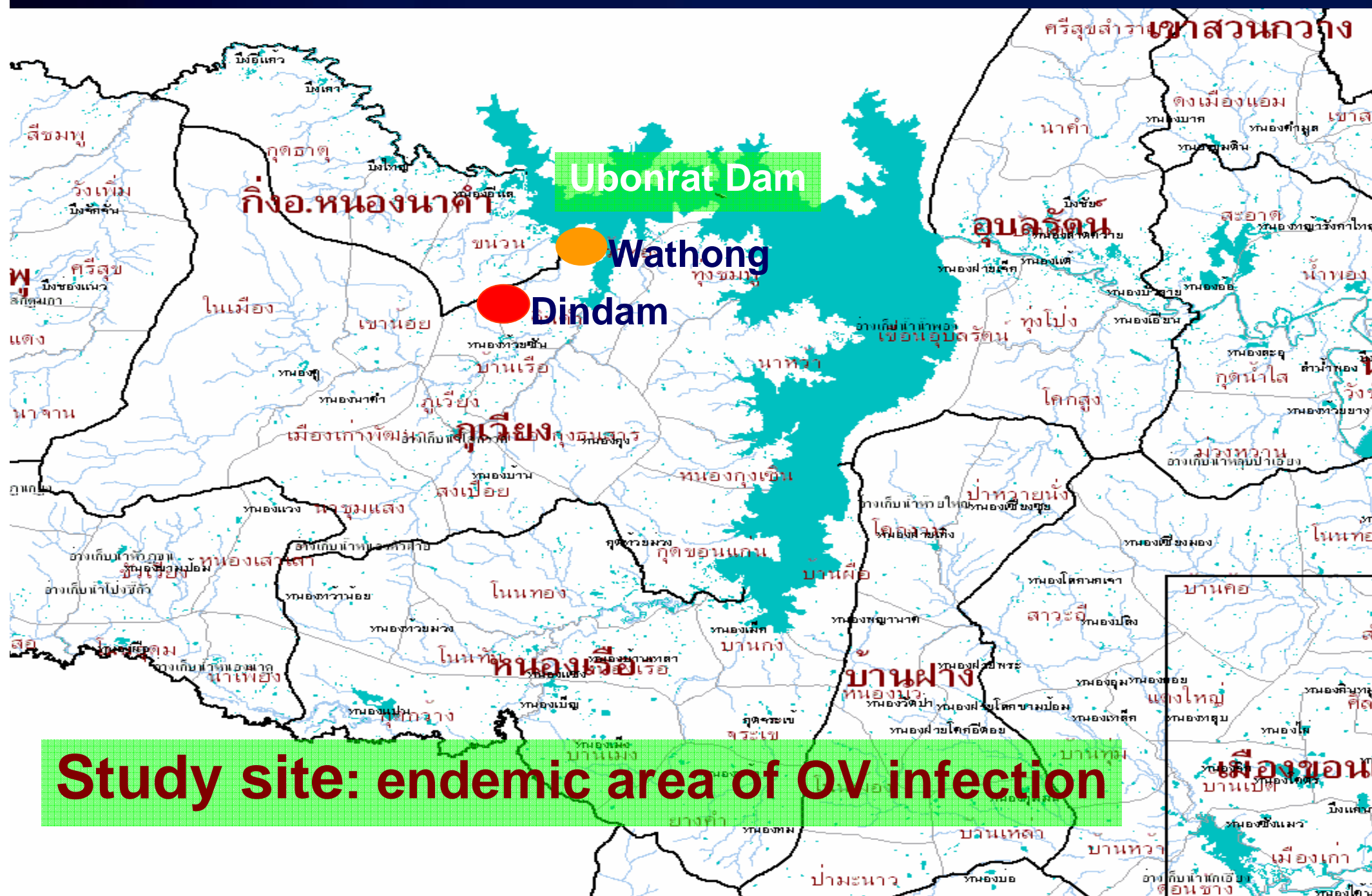
**Vitamin E, an antioxidant against lipid damage**

# OV-infection also causes DNA lipid damage





# Study site



# Endemic area of OV infection survey





# First visit at Univ. Hospital & Praziquantel Rx

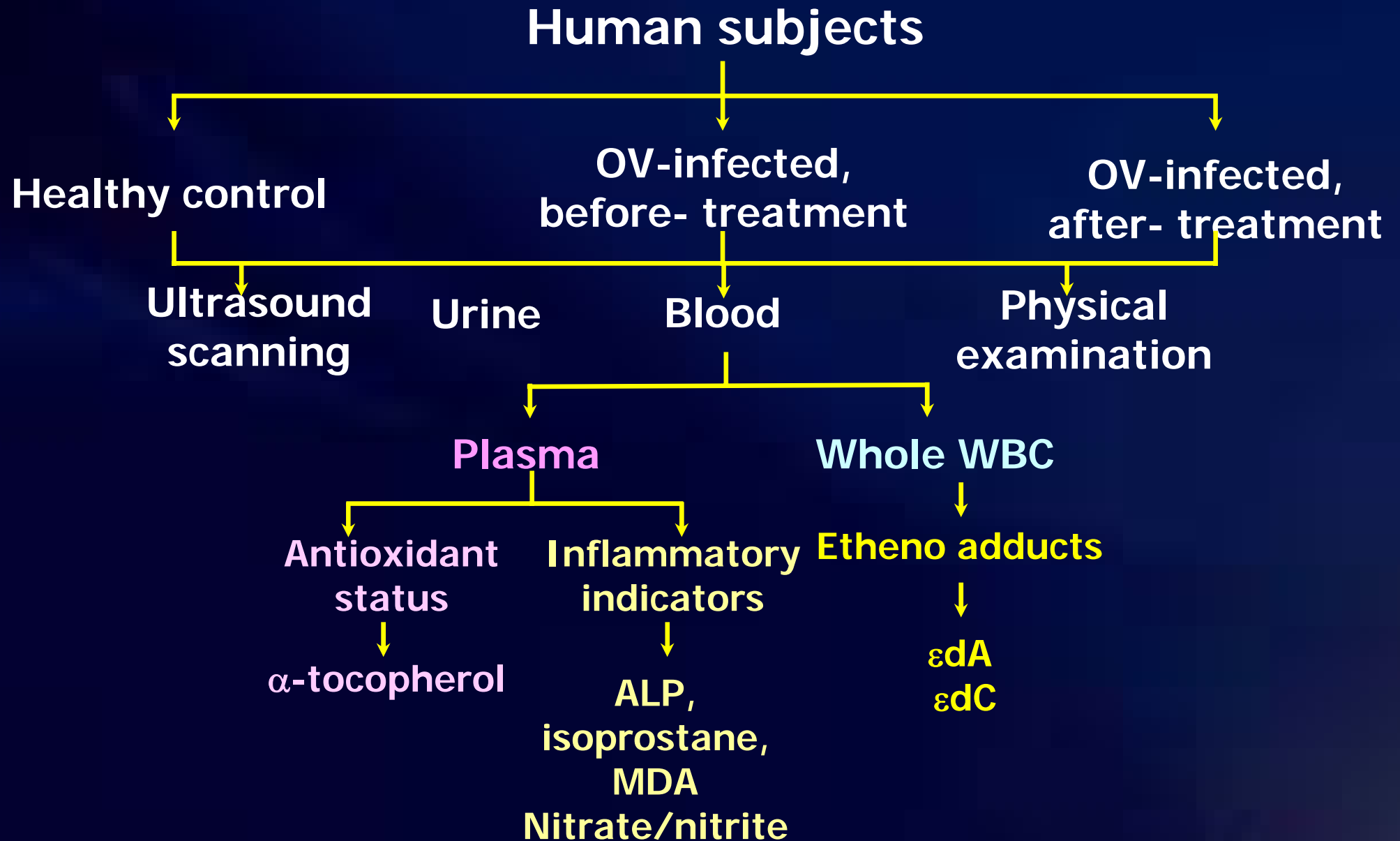




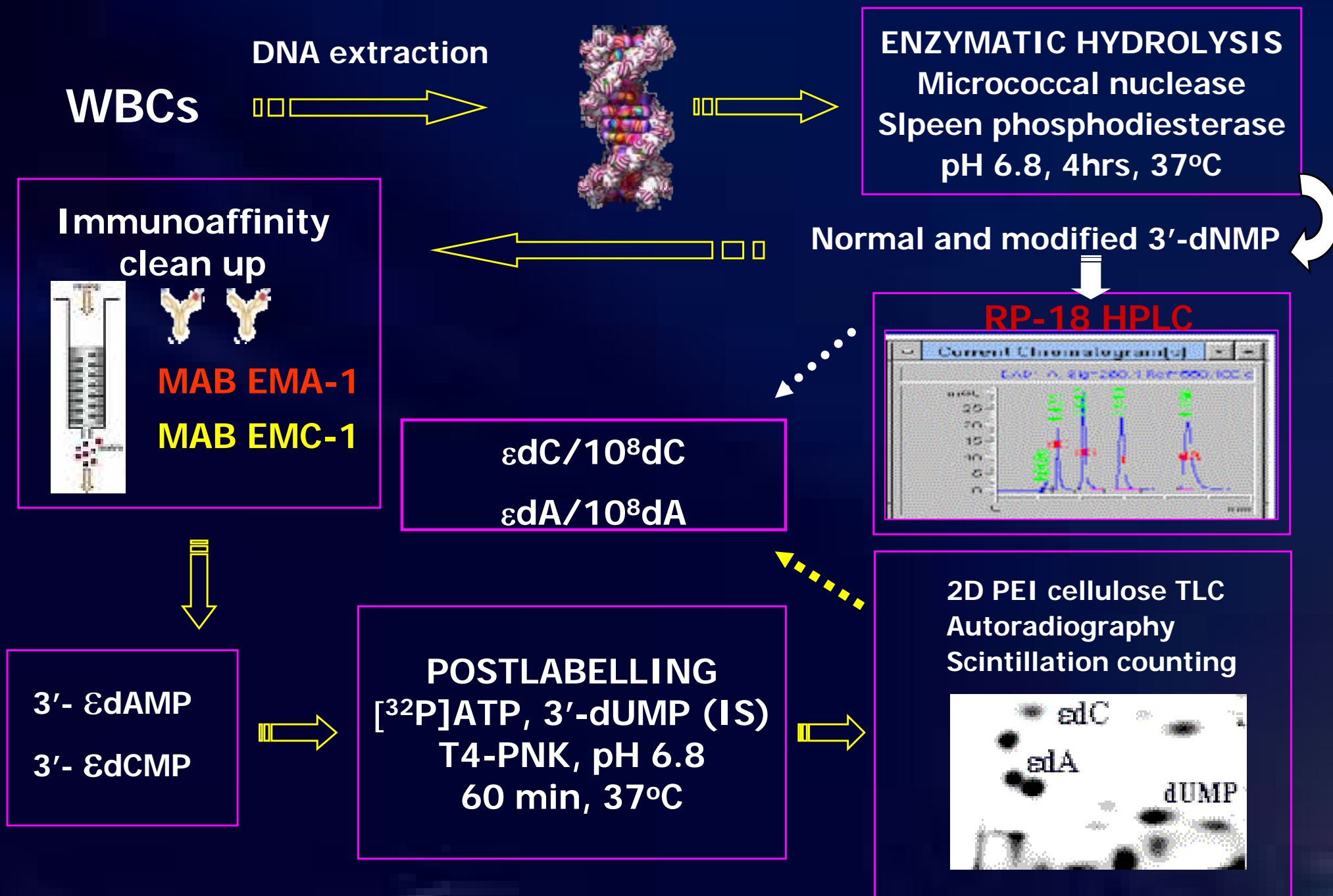
# Two-month followed up at Phuvieng study site



# Protocol of the study

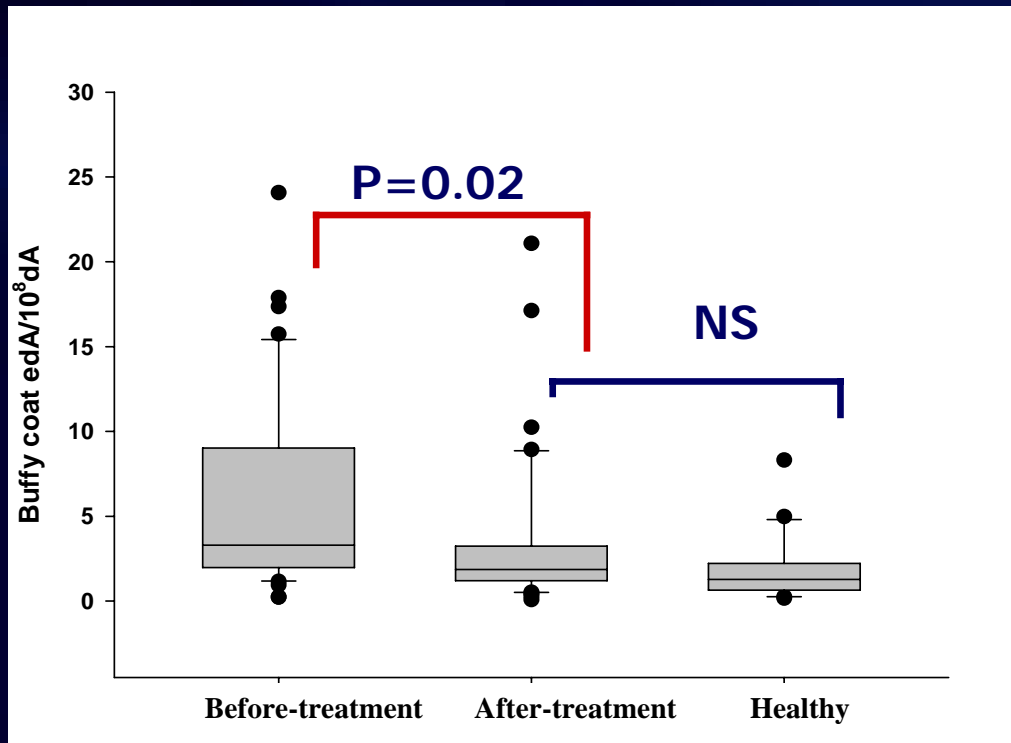


# Etheno-DNA adducts analysis in WBC

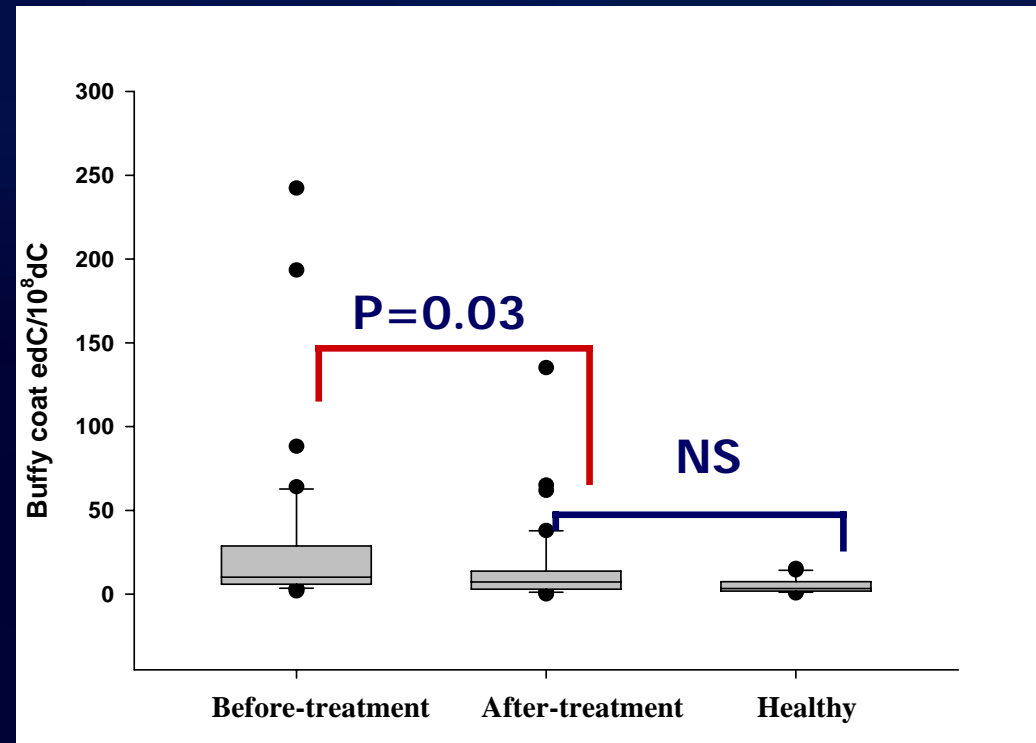


# Protection by Praziquantel against DNA damage

WBC  $\epsilon$ dA



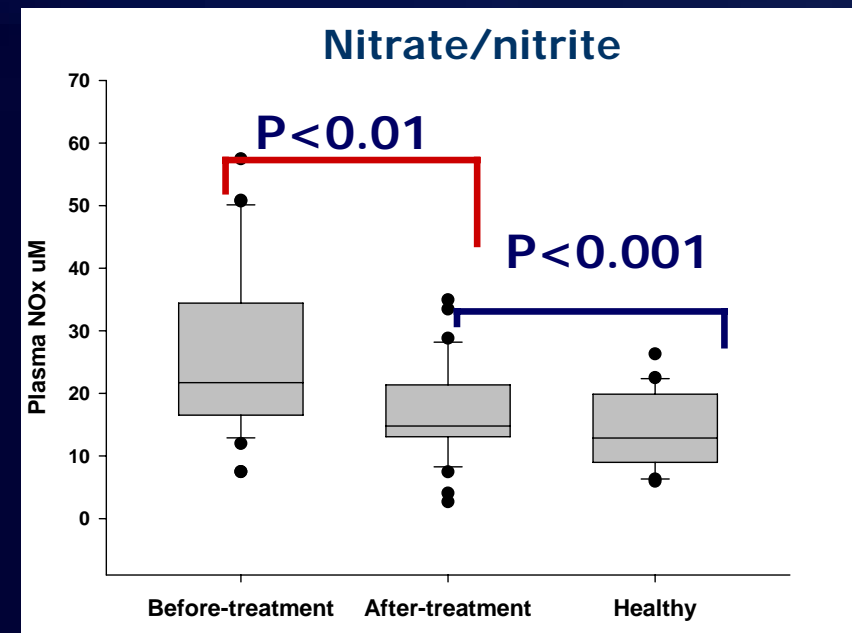
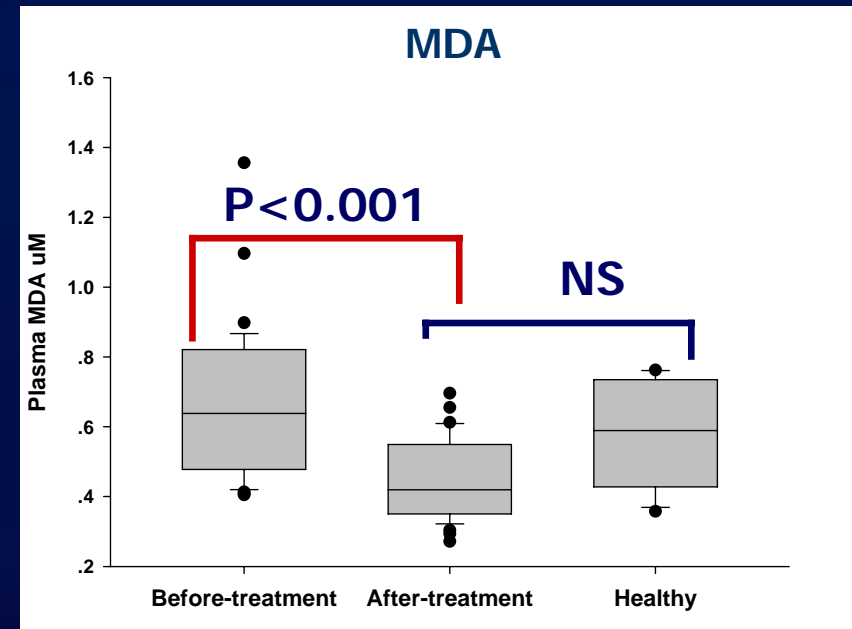
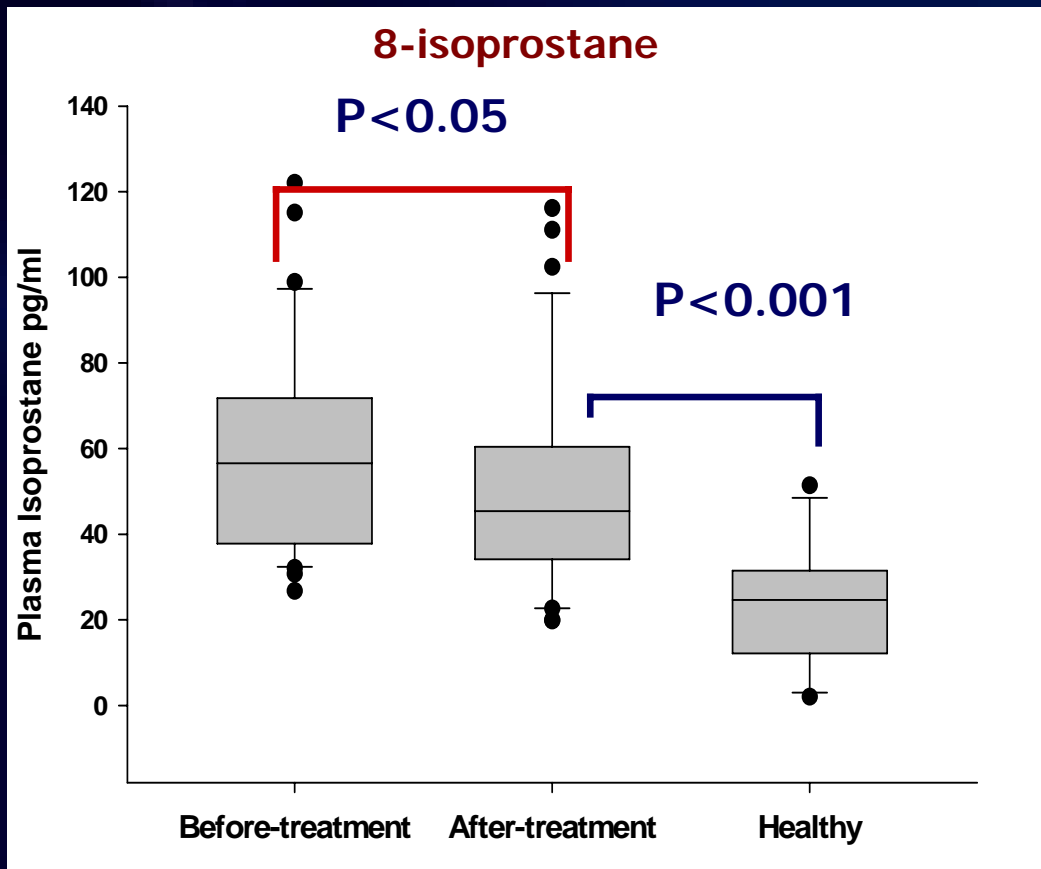
WBC  $\epsilon$ dC



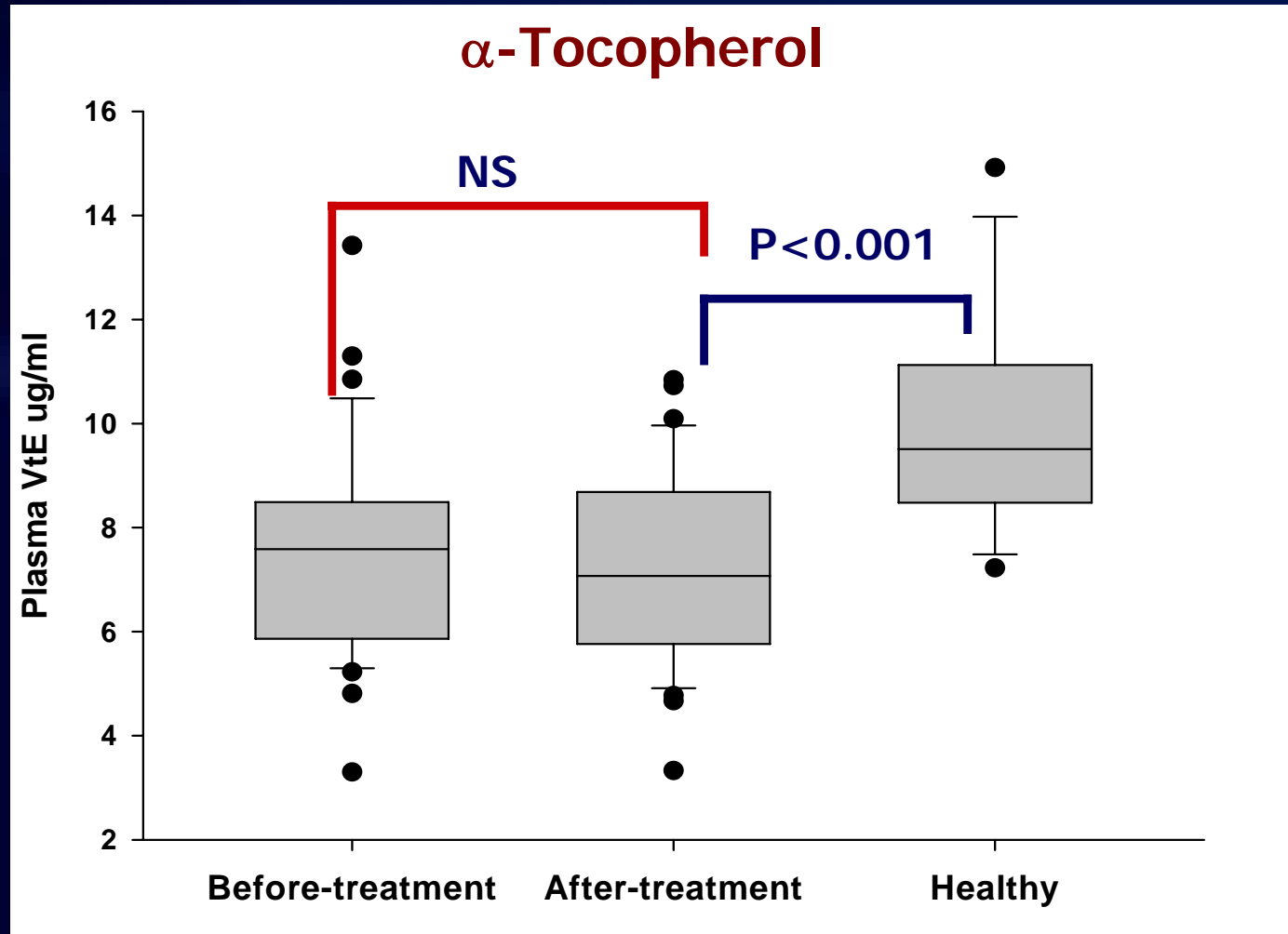
- Mann Whitney U Test
- Wilcoxon Signed Rank test



# Protection by Praziquantel against OV-induced inflammation



# An antioxidant status after praziquantel treatment



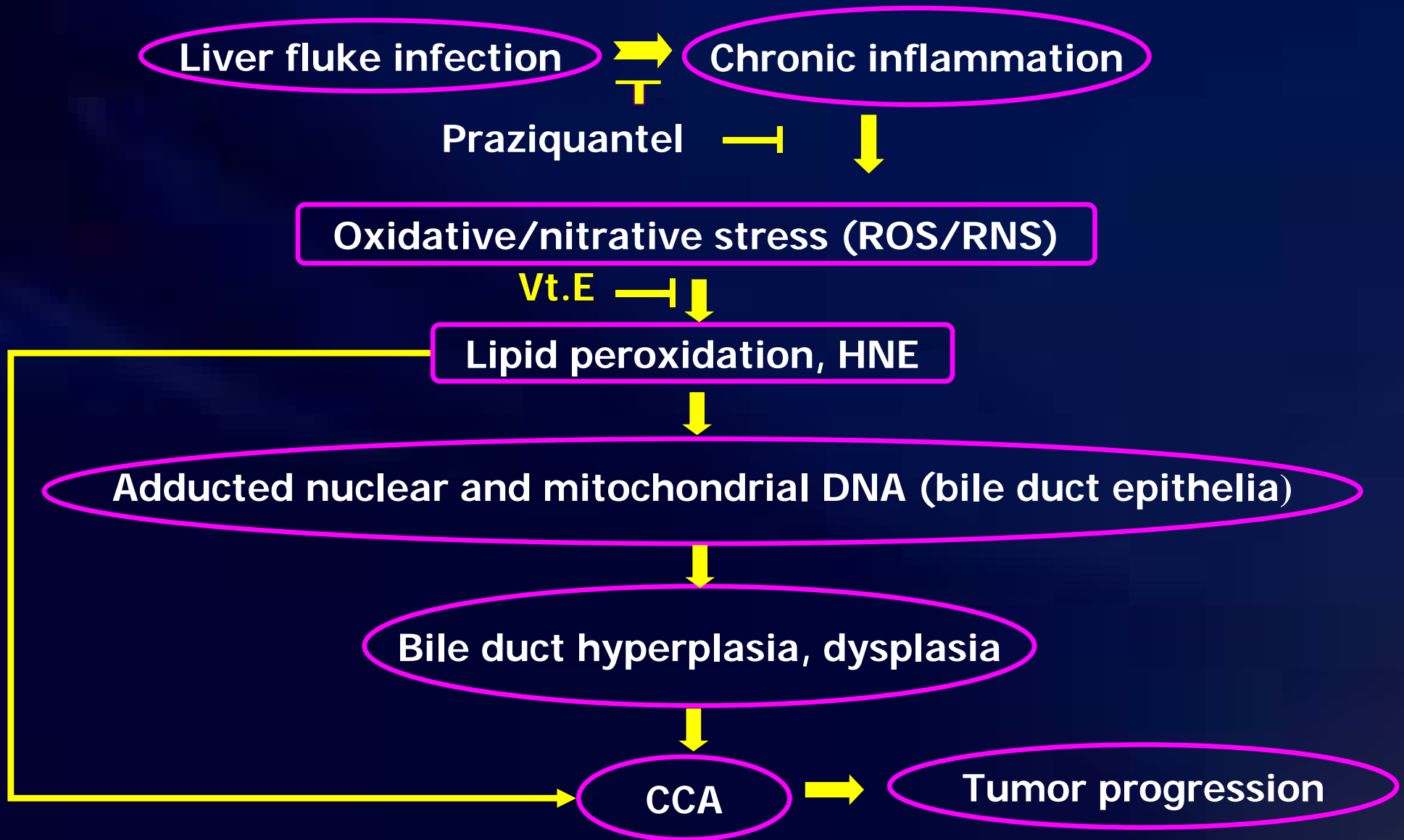
- Mann Whitney U Test
- Wilcoxon Signed Rank test

# The Spearman correlation of parameters

	$\alpha$ - tocopherol	8- isoprostane	MDA	Nitrate/ nitrite	ALP
$\varepsilon$ dA	-0.180 (0.105)	0.249 (0.032)	0.208 (0.048)	0.275 (0.008)	0.275 0.009
$\varepsilon$ dC	-0.218 (0.056)	0.233 (0.048)	0.204 (0.047)	0.149 (0.150)	0.346 (0.001)
$\alpha$ -tocopherol	1	-0.229 (0.058)	0.433 ( $<0.001$ )	-0.238 (0.032)	-0.238 0.038

$r^2$   
(P value)

# Conclusion



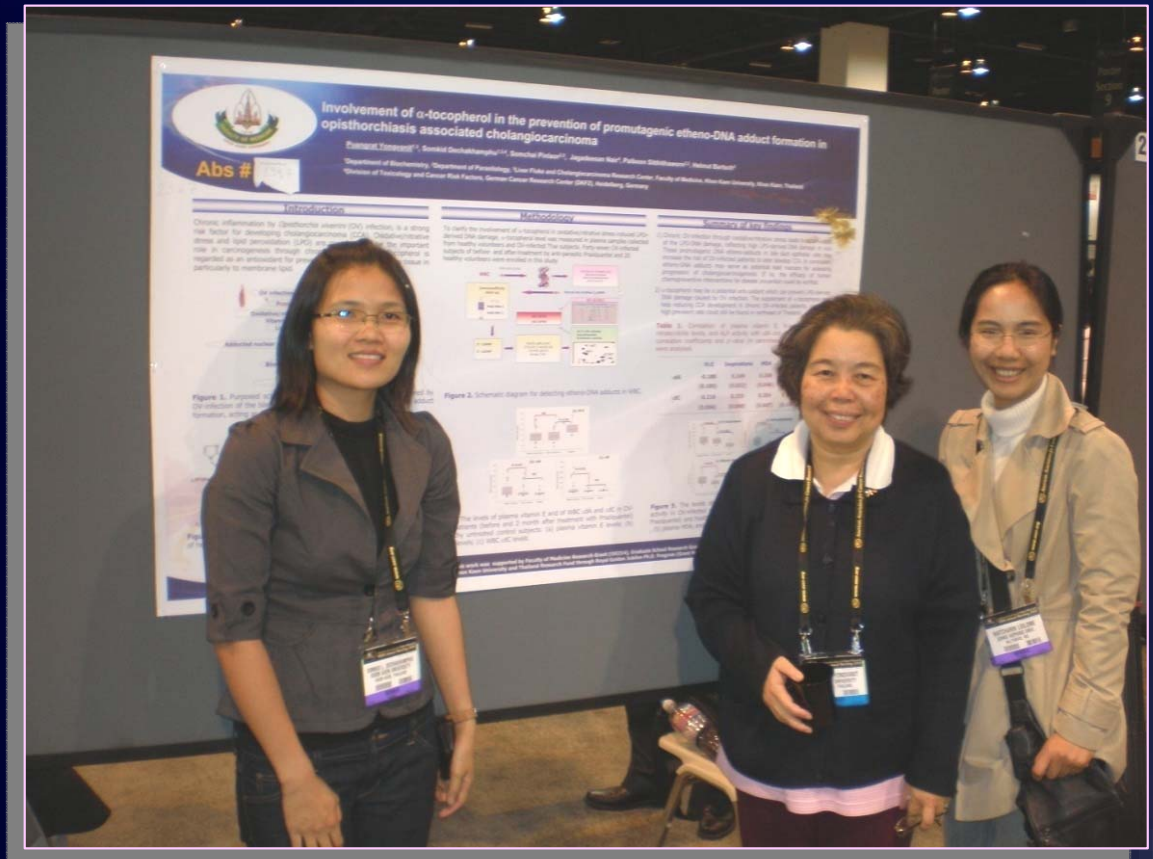
# Summary

- 1) Accumulation of inflammation-related oxidative- and LPO-induced DNA damage may play a key role in cholangiocarcinogenesis
- 2) Promutagenic DNA etheno-adducts in bile duct epithelial cells may increase the risk of OV-infected patients to later develop CCA
- 3) Praziquantel treatment & Vitamin E supplementation  
Can help reducing CCA development in chronic OV-Infected patients.



Dechakhamphu, S *et al.*  
Lipid peroxidation and etheno DNA adduct in  
white blood cells of liver fluke-infected patients :  
Protection by  $\alpha$ -tocopherol and praziquantel .  
In Press, *Cancer Epidemiol & Biomarker Prevent*,  
2010

100<sup>th</sup> AACR Annual Meeting  
Denver, 2009



# Acknowledgement

**dkfz.**

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**RGJ PhD program**

