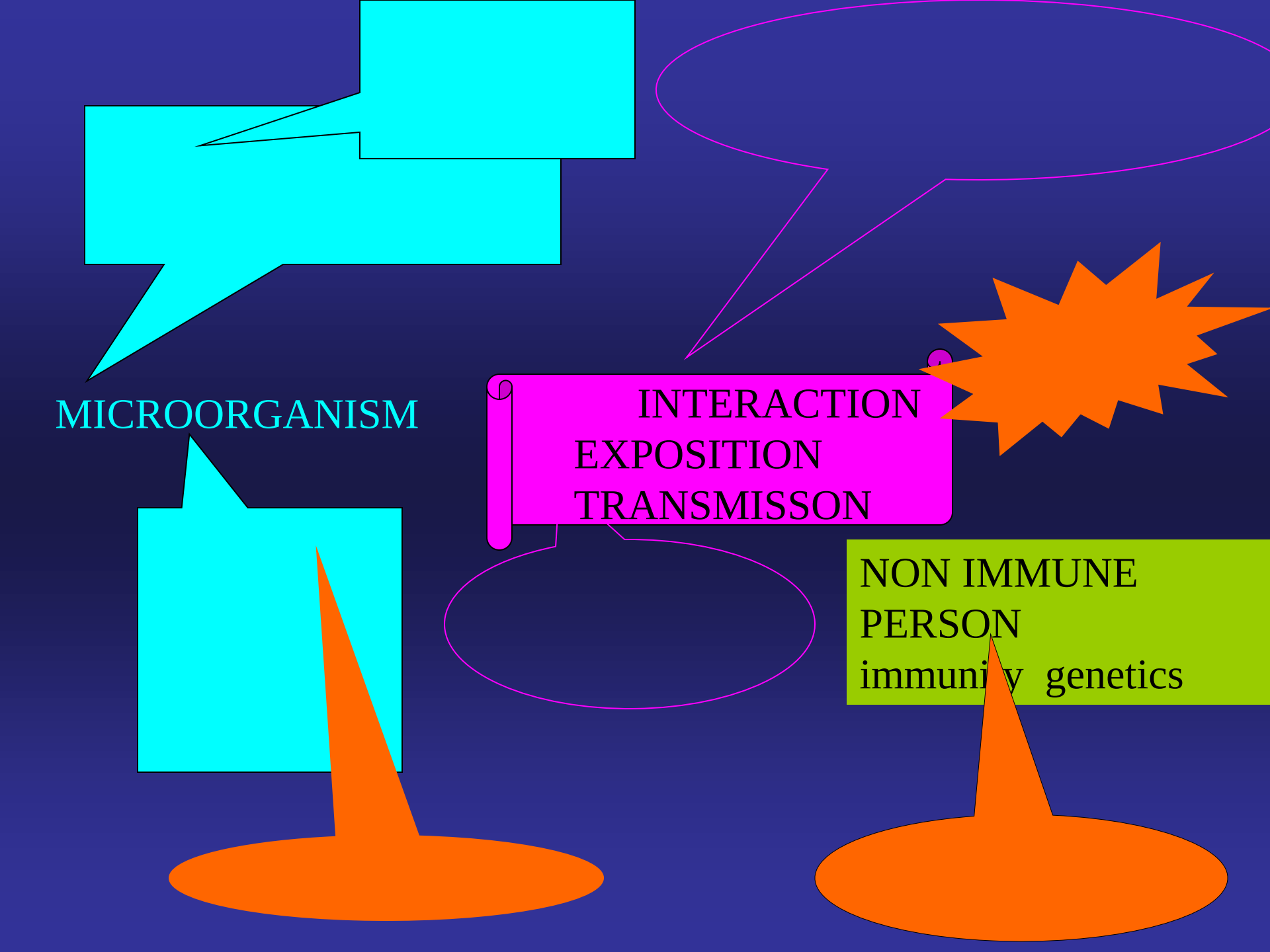
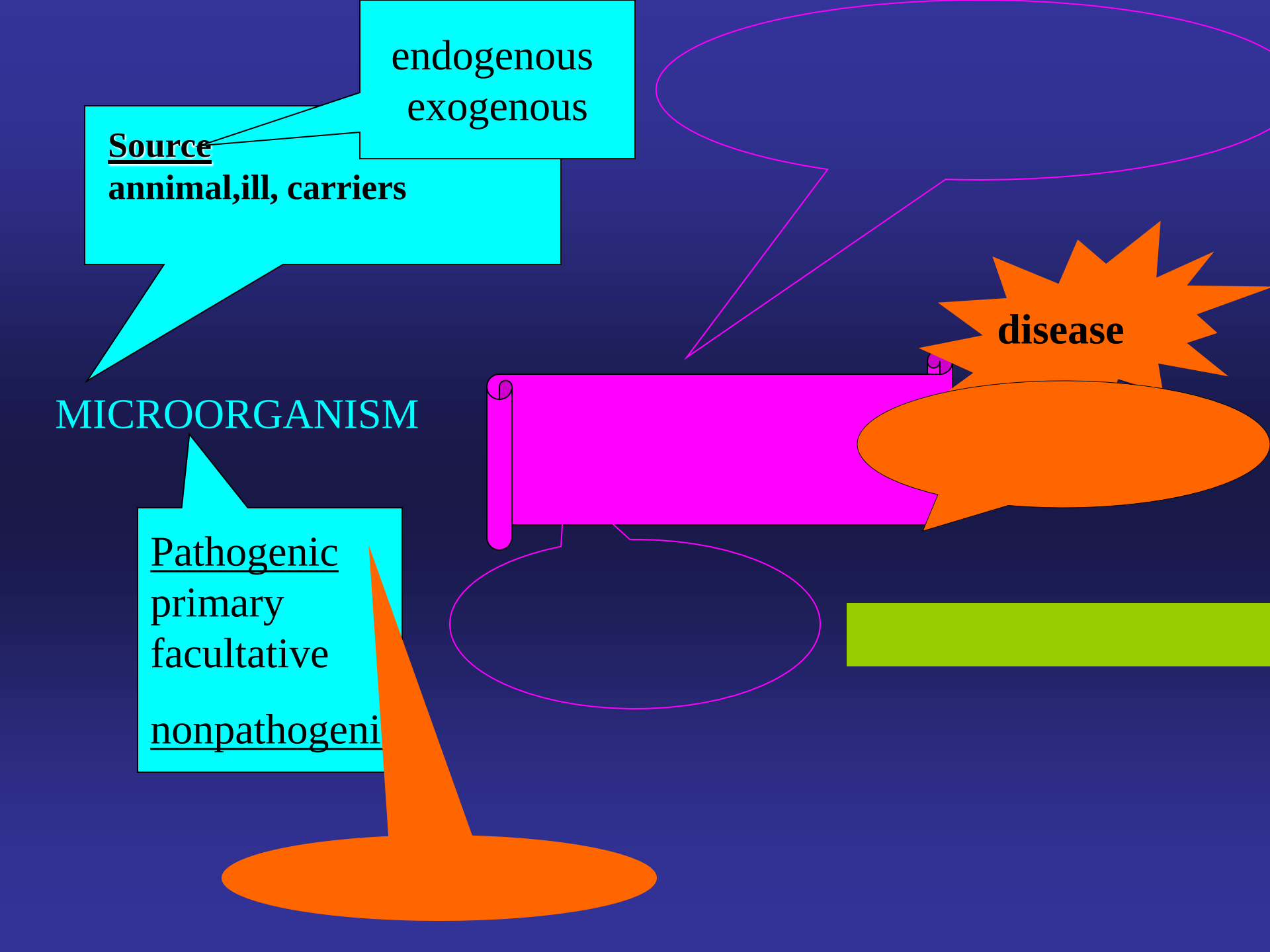
Patogenesis : process how the disease caused by microorganism starts (infection, intoxication, imunopathology)

- Microorganism
- Interaction
- Non immune person


MICROORGANISM
INTERACTION
EXPOSITION
TRANSMISSON
NON IMMUNE
PERSON
immuni y genetics

Patogenesis of microbial diseases

- multifactorial
- Influenced by
  - protective possibilities of host-immunity
  - pathogenity and virulence of microorganism
- Pathogenity – ability to cause the disease
- Virulence – quantitiy of pathogenicity, qualitative characteristic, determined by the infections dose


endogenous
exogenous
Source
annimal,ill, carriers
MICROORGANISM
disease
Pathogenic
primary
facultative
nonpathogeni

Pathogenesis

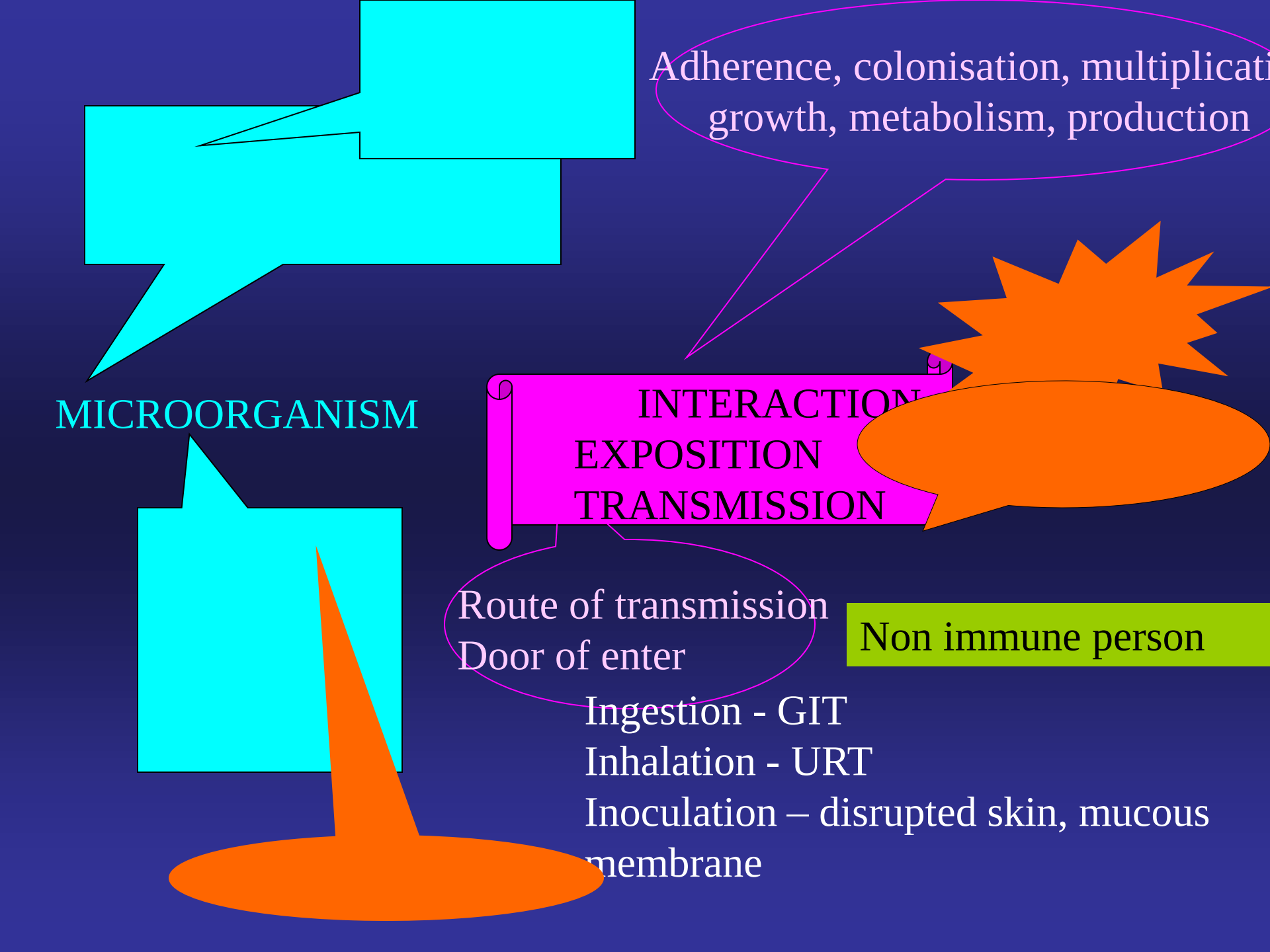
- Microorganism
  - source
  environment, annimal, ill, carrier
  exogenous , endogenous (microorganism of physiological flora)
  - pathogenic potential
  non pathogenic
  primary pathogenic
  facultatively pathogenic

Types of pathogens

- Facultative pathogens
  = not obligatory, oportunistic pathogens
  - in person with functional immunity the disease starts only very seldom. They cause the disease mostly when non specific immunity is commpromised.
  - frequently caused by IF. Low virulent.
- Non pathogenic - genetically not prepared to cause the disease in human
- Primary pathogenic
  - highly virulent
  - cause the disease in immunologically competent persons and if specific immunity is not present
  - influenced by the infectious doses and appropriate way of enter

Exposition and transmission
microorganism must enter in contact wiht macroorganism

- Endogenous microorganism – arising from FMF, if dysmicrobia or by transfer of IF to places that are not its fysiological place or are normally sterile
- Exogenous microorganism
  - route of transmission and the door of enter
  ingestion, inhalation, inoculation - typical
  - infectious dose, innoculum - (*200 bacteria Schigella sp., 10^8 Vibrio cholerae)*


Adherence, colonisation, multiplicati
growth, metabolism, production
MICROORGANISM
INTERACTION
EXPOSITION
TRANSMISSION
Route of transmission
Door of enter
Non immune person
Ingestion - GIT
Inhalation - URT
Inoculation – disrupted skin, mucous membrane

- Interaction -
  - not successful,
  - colonicsation
  - infection -disease,
  - recovery/death
-

  *exposition

  – conditions to meet the microorganism
  - route of transmission and door of enter

- Phases of diseases
  - adherence,
  - colonisation,
  - multiplication, growth, struggle for nutrion factors,
  - metabolism – production of toxins , tissue damage
  - spread to the organism – superficial,
    mucous,
    invasive,
  - reaction of organism
    – immunity or immunopathology

Sequelae for host

- 1) not infection – microorganism has no tool to start the infection
- 2) colonisation – microorganism is established on the surface on mucous membrane but – no infection
- 3) inaparent disease – host is not clinicall ill, reaction is detectable on the level of immunity
- 4) clinical infection – apparent disease
  - acute - (subacute, peracute), - chronic, persistent….
- 5) recovery and immunity
- 6) Death l- as the result of tissue damage caused by infection, immunity reaction, non infectious sequelae (poststreptococcal GNF), underlying diseases

Brána vstupu mikroorganizmov

- Ingestion – mouth stool transfe *Salmonella, Shigella, Yersinia enterocolitica, ETEC, Vibrio, Campylobacter, Clostridium botulinum, Bacillus cereus, Listeria, Brucella, Giardia, Entamoeba histolytica, cestodes, Enterovíruy, poliovírus, VHA, VHE*
- Inhalation – flying infectious dust – size of droplettes *Mycobacterium, Nocardia, Mycoplasma pneumoniae, Legionella, Bordetella, Chlamydia psittaci, pneumoniae, Histoplasma, Blastomyces, Coccidioides, Cryptococcus, RSV, orthomyxovírusy, Paramyxovírusy, VZV, HSV,*
- Inoculation - injury - *Clostridium tetani,*
  - injcetion - *VHB,HIV,VHC, Staf.aureus,*
  - insect *Borrelia, rickettsia, Yersinia,*
  - transplacentarly *Treponema pallidum, toxoplasma, rubeolla virus, CMV*
- Direct contact – contact of ill mucous membrane or skin with healthy mucous membrane and skin – sexually transmissible diseases *Neisseria gonorrhoe, Chlamydia trachomatis, HIV, Treponema pallidum*

Colonisation – adherence and replication

- adherence - made possible via adhesins at the surface of microobe that react with glykoprotein receptors at the surface of host cells
- Different kinds of adhesins are present in different kind of diseases (fimbrie)
- Adherence is responsible for strong reaction and resistence to peristaltic, urine stream, cough, sneezing, centripetal movement of cilliae

Mechanism of adherence

- St. aureus---*lipoteichoic acid*---?
- E.coli -------*P fimbriae*---------glycolipid
- Treponema pallidum---*P1,P2,P3*-----fibronectin
- Orthomyxovírusy---*hemaglutinin*---sialic acid
- HIV----------*gp120*---------CD4 T lymfocytes

Penetration and spread

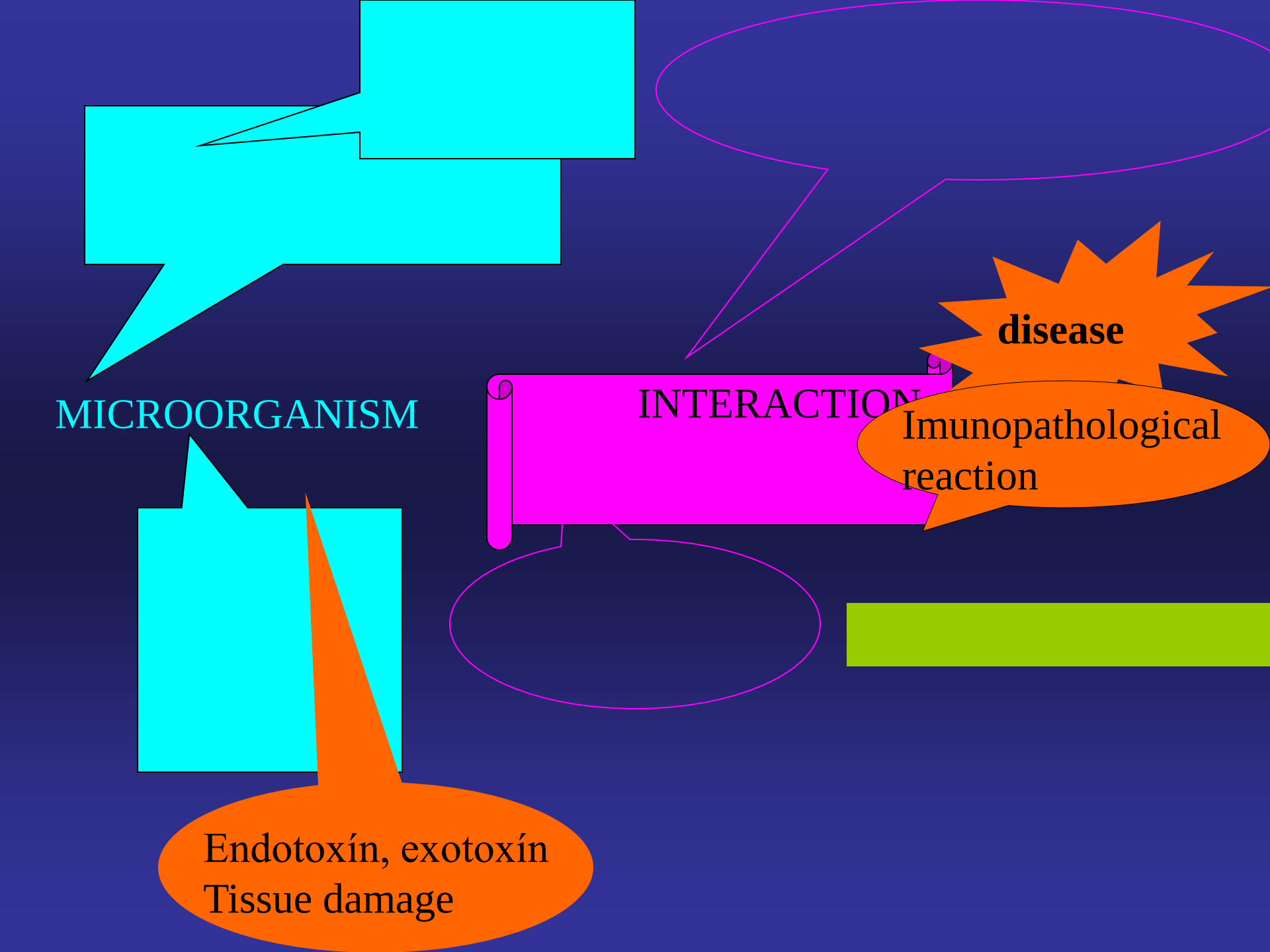
- Superfitial *(Vibrio cholerae, rhinovírusy - local infection, toxin production)*
- Penetratin to the cell, cell damage *(Shigella - ulceration)*
- Invasivity, spread via blood, lymfa or nerves *(Salmonella typhi – generalised infection)*

Surviving of the microbes in the host

- Appropriate place – tissue predilection – specific receptors, aviablility of growth factors
- Interaction of factors of virulence of microbe and immunity of host
- Degradation enzymes (hyaluronidase, nuclease, colagenase, elastase)
- Surviving of tools of immunity (fagocytosis – surviving in the fagosomes, releasing from it resistance to degradation ensymes)

How microorganism can survive immunity of the host

- Capsule – antifagocytic properties, antigenic mimicry – common type of antigens (*Str.pyogenes, Str.pneumoniae)*
- Antigenic changes - shift,drift (*V.influenzae)*
- Intracellular localisation (*Brucella)* – *must be able to survive the degradation in fagolysosomes - lysis of vesicles, they interfer with fusion of falgosome with lysosomes,*
- IgA protease against IgA antibodies (*H.influenzae*)
- Enzymes degradating fagocyting cells *(streptolyzín, alfa toxín Cl.perfringens)*


MICROORGANISM
INTERACTION
disease
Imunopathological reaction
Endotoxín, exotoxín
Tissue damage

Tissue damage

- Toxin - endotoxin, exotoxin
- Processes of specific immunity - imunopathogenicity
  – exhausted immunity - alergy
  - poorly degradable antigens – long persistence,
  - cross reacting antigens - autoimmunity

Toxins

- Endotoxin – lipopolysaccharide in cell wall of *G negative bacteria*.
  Lipid A – biological properties – Effects depends on the dosis. Clinically expressed after the cell disruption of the cell wall of G-bacteria (ATB) – fever, hypotension, Waterhause Friderichsen shock,
- Exotoxins -
  - ensymatic (*St. aureus - hyaluronidase)*
  - AB toxinsy (*difteric, tetanick cholera toxin)*
  - membranes degrading enzymes (*St.aureus delta)*

Lipopolysaccharide -endotoxin

- lipid A - intracelular part - hydrofobic - endotoxic activity –
  -high levels produces - shock and cardiovascular colaps,
  -low levels – activation of complement, inflamation mediators, TNF, IL-1,prostaglandís, is toxic to fibroblasts pyrogenic properties, resistence to phagocytosis,
- core - polysaccharide
- hydrofil O antigen – external part
- Termostability, released at the lysis of G-bacterium

AB toxins

- Consisting of 2 parts
  - B Binding part to the surface of host cell
  - A active part introduced to the cell membrane or cytoplasma, has biological properties
- 3 types
  - ADP ribosyl exotoxins (difteric choleratoxin)
  - 28S rRNA (Shiga toxin)
  - not complete (*B. antracis, botulotoxin, tetanospazmin)*

Biological properties of exotoxins

- Protein properties - antigenic – imunne systemes produces antitoxins aganist them (neutralising propertis)
  denaturable by physical a chemical ways that change them to anatoxin (is antigenic and not toxic)
- Tissue tropism
- Dose independent – cut off concentration will cause characteristic spectrum – clinical signs

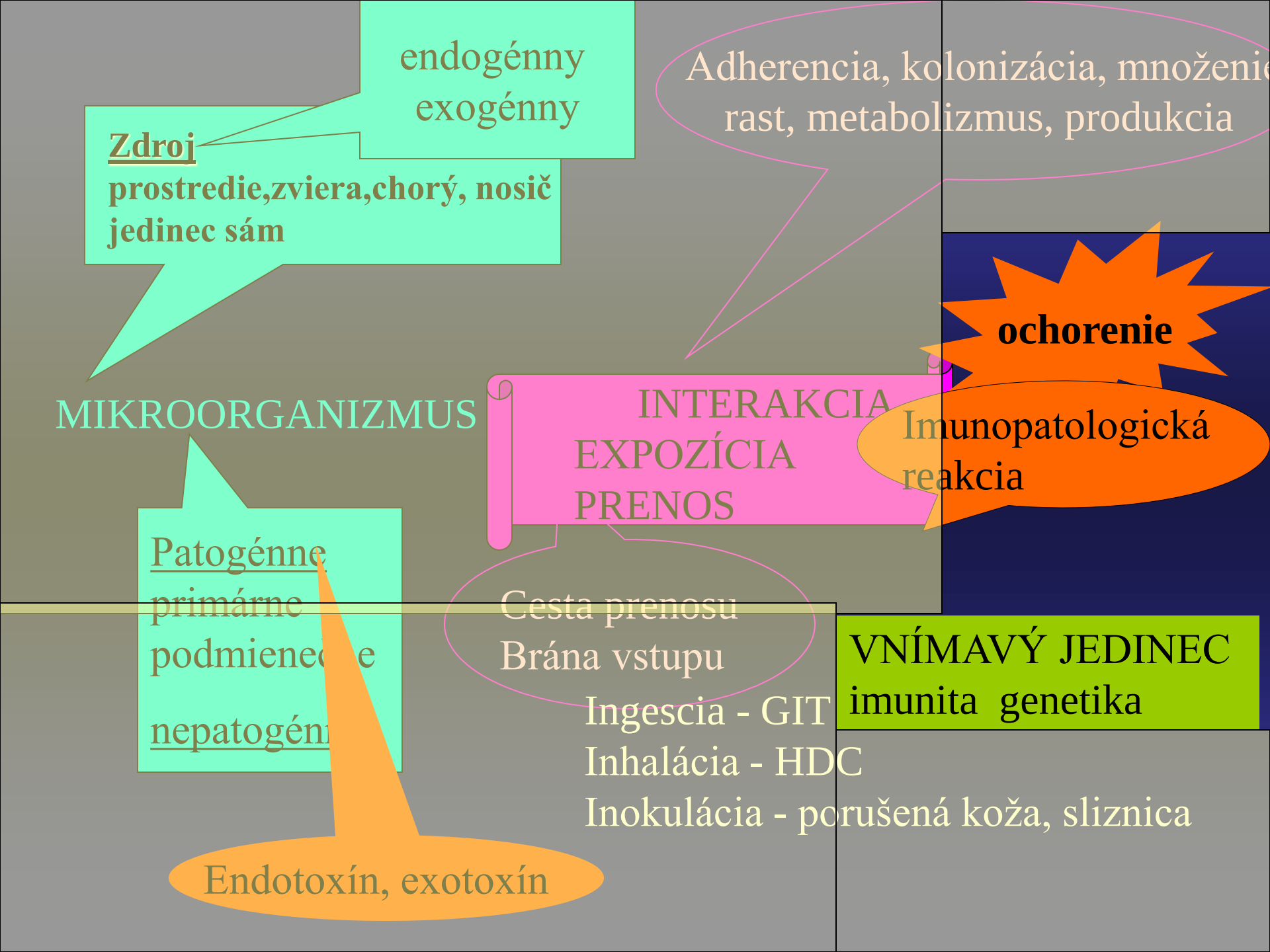
Exotoxins of ensymatic property

Ensymatically dissolving phospholipids or proteins of membranes or work as detergents

Fosfolipase C. perfringens – *disrupting cell membrane and blood cells that enable inflamatory cells gain the place of infection and help to produce anaerobic condition*

Extracelular toxins – ensymatic properties- cytolytic

- Proteases, kolagenase, hyaluronidase. Enable spread of bacteria. Effect is dose dependent
- *Cl. perfringens - kolagenase*
  Staphylococcus aureus - hyaluronidase, exfoliatin,


endogénny
exogénny
Zdroj
prostredie,zviera,chorý, nosič
jedinec sám
Adherencia, kolonizácia, množenie
rast, metabolizmus, produkcia
ochorenie
MIKROORGANIZMUS
INTERAKCIA
EXPOZÍCIA
PRENOS
Imunopatologická
reakcia
Patogénne
primárne
podmienec e
nepatogén
Cesta prenosu
Brána vstupu
Ingescia - GIT
Inhalácia - HDC
Inokulácia - porušená koža, sliznica
VNÍMAVÝ JEDINEC
imunita genetika
Endotoxín, exotoxín