

# Challenging Paediatric Brain Tumours

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# Overview

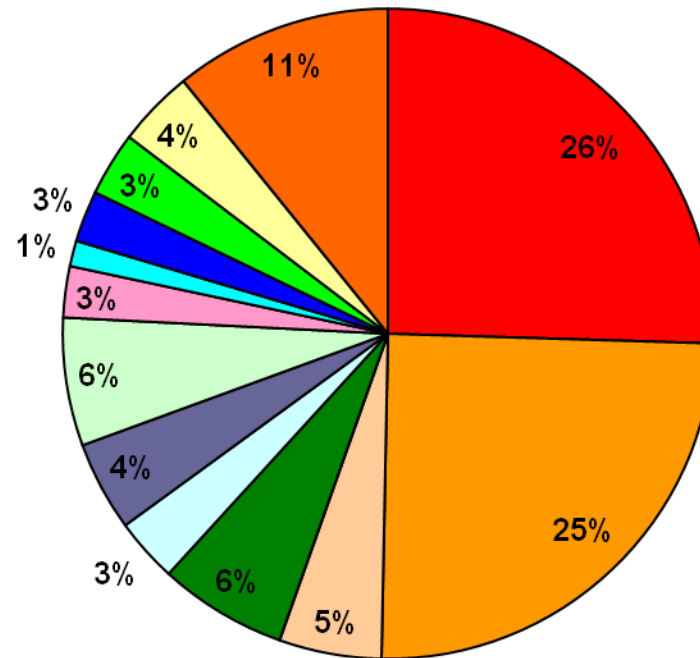
- (i) Paediatric malignancy
- (ii) Central nervous system tumours
- (iii) Diffuse Intrinsic Pontine Glioma

## (i) Paediatric malignancy

- ~1/500 children <16 years will develop a malignancy
- ~200 new cases/year in ROI
- A.L.L most common diagnosis
- CNS tumours most common solid malignancy of childhood

# 3.12 Malignant Haematology and Oncology main cancer primary groups in 2016

- Acute Lymphoblastic Leukaemia
- CNS (incl. Brain Tumours)
- Myeloid Malignancies
- Hodgkin's Lymphoma
- Non Hodgkin's Lymphoma
- Neuroblastoma
- Wilms' Tumour (incl. ERWT)
- Rhabdomyosarcoma
- Ewing's Sarcoma or ES/PNET
- Langerhans cell histiocytosis
- Osteosarcoma
- Germ Cell
- Other



## (ii) CNS tumour challenges (1)

- “Delay” in diagnosis
- Overlap with more common childhood illnesses
- Variety of presenting symptoms and signs
- Perceived as rare
- May result in:
- Lack of faith in medical profession
  
- (Headsmart initiative)

# CNS tumour challenges (2)

- Location
- Eloquent areas of brain, not always amenable to surgery
- Irreversible damage before treatment

# CNS tumour challenges (3)



Blood Brain Barrier  
protects:

- (i) from potentially damaging substances
- (ii) from hormones and transmitters
- (iii) Constant milieu
- (iv) NB: Area postrema / posterior pituitary etc)

Hey! We want in!



I'm sorry, but you are too highly charged, too large and not lipid soluble. You cannot enter the brain!

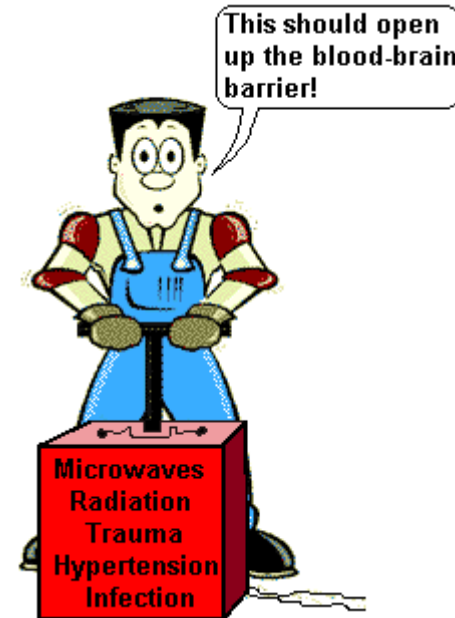


To the brain

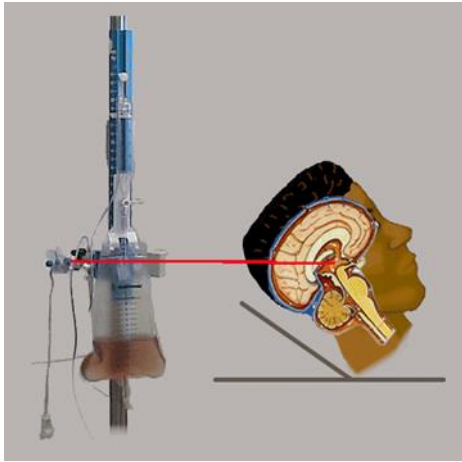


# CNS tumour challenges (3)

- To achieve adequate delivery of chemotherapeutic agents to intracranial/intraspinal tumours with minimal toxicities



# Ways in to the brain



# CNS tumour challenges (4)

- Late effects on developing brain
- Survival comes at a cost

# Sequelae of radiation

- Neuropsychological impairments( Attention, memory, visuospatial skills, motor functions, language, executive functioning)
- Psychosocial impairment (Employment, ability to drive, education, independent living, dating history)
- Neuro-endocrine impairment
- Second malignancy risk

# MDT working

- Dedicated neuro-oncology team:  
Oncologists, radiologists, surgeons, anaesthetists, pathologists, radiotherapists, ophthalmologists, audiologists, psychologists, nursing staff, pharmacists, physiotherapists, speech therapists, occupational therapists, dieticians, school teachers, social workers....
- PALLIATIVE CARE!!!!!!

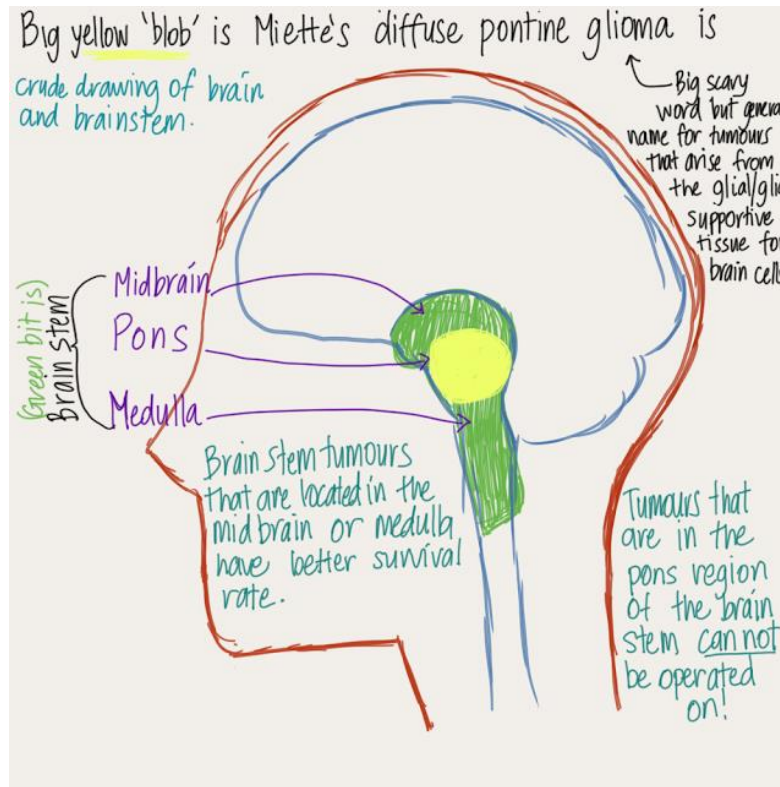
## (iii) Diffuse Intrinsic Pontine Glioma

- DIPG
- 10-15% of brain tumours
- Leading cause of brain tumour related death
- Median age 6-7 yrs
- Present with: Cranial nerve deficits, upper motor neuron signs, ataxia

# Diffuse Intrinsic Pontine Glioma

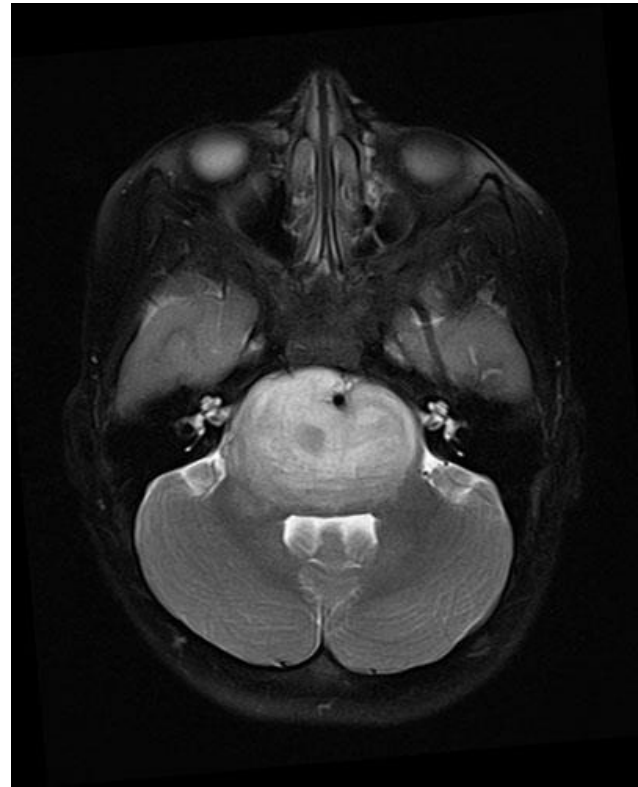
- Radiological diagnosis (MRI)
- T1 hypointense, T2 hyperintense, variably enhancing
- Expansile mass  $\geq 50\%$  of pons
- +/- leptomeningeal dissemination

# Diffuse Intrinsic Pontine Glioma

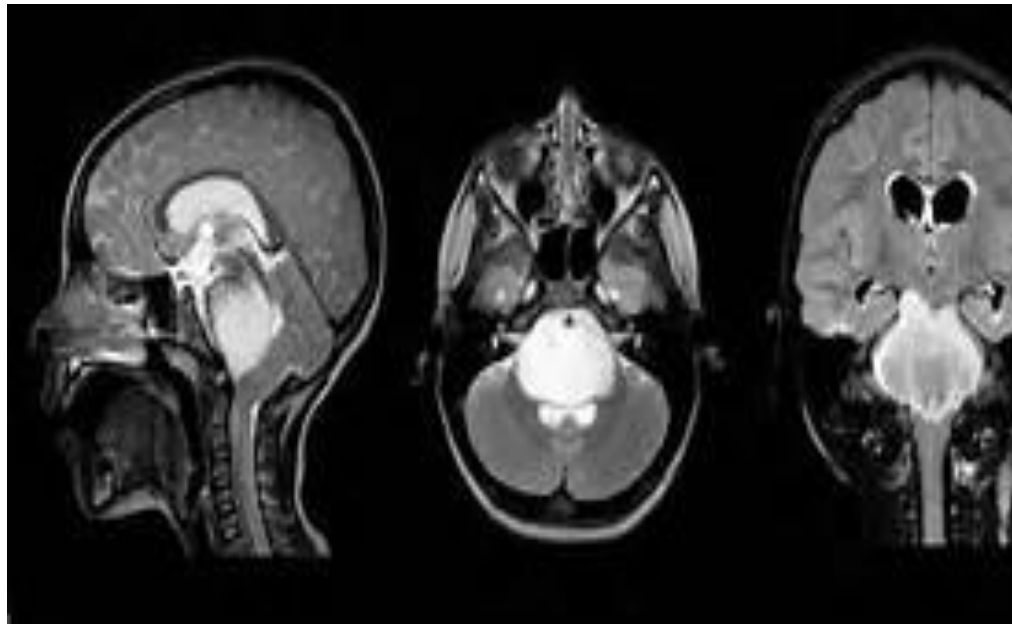




# Diffuse Intrinsic Pontine Glioma



# Diffuse Intrinsic Pontine Glioma



# Diffuse Intrinsic Pontine Glioma

- Median survival 9 months from diagnosis
- Radiotherapy *as palliation*
- Chemotherapy ineffectual
- Progress in treatment hampered by lack of tissue

# Diffuse Intrinsic Pontine Glioma

- International efforts to obtain tissue
- Post mortem
- Up front, stereotactically

# Diffuse Intrinsic Pontine Glioma

- DIPG Registries
- Database of demographic, clinical, radiological and pathology data
- Repository of molecular data
- To enable a solid research infrastructure

# DIPG : Diagnosis

- Clinical – radiological entity
- MRI
- Clinical symptoms: CN deficits, ataxia, long tract signs of <6 months duration
- Hemiplegia, dysphagia, hiccups, hoarseness
- Personality changes, night laughter
- Only ~20% present with hydrocephalus

# DIPG : Biology and histology

- TP53 mutations
- Amplification of EGFR
- Gain in PDGFRFA
- Gain in PARP 1
  
- Histone mutations

# DIPG : Treatment

- Steroids
- Focal radiotherapy
- 54Gy in 30 fractions
  
- 39Gy in 13 fractions + potential to repeat
  
- ~85% will respond
- Radiosensitising chemo shows no benefit



# DIPG : Clinical trials

- 21 trials listed
- Early phase, vaccine therapy, convection enhanced delivery, immunotherapy
- BIOMEDE: Biological Medicine for Diffuse Intrinsic Pontine Glioma Eradication

# DIPG : Prognosis

- Median survival of 9 months
- Median time from progression to death 1-4.5 months
- Favourable predictors include age  $\leq$  3years, longer symptom duration at diagnosis

# DIPG : End of life care

- Constipation
- Headache, seizures.
- Visual disturbance
- Sensitivity to noise
- Pain
- Nausea, vomiting
- Anxiety
- Sleep disturbance
- Fatigue
- Dysarthria
- “Locked in syndrome”
- Dysphagia
- Nutrition
- Urinary retention
- Secretions
- Dyspnoea
- Advanced care planning

# DIPG: Other challenges

- Health tourism
- Social media
- Fundraising
- Unrealistic expectations

# DIPG

## THE BASIC FACTS

**9 MONTHS**

THE MEDIAN SURVIVAL  
RATE FROM DIAGNOSIS.

**90%**

OF KIDS WILL DIE WITHIN 2  
YEARS OF A DIPG DIAGNOSIS.

DIPG HAS A  
SURVIVAL RATE  
OF LESS THAN

**1%**

DIPG MOST COMMONLY  
STRIKES KIDS BETWEEN

**4 TO 11**

YEARS OF AGE.

**BRAIN TUMORS**

ARE THE LEADING CAUSE OF  
CANCER RELATED DEATHS IN  
CHILDREN UNDER AGE 10.

# DIPG

LEAVES KIDS MENTALLY INTACT, BUT STEALS ESSENTIAL BODILY  
FUNCTIONS OVER TIME AS THE TUMOR GROWS. SUCH AS VISION,  
CHEWING, SWALLOWING, WALKING, AND BREATHING.

[www.DefeatDIPG.org](http://www.DefeatDIPG.org)

**Brain Tumours are the #1 cancer killer of UK Children.  
The most FATAL Childhood Brain Cancer is DIPG**

**No Treatment. No Cure. 0% Survival Rate.**

It is described as a 'Rare' cancer  
**BUT every 9 Days a UK child like  
Rebekah is diagnosed with DIPG**

**Median Survival is 9 - 12 months  
Rebekah was taken in *just FIVE***

Support vital DIPG Research and the work  
of Abbie's Army to help Make a Difference  
& change the outcomes for other Children

**Text: DIPG20 £ to 70070**

Learn more about: [www.abbiesarmy.co.uk](http://www.abbiesarmy.co.uk)



80%  
Survival Rate?  
for childhood cancer

For  
every  
children  
diagnosed  
with cancer

8

1  
will not survive

will suffer late  
effects such as  
secondary cancers,  
muscular difficulties  
and infertility.

Although survival rates  
have increased, there are  
still childhood cancers,  
like DIPG, that are

**TERMINAL  
AT  
DIAGNOSIS**

TEAM  
*Jacob*  
FOUNDATION

# Looking forward.....

- Increased international collaboration
- Working together
  - - with palliative care
  - - with parent groups
- **STRONGER TOGETHER**
- Things can only get better.....





- Any questions?

- Any comments?

**Thank you, enjoy your lunch!**

