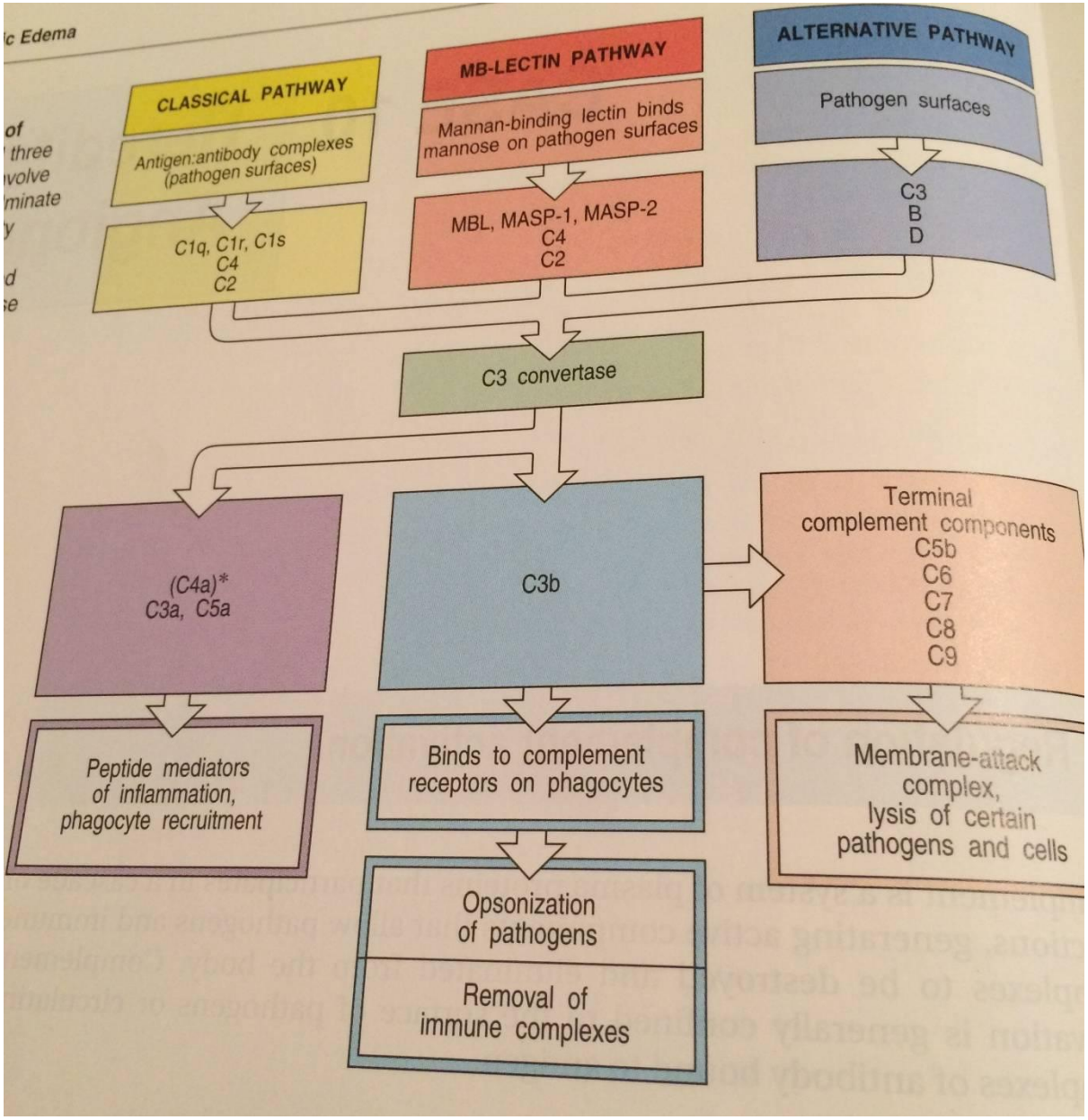
Hereditary Angioneurotic Edema

Case Study

C1 esterase inhibitor (C1INH)

Potent Inhibitor of the classical pathway

Sole known inhibitor of C1


c Edema
of
three
volve
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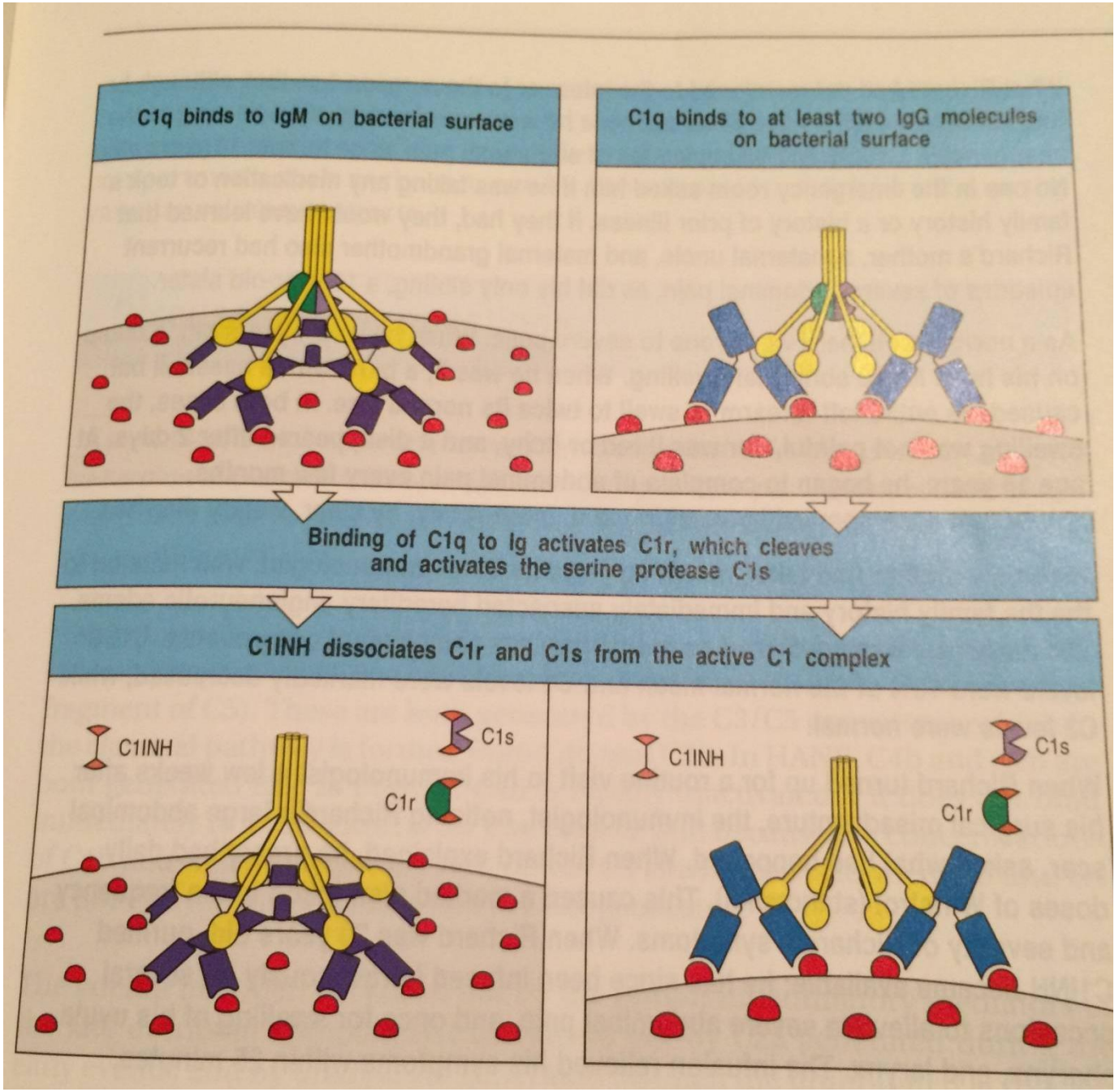
CLASSICAL PATHWAY
Antigen:antibody complexes (pathogen surfaces)
C1q, C1r, C1s
C4
C2
MB-LECTIN PATHWAY
Mannan-binding lectin binds mannose on pathogen surfaces
MBL, MASP-1, MASP-2
C4
C2
ALTERNATIVE PATHWAY
Pathogen surfaces
C3
B
D
C3 convertase
(C4a)*
C3a, C5a
C3b
Terminal complement components
C5b
C6
C7
C8
C9
Peptide mediators of inflammation, phagocyte recruitment
Binds to complement receptors on phagocytes
Membrane-attack complex, lysis of certain pathogens and cells
Opsonization of pathogens
Removal of immune complexes


C1q binds to IgM on bacterial surface
C1q binds to at least two IgG molecules on bacterial surface
Binding of C1q to Ig activates C1r, which cleaves and activates the serine protease C1s
C1INH dissociates C1r and C1s from the active C1 complex
C1INH
C1s
C1r
C1INH
C1s
C1r

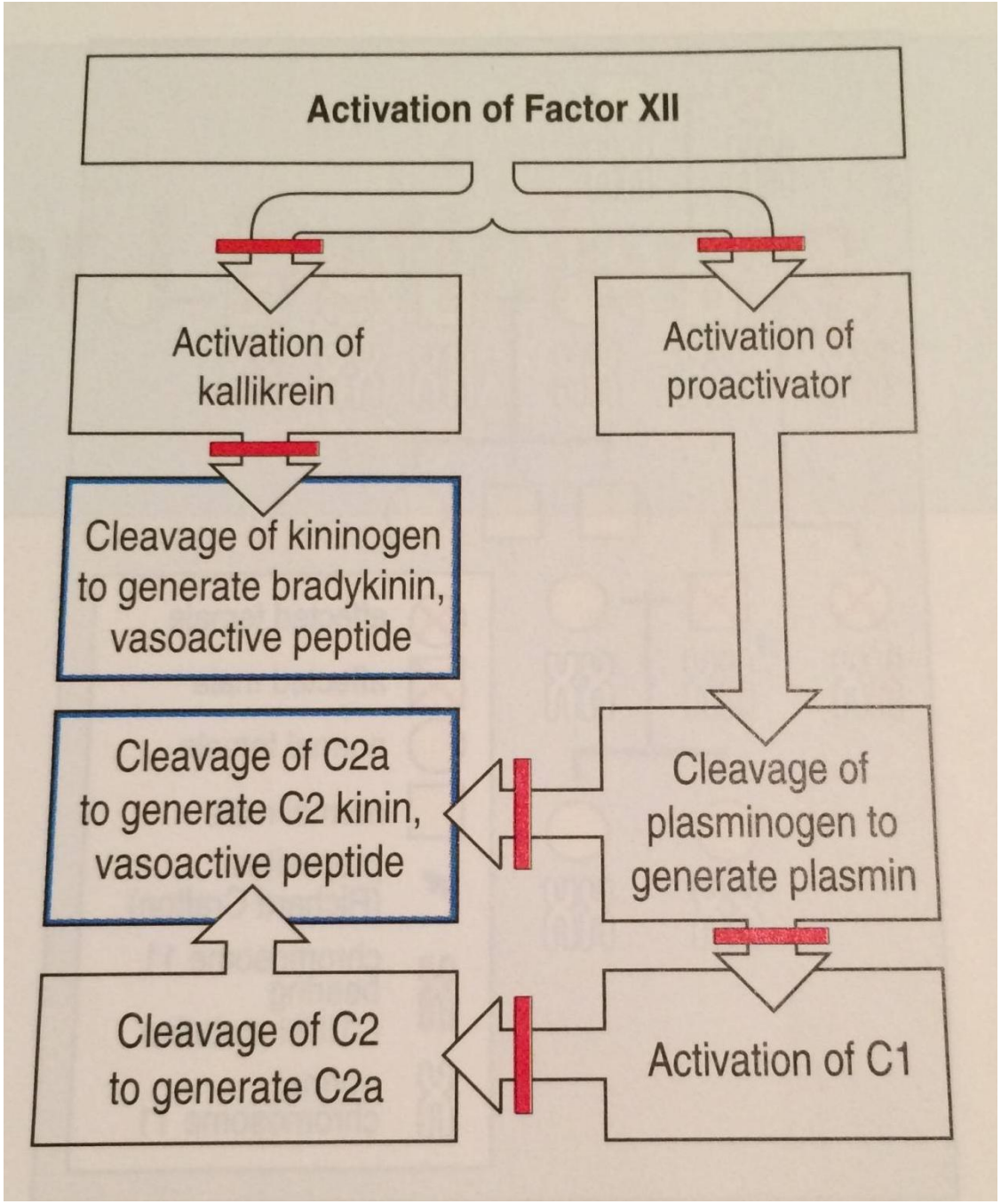
Case of Richard Crafton

Swelling of skin

Intestine (Abdominal pain, vomiting)

Colon= Severe watery diarrhea

Larynx= choking


Activation of Factor XII
Activation of kallikrein
Activation of proactivator
Cleavage of kininogen to generate bradykinin, vasoactive peptide
Cleavage of C2a to generate C2 kinin, vasoactive peptide
Cleavage of plasminogen to generate plasmin
Cleavage of C2 to generate C2a
Activation of C1

Why is Richard's C4 low?

Cleaved by C1

What other complement component should be low?

C2

Is the alternative pathway affected?

No

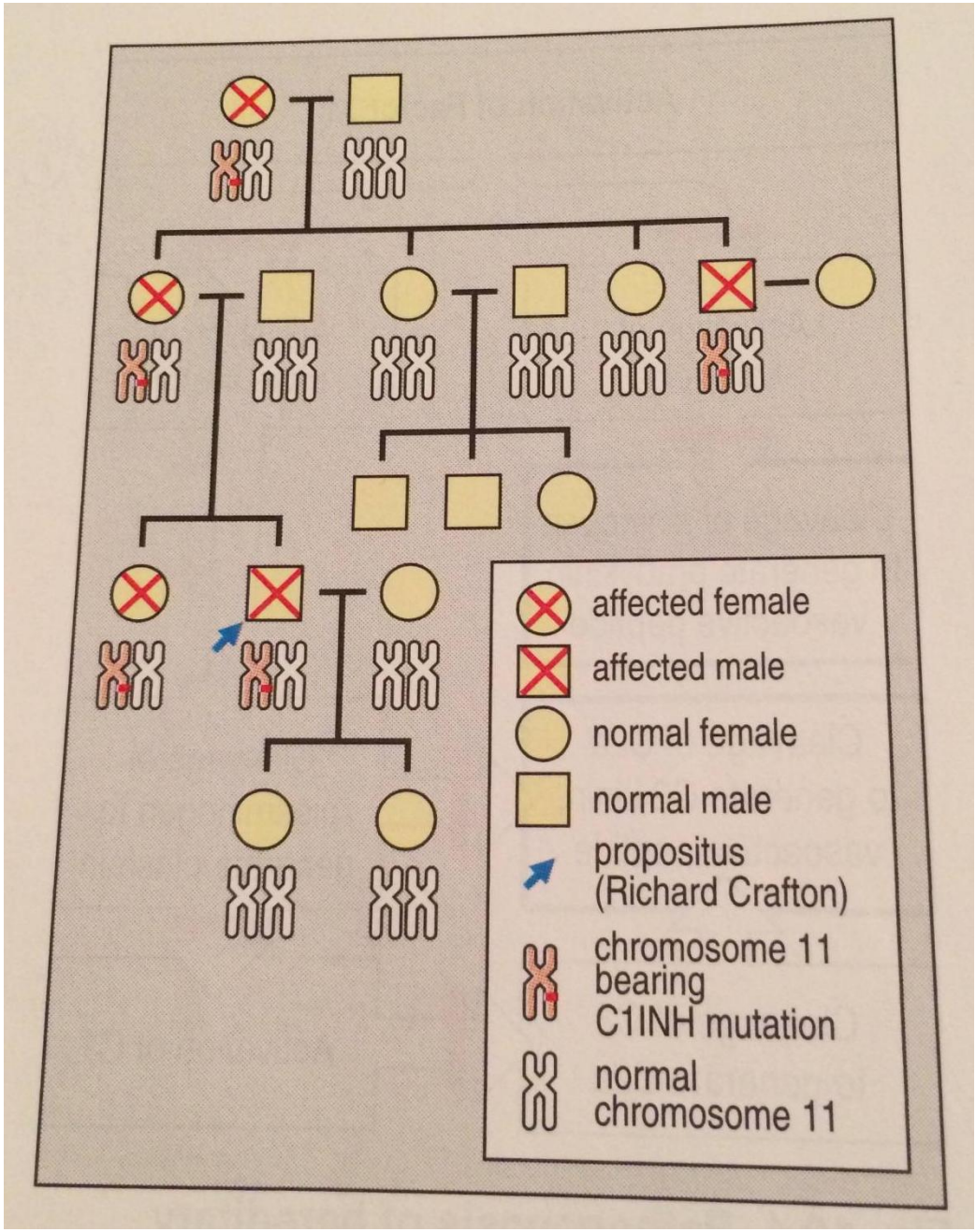
Are these patients more prone to infections?

No (Alternative pathway compensates)

In airway obstruction case in ER, how to decide if it is C1INH deficiency case or anaphylactic shock?

Administer epinephrine in any case and monitor response

Can Richard ‘s children pass the disease to their offspring?



Affected males vs. Females?

Disease skipping generations?

Autosomal dominant pattern